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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Phenotypic data was collected from the electronic health record and genetic data using the Million Veteran Program (MVP) Axiom array.
Data analysis	Imputation was performed using MiniMac3/EAGLE v2, and data was collected and cleaned using the EasyQC package, SNPTESTv2.5.4, EIGENSOFT v6, METAL (released 2011), and KING 2.0 software programs as outlined in the online methods. Clear code for analysis is available at their associated website (see text). Additional analyses were performed in R-3.2.

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The full summary level association data from the MVP trans-ancestry PAD meta-analysis from this report are available through dbGAP, accession code

phs001672.v2.p1. Additional data that support the findings of this study are available on request from the corresponding author SMD; these data are not publicly available due to U.S. Government and Department of Veteran's Affairs restrictions relating to participant privacy and consent. Data contributed by CARDIoGRAMplusC4D investigators are available online (http://www.CARDIOGRAMPLUSC4D.org/). Data on large artery stroke have been contributed by the MEGASTROKE investigators and are available online (http://www.megastroke.org/). The genetic and phenotypic UK Biobank data are available upon application to the UK Biobank.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	All samples available of three ancestries (European, African, Hispanic) were used for analysis (after quality control, see Supplementary Table 1 for full details). Sample size was determined based on using all genetic data available from MVP/UK Biobank. Participants were excluded if they failed to meet case or control definitions.
Data exclusions	Data were excluded if they did not pass our pre-established quality control metrics, or if they did not fall within the three main ancestries used for analysis.
Replication	Replication was performed using data from UK Biobank of 25 genome-wide significant loci identified in MVP. Of the 6 signals that did not replicate, 2 were rare variants that were not available in UK Biobank following quality control (European MAF < 0.005), and the remaining four did not meet the pre-specified $P < 0.05$ for independent replication (see Supplementary Table 6).
Randomization	Randomization is not applicable, as this is a population based case-control analysis of prevalent data.
Blinding	Blinding is not applicable, as this is a population based case-control analysis of prevalent data.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants

Methods

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Demographics and participant counts for the European, African, and Hispanic MVP participants (European - Mean Age PAD cases = 74.4 years, 97.5% male, Mean Age PAD controls = 66.9 years, 91.9% male; African - Mean Age PAD cases = 69.6 years, 96.1% male, Mean Age PAD controls = 60.4 years, 85.2% male; Hispanic - Mean Age PAD cases = 71.6 years, 97.9% male, Mean Age PAD controls = 59.0 years, 89.7% male) that passed our quality control and were included in the analysis are depicted in Supplementary Table 1 and Supplementary Table 7.
Recruitment	Individuals aged 19 to 104 years have been recruited voluntarily from more than 50 VA Medical Centers nationwide for participation in the Million Veteran Program biobank study. Recruitment is currently occurring in person at selected sites in the VHA health care system. Every Veteran is assigned a study ID number, which is used to track them throughout the entire process of recruitment, enrollment, sample collection and use; this approach also provides a level of protection for personal identifiers from the outset. Given that study enrollment is voluntary, biases of this study are similar to those of any mega-biobank with voluntary enrollment, including survivorship bias. A complete description of the entire MVP Biobank study including recruitment can be found at PMID: 26441289.

In UK Biobank, individuals aged 45 to 69 years old were recruited from across the United Kingdom for participation. Given that study enrollment is voluntary, biases of this study are similar to those of any mega-biobank with voluntary enrollment, including survivorship bias. A complete description of the entire UK Biobank study including recruitment can be found at PMID: 30305743.