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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☒	☐ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No software was used to collect data for this study.
Data analysis	SAIGE v0.39.1 and REGENIE v3.0.3 were used to perform genome-wide association analysis; phasing was performed in Eagle (v2.3-2.4 across studies); METAL (release 5/2020, https://github.com/statgen/METAL) was used to perform GWAS meta-analysis; GCTA-COJO v1.94.0 was used to perform conditional analysis; and LDSC v1.0.1 was used to calculate genetic correlations and intercepts; KING v2.1.3 was used to calculated relatedness among individuals. PRS-CS v1.0.0 was used to generate genome-wide polygenic scores. Base R functionalities and the 'coloc' v4, 'PoPS' v0.2, 'PheWAS' v1.0, and 'ggplot2' v3.4 packages were additionally used to perform analyses and generate figures. Code for all packages is publicly available, and all custom code used in the study is available at https://github.com/buutrg/HDP.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

GWAS summary statistics for preeclampsia/eclampsia and gestational hypertension and genome-wide polygenic scores for preeclampsia/eclampsia, gestational hypertension, and systolic blood pressure are available for download at https://doi.org/10.6084/m9.figshare.22680904.v1. Summary statistics used in this meta-analysis are publicly available for FinnGen r6 (https://www.finngen.fi/en/access_results) and for BioBank Japan (https://pheweb.jp/pheno/PreEclampsia). Preeclampsia GWAS summary statistics from the InterPregGen consortium are available at https://ega-archive.org (dataset IDs EGAD00010001984 [European maternal meta-analysis], EGAD00010001985 [Central Asian maternal meta-analysis], and EGAD00010001983 [European and Central Asian fetal meta-analysis]). Placental transcriptome data are publicly available at https://www.obgyn.cam.ac.uk/placentome/.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Sex, rather than gender, was available in contributing cohorts. This research focuses on hypertensive disorders of pregnancy, a sex-specific condition that affects parous female individuals only. All included genotyped cohorts, except for control individuals in GOPEC within the InterPregGen consortium, included female individuals only. Single-nuclei RNA sequencing analyses used aortic tissue specimens from male individuals.
Population characteristics	The population studied in this manuscript is primarily genotyped women with available phenotyping of pregnancy history, history of preeclampsia/eclampsia, and/or history of gestational hypertension. Supplementary Tables 1-3 summarize the phenotype definitions used in each cohort included in the meta-analysis. Average age of women included in these genotyped cohorts varied across studies, ranging from 27.0 years in the nuMoM2b cohort to 61.5 years in BioBank Japan. For single-nuclei RNA sequencing of human aortic tissue, both individuals contributing aortic tissue specimens were male individuals of European ancestry, aged 49 and 51 years.
Recruitment	This study included multiple cohorts with different recruitment approaches. Cohorts include those that are population- or community-based (FinnGen, Estonian Biobank, Genes & Health, UK Biobank, HUNT) and those in which participants were recruited from hospitals or healthcare settings (Michigan Genomics Initiative, Mass General Brigham Biobank, Biobank Japan, BioMe, Penn Medicine Biobank). Aortic specimens were collected from a local biorepository for vascular research in Boston, Massachusetts, USA.
Ethics oversight	FinnGen: Coordinating Ethics Committee of the Helsinki and Uusimaa Hospital District Estonian Biobank: Estonian Committee on Bioethics Genes & Health: London - South East Research Ethics Committee Michigan Genomics Initiative: University of Michigan Medical School Institutional Review Board Mass General Brigham Biobank: Mass General Brigham Institutional Review Board Biobank Japan: Approved by the ethics committees of the Institute of Medical Science, the University of Tokyo, and of the RIKEN Yokohama Institute BioMe: Icahn School of Medicine at Mt. Sinai Institutional Review Board HUNT: Regional Committee for Ethics in Medical Research, Norway Penn Medicine Biobank: University of Pennsylvania Institutional Review Board UK Biobank: North West Multi-center Research Ethics Committee nuMoM2b: Approved by the institutional review boards of each participating site (Case Western Reserve University, Columbia University, Indiana University, University of Pittsburgh, Northwestern University, University of Pennsylvania, University of California at Irvine, and University of Utah) Aortic specimens were collected with approval from the Mass General Brigham Institutional Review Board

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	All cohorts with genotype/imputed data and phenotyping of relevant pregnancy outcomes who either had made association summary statistics publicly available or who were willing to collaborate on this study were included in this multi-ancestry GWAS meta-analysis. Discovery cohorts for preeclampsia/eclampsia were approximately 40% larger than combined discovery and replication sample sizes from the largest previous preeclampsia GWAS, implying adequate power to detect genomic loci associated with preeclampsia/eclampsia and gestational hypertension, including those with modest magnitude of effect.
Data exclusions	Samples and variants were excluded according to standard GWAS quality control procedures as detailed in the manuscript. Wherever possible, women who never had never experienced childbirth were excluded from cohorts. In some cohorts, women with pre-pregnancy chronic hypertension were excluded.
Replication	Replication of GWAS findings was performed using the same procedure of multi-ancestry GWAS meta-analysis of the HUNT, Penn Medicine Biobank, UK Biobank, and nuMoM2b cohorts. For preeclampsia/eclampsia, we replicated 7 of 12 significant associations identified in discovery analysis (P<0.05 in follow-up cohorts with consistent direction of effect), and 11 of 12 associated loci retained genome-wide significance in combined meta-analysis of discovery and follow-up cohorts (along with two additional loci attaining genome-wide significance in combined meta-analysis). Furthermore, there was no discernible heterogeneity of associations across cohorts. For gestational hypertension, we replicated 4 of 7 significant associations identified in discovery analysis, and 6 of 7 loci retained genome-wide significance in combined discovery and follow-up meta-analysis (along with an additional locus attaining genome-wide significance in combined meta-analysis). In addition, we performed external validation of polygenic scores in HUNT and nuMoM2b. Polygenic scores were predictive in both cohorts. In nuMoM2b, which includes detailed information on first-trimester clinical characteristcs, polygenic risk significantly improved the C-statistic for predicting preeclampsia/eclampsia and gestational hypertension beyond clinical risk factors alone and significantly reclassified eligibility for low-dose aspirin to prevent preeclampsia.
Randomization	There was no randomized intervention in this observational study.
Blinding	There was no intervention performed in this observational study.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging