nature portfolio

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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<br>*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<br>*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 for data collection. |
| Data analysis | All code for analyses in this study is available for download from GitHub at https://github.com/YanLuoCityU/cardiomicscore.<br><br>Data analysis was performed using Python and R with the following settings:<br>- Python version 3.8.5, Linux<br>- R version 4.3.3, Windows 10 x64<br><br>Main softwares:<br>- Main Python software:<br>- scikit-learn v1.3.2<br>- pytorch v1.11.0 (CUDA 11.3, cuDNN 8.2.0)<br>- optuna v4.0.0<br>- shap v0.46.0<br>- lifelines v0.27.8<br>- xgboost v2.0.3<br>- lightgbm v4.4.0<br><br>- Main R software:<br>- tidyverse v2.0.0<br>- dplyr v1.1.4 |

- data.table v1.17.0
- stringr v1.5.1
- arrow v17.0.0.1
- gtsummary v2.3.0
- flextable v0.9.9
- skimr v2.1.5
- janitor v2.2.1
- ggplot2 v3.5.2
- patchwork v1.3.1
- ggsci v3.2.0
- ggtext v0.1.2
- geomtextpath v0.1.5
- MetBrewer v0.2.0
- showtext v0.9-7
- survival v3.8-3
- cmprsk v2.2-12
- dcurves v0.5.0
- pracma v2.4.4
- foreach v1.5.2
- doParallel v1.0.17
- futile.logger v1.4.3

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

This study used data from the UK Biobank under application number 79146. The UK Biobank has approval from the North West Multi-Centre Research Ethics Committee as a Research tissue biobank (REC reference 11/NW/0382). All participants provided written informed consent.

The UK Biobank data used in this study are not publicly available due to the resource's strict privacy protection policies. Researchers can gain access to the individual-level data by submitting an application to the UK Biobank and obtaining approval (https://www.ukbiobank.ac.uk/).

## Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

| | |
|---|---|
| Reporting on sex and gender | Self-reported sex (UK Biobank Field ID: 31) was defined as male or female. The distribution of sex is presented in Supplementary Tables 1-3. The main analyses, performed in the whole samples, included sex as a covariate. Additional analyses stratifying by sex are presented in Supplementary Figure 13. |
| Reporting on race, ethnicity, or other socially relevant groupings | Ethnicity (UK Biobank Field ID: 21000) was included as a covariate in the main analyses. |
| Population characteristics | Detailed baseline characteristics for the study population are provided in Supplementary Data 1–3. |
| Recruitment | The UK Biobank is a prospective cohort study that has collected extensive genetic and phenotypic data from approximately 500,000 participants who were recruited from 22 centers across the UK during 2006–2010. |
| Ethics oversight | The UK Biobank has approval from the North West Multi-Centre Research Ethics Committee as a Research tissue biobank (REC reference 11/NW/0382). All participants provided written informed consent. |

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 | This study utilized the UK Biobank data, which were collected from approximately 500,000 participants. No a priori sample size was determined; instead, the study included all available participants with clinical, genomics, metabolomics, and proteomics data to maximize statistical power and ensure comprehensive analyses. |
| Data exclusions | Participants with missing key variables or with prevalent cardiovascular disease at baseline, as defined in this study, were excluded. Further details are provided in the Methods section. |
| Replication | Analyses were performed using the UK Biobank data, a widely used resource in biomedical research. Full methodological descriptions are provided to ensure transparency and enable replication with the same data and procedures. |
| Randomization | This is an observational cohort study and thus randomization is not relevant. |
| Blinding | This is an observational cohort study and thus blinding is not relevant. |

# 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 |
| ☒ | ☐ Plants |

## Methods

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

## Plants

| | |
|---|---|
| Seed stocks | Not applicable. |
| Novel plant genotypes | Not applicable. |
| Authentication | Not applicable. |