

## STATE-OF-THE-ART REVIEW

# Systematic Review of International Population Studies With Cardiac Magnetic Resonance and Genomics Research Data (“Imagenomics”)

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## ABSTRACT

Epidemiological population studies may include cardiac magnetic resonance (CMR)-derived phenotyping and large-scale genotyping, providing unprecedented level of detail to investigate novel gene-lifestyle-disease interactions. The systematic review presents high-level summaries and critically appraises contemporary challenges and biobank opportunities. The authors identified 17 relevant biobanks by searching “CMR,” “genome” and “population study” on MEDLINE, EMBASE, and Web of Science 2025. Collectively, studies recruited ~1 million participants with stored blood samples for extensive genomic analyses, of whom >180,000 have or will undergo CMR. Use of expansive personal data must safeguard participant confidentiality, encourage technological standardization, and champion inclusivity and sustainability. Application of genotypic and imaging-derived phenotypic information will be readily translatable to clinical practice through investigation of, among others, new therapeutic targets and highly sensitive and specific biomarkers. Imaging biobanks are accessible to researchers by application. This systematic review should inspire greater use and cross-collaboration and facilitate powerful discoveries in more heterogeneous population samples. (JACC Cardiovasc Imaging. 2026;■:■-■) © 2026 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

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**ABBREVIATIONS  
AND ACRONYMS****CAC** = coronary artery calcium**CMR** = cardiac magnetic resonance**CT** = computed tomography**CV** = cardiovascular**CVD** = cardiovascular disease**LVMWT** = left ventricular maximum wall thickness**MRI** = magnetic resonance imaging**PRS** = polygenic risk score**SNP** = single nucleotide polymorphism**WES** = whole exome sequencing**WGS** = whole genome sequencing

Over the last 20 years patient data volume, variety, and processing velocity have expanded at an exponential rate in cardiovascular (CV) epidemiology and health services research (eg, subspecialty, disease, and procedural registries).<sup>1,2</sup> Such information is important for health care services quality control to improve patient care and for studies that address the prognosis of a specific disease, but they are of limited use to understand risk factors for diseases and in the area of primary prevention.<sup>3,4</sup>

Instead, population cohort studies longitudinally assess exposure-outcome relations by: 1) recruiting several thousand participants; 2) comprehensively phenotyping them at baseline by gathering sociodemographic, lifestyle, anthropometric, and biochemical characteristics; and 3) collecting detailed outcome data through scheduled follow-up visits and synchronization to electronic health records and other registries.<sup>5</sup> Because participants are recruited from the general population, these cohort studies can investigate the incidence of disease among those who did not have the disease at the time when the exposures were assessed. More recently, such studies include omics data (eg, genomics data from whole genome sequencing [WGS], whole exome sequencing [WES], and single nucleotide polymorphism [SNP] genotyping relevant to GWAS [genome-wide association study] and polygenic risk scores [PRS]) and specialized imaging (eg, cardiac magnetic resonance [CMR]).<sup>5</sup> In this review, we term this combination as “imagenomics,” signifying a rich genomic-imaging phenotype.<sup>5</sup> Example studies include the MESA (Multi-Ethnic Study of Atherosclerosis), the UKBB (United Kingdom Biobank), and NAKO (German National Cohort).<sup>5</sup>

Such large-scale studies have opportunities, challenges, strengths, and weaknesses. Imaging and gene information provide a new level of detail to investigate novel disease mechanisms, associations, and therapeutic targets.<sup>6-8</sup> On the other hand, this sensitive data must be handled legally and ethically in line with confidentiality safeguards; it must be stored securely with clear governance plans and data access policies.<sup>2,9,10</sup> Finally, research that amalgamates

existing epidemiological studies may mitigate inherent biases and be even more powerful.

The aim of this review is to systematically summarize and broadly appraise CV population cohort studies with CMR imaging and genomic and outcome data. By synthesizing these CV imagenomics data sets for secondary analysis, we hope to inspire, guide, and maximize use and cross-collaboration, facilitating powerful discoveries in more heterogeneous population samples.

**METHODS**

The search protocol, including search methods, inclusion criteria, and data collection, were pre-specified. In line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, we conducted our search in 4 steps: identification, screening, eligibility, and inclusion.<sup>11</sup>

**DATA SOURCES AND SEARCHES.** MEDLINE, EMBASE, and Web of Science databases were searched for population studies with CMR imaging and genomic and outcome data. The scope of the systematic review was from date of database inception until date of the search in November 2025. Our search strategy was customized in the advanced search function of the respective database. Broadly, the search syntax used 4 elements formed and separated by Boolean terms (OR, AND):

1. [(Cardiac magnetic resonance imaging) OR (Cardiovascular magnetic resonance imaging) OR (CMR)] AND
2. [(Genome) OR (Exome)] AND
3. [(Population) OR (Cohort)] AND
4. (Study)

**STUDY SELECTION.** Included studies had to be population cohort studies with CMR and genomics data. The cardiac imaging modality of choice was CMR because it is the reference standard for cardiac volume, functional quantification, and in vivo tissue characterization with good interobserver and intra-observer reliability.<sup>5-7</sup> Genomics was the preferred type of omics data as health care systems such as the NHS (National Health Service) move closer to integrating genomic medicine into its infrastructure to ultimately deliver personalized medicine.<sup>12</sup> Another important inclusion criterion was clinical

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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outcome data (eg, diagnoses and procedures) that continue to be collected from study follow-up appointments and from other population databases (eg, electronic health records, death registries, and primary care data). We excluded studies that did not provide contact information and/or describe data access procedures. Non-English language studies were considered provided that the study rationale, methodology, and governance were available in English.

**DATA EXTRACTION.** Titles and abstracts from search results were imported to an online systematic review management platform Rayyan for data screening, eligibility assessment, and extraction by the reviewer (K.H.).<sup>13</sup> First, titles and abstracts were screened for terms related to CV imaging (eg, CMR, cardiac imaging, cardiac morphology, and so on), genomics (eg, Mendelian randomization, GWAS, genetic variants, and so on), and/or population cohort study (eg, population-based imaging, healthy population longitudinal study, exposure-based cohort study, and so on). Then, for each candidate population study, the full text of the respective citation, advertised websites, and published protocols were read for availability of CMR, genomic, and outcome data. Finally, if the study met all prespecified inclusion criteria, data were extracted from their advertised website and published protocols and tabulated by topics of interest to the general researcher: aims and enrollment of target population; scope, detail, and linkage to other databases; data completeness, validation, and reliability; governance and data access; and exemplar research output and ongoing projects. Study principal investigators were contacted to add and confirm further pertinent information that was not readily available in the public domain.

## RESULTS

The search yielded 1,302 citations linked to abstracts and/or full text articles. Of these citations, 248 were duplicates and 925 did not meet the inclusion criteria (Figure 1). In total, there were 14 population studies from 120 citations, 3 additional cohorts from article reference screening, and 1 unpublished imaging biobank from expert discussions. Although a further 4 studies had both CMR and genomic data, limited contact and data access information precluded their inclusion. We noted an additional 19 population studies that used other cardiac imaging modalities (eg, echocardiography and/or computed tomography [CT]), but their summary was outside the scope of this systematic review (Figure 1). Included studies were summarized by the reviewer (K.H.). Tables 1 to 3

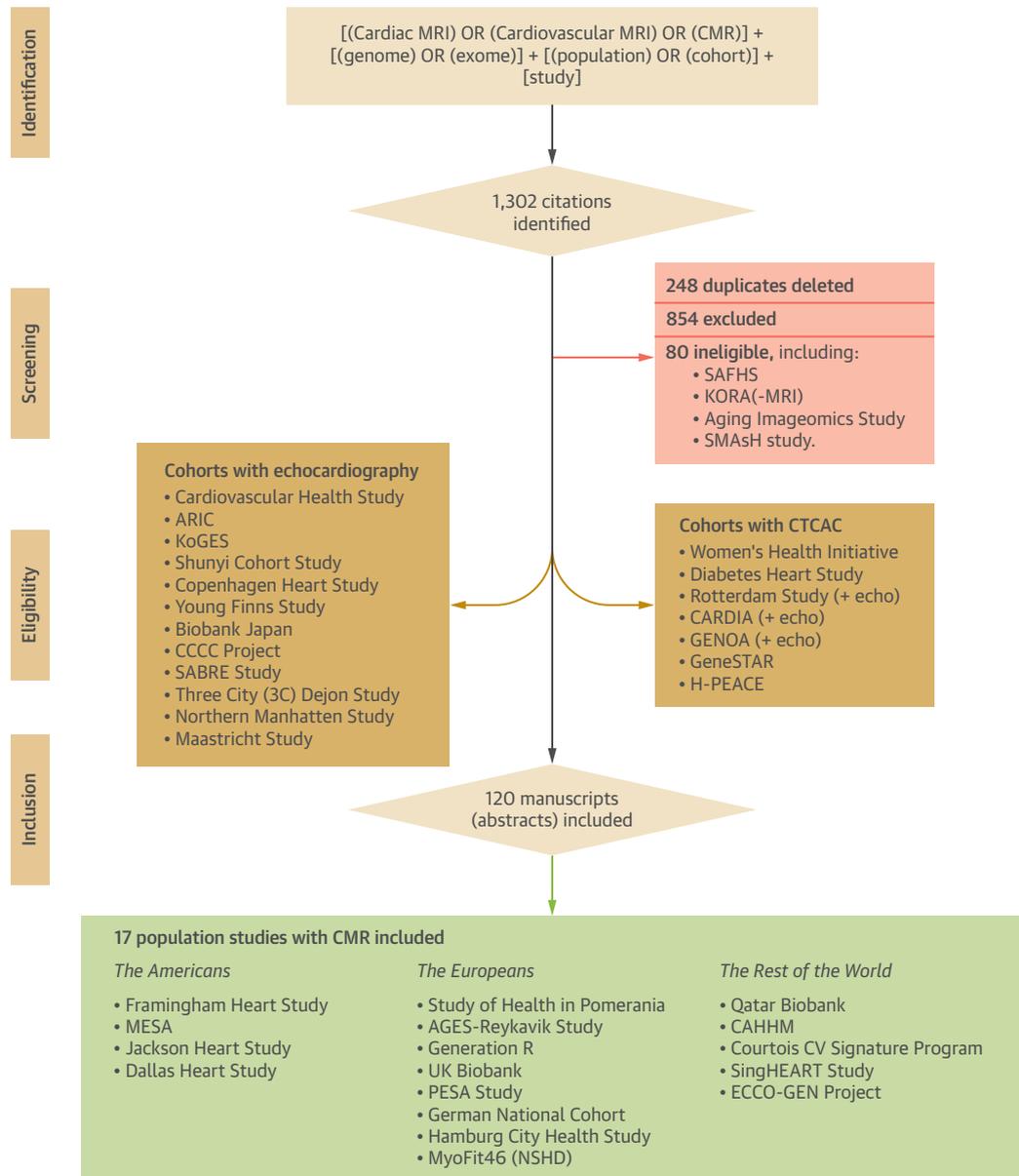
and Figure 2 present study name and contact information; number and ethnicity of participants; available CMR imaging; and comprehensive genomic sequence summaries for American, European, and other population studies, respectively. We also provided estimated participant numbers with paired CMR and genomic data; the information was confirmed by data custodians from 15 of 17 studies.

## STUDY VIGNETTES

Included population studies were collated into 3 separate sections: 1) the United States-based; 2) the European-based; and 3) the rest of the world.

**THE UNITED STATES. Framingham Heart Study.** The FHS (Framingham Heart Study) is the longest-running and perhaps most well-recognized CV epidemiological study.<sup>14,15</sup> In Framingham, Massachusetts, USA, during 1948, 5,209 men and women 30-59 years of age who were free of clinical cardiovascular disease (CVD) were enrolled to investigate the risk factors and etiology of coronary heart disease. Between 1971 and 2002, the study expanded to include 2 generations of descendants (offspring and third-generation cohorts) as well as ethnic minority groups (omni-1 and omni-2).<sup>14,15</sup> Their recruitment is a specific strength of the FHS, facilitating the detailed understanding of genetic determinants and temporal trends in CV risk factors and disease. The FHS was instrumental in identifying modifiable and nonmodifiable CV risk factors; it introduced the use of clinical prediction models (eg, the Framingham Risk Score) to estimate future risk of CVD.<sup>47</sup> CMR data are available from 1,776 participants of the offspring cohort. Separately, genomic data include at least 3,000 WES, 7,000 WGS, as well as 9,000 Affymetrix and Illumina microarray-based SNP genotype panels.<sup>14,15</sup>

**Multi-Ethnic Study of Atherosclerosis.** The MESA study took the epidemiological study of CVD a step further. Two of its legacies are the recruitment of an ethnic diverse population and the introduction of large-scale CV imaging. Between 2000 and 2002, 6,814 participants (50% female) 45-84 years of age without overt CVD were recruited across 6 centers in the United States. Study participants were from 4 ethnic backgrounds: 38% White, 28% Black, 23% Hispanic, and 11% Chinese.<sup>17</sup> CMR scans were performed at baseline in 5,004 participants and at follow-up 10 years later in 3,015 participants to investigate the progression of subclinical disease and to establish imaging-derived phenotypes as novel risk factors.<sup>17</sup> This was complemented by the genotyping of ~1 million SNPs using the Affymetrix Genome-Wide

**FIGURE 1 Study Selection Flowchart**

AGES = Age, Gene/Environment Susceptibility Study; ARIC = Atherosclerosis Risk In Communities Study; CAC = coronary artery calcium; CARDIA = Coronary Artery Risk Development in Young Adults Study; CCCC = Chin-Shan Community Cardiovascular Cohort; CAHHM = Canadian Alliance for Healthy Hearts and Minds; CMR = cardiac magnetic resonance; CT = computed tomography; CV = cardiovascular; ECCO-GEN = Egyptian Collaborative Cardiac Genomics Project; GENOA = Genetic Epidemiology Network of Arterioopathy; H-PEACE = Health and Prevention Enhancement; KoGES = Korean Genome and Epidemiology Study; KORA = Cooperative Health Research in the Region of Augsburg; MESA = Multi-Ethnic Study of Atherosclerosis; MRI = magnetic resonance imaging; MyoFit46 = MRC National Survey of Health and Development; NSHD = National Survey of Health and Development; PESA = Progression of Early Atherosclerosis Study; SABRE = Southall and Brent Revisited; SAFHS = San Antonio Family Heart Study; SMAsH = Subclinical Myocardial Abnormalities in HIV.

**TABLE 1 Summary of Participant Ancestry, Paired Imagenomics Data, and Contact Information for Included American Studies**

Study	Participant Information	CMR Details	Other CV Imaging/ Investigations	Genomic Data	Paired Data
Framingham Heart Study (FHS) <sup>14-16</sup> <a href="https://www.framinghamheartstudy.org">https://www.framinghamheartstudy.org</a> Contact: <a href="mailto:fhs@bu.edu">fhs@bu.edu</a>	Original (n = 5,209), Offspring (n = 5,124), third-generation (n = 4,095) cohorts: White of European descent Omni-1 (n = 506), Omni-2 (n = 403) cohorts: African American, Hispanic, Asian, Indian, Native American, and Pacific Islander descent	1,776 from Offspring cohort had CMR (1.5-T) ~30 y after recruitment Localizers; bSSFP cine 2Ch, 4Ch, and SAX stack	Echo: 2D, Doppler, tissue Doppler, M-mode and speckle-tracking CT-CAC: 8-detector-row noncontrast CT with prospective ECG gating, 2.5 mm slices BP, 12-lead ECG, Smartwatch data, US carotid	~9,300 had 550K SNPs genotyped on Affymetrix GeneChip Human Mapping 500K Array and 50K Human Gene Focused Panel; SNP imputation with HAPMAP, 1000G, HRC (SHARe) Other SHARe SNP genotyping panels: Affymetrix 100K GWAS array (n = 1,345), Illumina HumanOmni5M-4v1 Array (n ~2,500 Offspring), Affymetrix Axiom Genome-Wide BioBank array (n = 845) >7,500 had 50,000 SNPs genotyped on Illumina Cardiochip (CARE) >8,000 had ~200,000 exome variants genotyped on Illumina HumanExome BeadChip WES in 464 from ESP and >3,000 from CHARGE-S >7,000 had 30X WGS on Illumina HiSeq X technology (NHLBI TOPmed project)	All participants with CMR have linkable genomics of variable completeness
Multi-ethnic Study of Atherosclerosis (MESA) <sup>17</sup> <a href="https://mesa-nhlbi.org">https://mesa-nhlbi.org</a>	6,814 (50% female) aged 45-84 y from 4 ethnicities: 38% White, 28% Black, 23% Hispanic, and 11% Chinese	CMR (1.5-T) at baseline in 5,004 and at follow-up in 3,015 Localizers; fGRE cine 2-4Ch and SAX stack; phase-contrast of aorta; mid-LV slice for pre- and post-contrast T1 mapping, ECV and LGE; tagging	Echo: 2D, Doppler, tissue Doppler, speckle-tracking CT-CAC: Either cardiac-gated EBCT or prospective ECG-gated MDCT with 2.5-mm slices BP, 12-lead ECG, Ziopatch CPET, 6-min walk test ABPI, MRI/PET and US carotid, arterial stiffness MRI brain Polysomnography	8,402 from MESA and ancillary studies had ~1M SNPs genotyped on Affymetrix Genome-Wide Human SNP Array 6.0 as part of SHARe Also contributed to CARE 423 had selected exome variants genotyped through ESP	Linkable CMR and genotyping available for >4,500 participants
Jackson Heart Study (JHS) <sup>18,19</sup> <a href="https://www.jacksonheartstudy.org">https://www.jacksonheartstudy.org</a>	5,306 African Americans recruited. This included 6.6% aged 35-84 yrs in Jackson, Mississippi, USA; 252 aged 21-34 yrs; and 14 aged 85 yrs from the nested Family study	~1,600 had CMR (1.5-T) between 2009 and 2013 during Exam 3, a subset of whom had repeat imaging Localizers; bSSFP cine 2-4Ch and SAX stack; tagging at base, mid and apex; phase-contrast of aorta; LGE	Echo: 2D, M-mode, (tissue) Doppler (Exam 1, 2000-2004) CT-CAC: Prospective ECG-gated MDCT with 2.5-mm slices (Exam 2, 2005-2008) 12-lead ECG (Exam 1 and 3) BP (Exam 1-3) ABPM (Exam 1) Accelerometer and step counter ABPI, US carotid (Exam 1)	3,029 had >906,600 SNPs genotyped, using Affymetrix 6.0 (CARE) 2,790 had selected exome variants genotyped using Illumina HumanExome BeadChip (ESP) 3,374 had WES (CHARGE-S) 3,406 had WGS (NHLBI TOPmed project)	Linkable CMR and genotyping available for >700 participants
Dallas Heart Study (DHS) <sup>20-22</sup> <a href="https://www.utsouthwestern.edu/departments/internal-medicine/research/dallas-heart/">https://www.utsouthwestern.edu/departments/internal-medicine/research/dallas-heart/</a> Contact: <a href="mailto:dallasheartstudy@utsouthwestern.edu">dallasheartstudy@utsouthwestern.edu</a>	6,101 (56% African American, 23% White, 19% Hispanic, 2% other) were recruited to DHS-1, of whom 3,401 participated in DHS-2	~2,800 had baseline CMR (1.5-T); ~1,300 had repeat CMR (3.0-T) bSSFP cine including SAX stack and CMR-FT; phase-contrast and angiography of aorta	CT-CAC: EBCT (DHS-1) and MDCT (DHS-2) calcium score, volume, mass, distribution BP, 12-lead ECG ETT, accelerometer ABPI, MRI carotid MRI abdomen/liver (body fat content)	Participants had selected exome variants genotyped with Illumina HumanExome Beadchip	All participants with CMR have linkable targeted sequencing

2D = 2-dimensional; ABPI = ankle brachial pressure index; ABPM = ambulatory blood pressure monitor; BP = blood pressure; bSSFP = balanced steady-state free precession imaging; CAC = coronary artery calcium; CARE = Candidate Gene Association Resource; CHARGE-S = Cohorts for Heart and Aging Research in Genomic Epidemiology Sequencing; CMR = cardiac magnetic resonance; CMR-FT = cardiac magnetic resonance feature tracking; CPET = cardiopulmonary exercise test; CT = computed tomography; CV = cardiovascular; EBCT = electron beam computed tomography; ECG = electrocardiogram; Echo = echocardiogram; ECV = extracellular volume; ESP = Exome Sequencing Project; ETT = exercise tolerance test; fGRE = fast gradient recovery echo; GWAS = genome-wide association study; HAPMAP = haplotype map; HRC = Haplotype Reference Consortium; LGE = late gadolinium enhancement; LV = left ventricle; MDCT = multidetector computed tomography; MRI = magnetic resonance imaging; NHLBI = National Heart Lung and Blood Institute; PET = positron emission tomography; SAX = short axis; SHARe = SNP Health Association Resource; SNP = single nucleotide polymorphism; TOPmed = Trans-Omics for Precision Medicine; US = ultrasound; WES = whole-exome sequencing; WGS = whole-genome sequencing.

**TABLE 2** Summary of Participant Ancestry, Paired Imagenomics Data, and Contact Information for Included European Studies

Study	Participant Information	CMR Details	Other CV Imaging/ Investigations	Genomic Data	Paired Data
Study of Health in Pomerania (SHIP) <sup>5,23</sup> <a href="https://transfer.ship-med.uni-greifswald.de/FAIRequest/">https://transfer.ship-med.uni-greifswald.de/FAIRequest/</a> Contact: <a href="mailto:transferstelle@med.uni-greifswald.de">transferstelle@med.uni-greifswald.de</a>	SHIP-START (n = 4,308), SHIP-TREND (n = 4,420) and SHIP-NEXT (target n = 4,000): exclusively, White	528 (SHIP-START), 997 (SHIP-TREND) had CMR (1.5-T) bSSFP cine 2-4Ch, SAX stack and axial stack; PSIR LGE; whole body T1 FLASH 3D angiography (with and without contrast, only in men)	Echo: M-mode, 2D, Doppler, tissue Doppler, and speckle-tracking BP, 12-lead ECG, CPET, accelerometry ABPI, US carotid, arterial stiffness MRI brain, MRI whole body and MR angiography Polysomnography	Genome-wide genetic data generated on Affymetrix Genome-Wide Human SNP Array 6.0 (SHIP-START), Illumina Infinium HumanOmin2.5 BeadChip (SHIP-TREND subgroup), Illumina Infinium Global Screening Array (SHIP-TREND subgroup), Illumina Infinium HumanExome BeadChip (SHIP-START/SHIP-TREND) WGS data available (SHIP-TREND subgroup) DNA methylation performed with Illumina Infinium Methylation EPIC BeadChip Kit (SHIP-TREND subgroup) Genomic analyses planned for SHIP-NEXT	Linkable CMR and genotyping available for most participants with CMR
Age, Gene/Environment Susceptibility Study (AGES) <sup>24,25</sup> <a href="https://hjarta.is/en/research/ages-phase-1/">https://hjarta.is/en/research/ages-phase-1/</a> Contact: <a href="mailto:afgreidsla@hjarta.is">afgreidsla@hjarta.is</a>	5,764 participants, from the original Reykjavik Study: Only White	970 participants had CMR (1.5-T) bSSFP cine LAX and SAX; PSIR LGE	Echo: 2D, Doppler, tissue Doppler, M-mode CT-CAC BP, 12-lead ECG US carotid MRI brain	Participant genotypes were imputed to the TOPmed panel Subset had WES and WGS As part of the CHARGE Consortium, AGES has contributed to multiple meta-analyses of GWAS studies	All participants with CMR have linkable genotyping
Generation R Study <sup>26,27</sup> <a href="https://generationr.nl/researchers/">https://generationr.nl/researchers/</a> Contact: <a href="mailto:info@generationr.nl">info@generationr.nl</a>	9,778 mothers (62% Dutch/European, 8% Surinamese, 7% Moroccan, 8% Turkish, 4% Dutch Antilles, 3% Cape Verdian, 8% other), who gave birth to 9,749 live born children	>7,000 children had noncontrast CMR (3.0-T) Biomarkers included LVM, LVEDV, LVESV, LVEF	Echo at 6 and 24 months (n = ~1,000) Echo at 6 and 10 y (n = ~7,000 and 6,000, respectively) BP at 0.5, 2, 6, 10, 14, 18 y Arterial stiffness at 10, 22 y MRI brain (3D T1w GRE, 2D PDw TSE, DTI, resting fMRI)	Genome-wide genetic data generated on Illumina 670K platform for children Parent DNA used for candidate gene and replication studies DNA methylation performed in subset of children with Illumina Infinium Human Methylation450 BeadChip	Linkable CMR and genotyping available for 500-5,000 children
UK Biobank (UKBB) <sup>6,28</sup> <a href="https://www.ukbiobank.ac.uk">https://www.ukbiobank.ac.uk</a> Contact: <a href="mailto:ukbiobank@ukbiobank.ac.uk">ukbiobank@ukbiobank.ac.uk</a>	500,000 participants, aged 40-69 y: 95% White, 1.6% Black/Black British, 1.2% Indian, 0.4% Pakistani, 0.3% Chinese, 0.6% mixed, 0.9% other	Target 100,000 to have baseline CMR (1.5-T) with ~50% to have repeat imaging Localizers: bSSFP cine 2-4Ch and SAX stack; transverse aortic cine at level of PA; phase contrast; tagging; mid-LV slice for native T1 mapping	BP, serial 12-lead ECG ETT, accelerometry US carotid, arterial stiffness MRI brain (T1, T2/FLAIR, T2*, resting and task fMRI)	500,000 had WGS, using Illumina NovaSeq technology 470,000 had WES, using IDT xGen Exome Research Panel v1.0 488,000 genotyped on 2 separate arrays by Affymetrix, using 805,426 markers	All participants with CMR have linkable genomics
Progression of Early Atherosclerosis Study (PESA) <sup>29,30</sup> <a href="https://estudiopesa.org/">https://estudiopesa.org/</a> Contact: <a href="mailto:pesa-h@cnic.es">pesa-h@cnic.es</a>	4,184 asymptomatic employees of Santander Bank aged 40-54 y: >95% White	750 had CMR (3.0-T) bSSFP cine SAX stack and LGE Subcohort had myocardial stress perfusion	Echo Serial CT-CAC at 0, 3, 6, 10, and 15 y: subset had CTCA w/ FFR, NaF PET/CT, <sup>18</sup> FDG-PET MRI BP, 12-lead ECG Accelerometry 2D/3D vascular US: subset had hybrid vascular PET-MR Polysomnography	Whole genome wide SNPs available High sensitivity targeted sequencing of 54 clonal hematopoiesis-related genes in 3,692 participants WGS planned	All participants with CMR have linkable genotyping, targeted sequencing
German National Cohort (NAKO) <sup>31-33</sup> <a href="https://nako.de/en/research/">https://nako.de/en/research/</a> Contact: <a href="mailto:transfer@nako.de">transfer@nako.de</a>	205,415 aged 19-74 yrs: 83% no migration background, 5.1% second generation, 1.8% resettlers, 2.6% Western, 3.4% Eastern Europe, 1.5% Turkish, 2.7% other migrants	30,861 had whole-body MRI, including CMR (3.0-T) bSSFP cine 2-4Ch and SAX stack; native T1 mapping (SAX slice); thoracic MR angiogram	3D echo at baseline and 5 y (n = 41,040): results from reading of images available from subset BP, 12-lead ECG at baseline and 5 y (n = 50,817) 7-day accelerometry	Genotyping of all study participants is ongoing; data to be available 2026/27 WGS is ongoing for 15,000 participants; data to be available 2026	All participants with CMR will have linkable genotyping (±WGS)

Continued on the next page

TABLE 2 Continued

Study	Participant Information	CMR Details	Other CV Imaging/ Investigations	Genomic Data	Paired Data
Hamburg City Health Study (HCHS) <sup>34,35</sup> <a href="https://hchs.hamburg">https://hchs.hamburg</a> Contact: <a href="mailto:hchs@uke.de">hchs@uke.de</a>	45,000 aged 45-74 y: 98% White, <1% Black, 1% other	12,362 had CMR (3.0-T): enriched for participants at increased risk of CAD, AF and HF as well as reference cohort of 1,500 bSSFP cine; pre-/post- contrast T1 and T2 mapping; phase contrast of aorta; rest and stress perfusion; LGE	Echo: 2D, 3D, Doppler and tissue Doppler, speckle-tracking BP ECG: 12-lead, 2-min rhythm strip Accelerometry (Actigraphs) ABPI, US peripheral arteries MRI brain	WGS available	All participants with CMR have linkable WGS
MyoFit46 <sup>36,37</sup> <a href="https://myofit46.com">https://myofit46.com</a> Contact: <a href="mailto:mrclha.enquiries@ucl.ac.uk">mrclha.enquiries@ucl.ac.uk</a>	550 native born British, aged ≥75 y from the original 5,326 MRC NSHD	550 had CMR (3.0-T) Localizers; bSSFP cine 2-4Ch and SAX stack; LGE; T1, T2 mapping and ECV; rest and stress perfusion; phase-contrast and 4D flow of aorta	ECGi to map epicardial electrograms on CMR data BP, 12-lead ECG, heart rate variability Historical data: 2D echo (LAX, SAX, Doppler and tissue Doppler), ECG, heart rate variability, US vascular, MRI brain	DNA samples from >2,900 original study members collected at 53 and 60-64 y Genotyping performed using Illumina DrugDev Array and NeuroX2 chip (imputed to TOPmed)	Linkable CMR and genotyping available for ~85% of participants

<sup>18</sup>FDG = 18-fluorodeoxy-glucose; AF = atrial fibrillation; CAD = coronary artery disease; CTCA = computed tomography coronary angiography; DTI = diffusion tensor imaging; ECGi = electrocardiographic imaging; FFR = fractional flow reserve; FLAIR = fluid-attenuated inversion recovery; FLASH = fast low-angle shot; fMRI = functional magnetic resonance imaging; GRE = gradient recovery echo; HF = heart failure; IDT = Integrated DNA Technologies; LAX = long axis; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVM = left ventricular mass; MR = magnetic resonance; MRC = Medical Research Council; MyoFit 46 = MRC National Survey of Health and Development; NaF = sodium fluoride; NSHD = National Survey of Health and Development; PA = pulmonary artery; PDw = proton density-weighted; PSIR = phase sensitive inversion recovery; TSE = turbo spin echo; other abbreviations as in Table 1.

Human SNP Array 6.0 platform in 8,402 participants.<sup>17</sup> Among the notable findings, CT-measured coronary artery calcium (CAC) improved overall CVD risk stratification; CMR-derived elevated mass-to-volume ratio was more predictive of incident CVD than elevated left ventricular mass; and higher postcontrast extracellular volume, a marker of diffuse fibrosis was associated with previous CV events.<sup>48-50</sup>

**Jackson Heart Study.** The JHS (Jackson Heart Study) investigated racial disparities in CVD by recruiting 5,302 African American participants 35-84 years of age from Jackson, Mississippi, USA, in 1998.<sup>51</sup> More importantly, the JHS sought to address health inequalities by involving participants in the study design as well as supporting the next generation of health care professionals through local secondary school outreach programs and undergraduate scholarship schemes.<sup>18,51</sup> Approximately 1,600 underwent CMR scans during exam 3 with repeat imaging available in a subset. Separately, >3,000 had WES, WGS as well as Affymetrix microarray-based SNP genotype panels sequenced.<sup>18</sup>

**Dallas Heart Study.** The DHS (Dallas Heart Study) sought to define the factors and mechanisms that contributed to ethnic differences in CV health.<sup>20</sup> The study's novelty is derived from the probability-based

recruitment of 6,101 residents 18-65 years of age across 10 geographic strata in Dallas County, Texas, USA, between 2000 and 2002.<sup>21</sup> By sourcing a sample that was representative of the local population by age, sex, ethnicity, and education level, study outcomes would be readily applicable at population level.<sup>21</sup> Approximately 2,800 had baseline CMR scans with repeat imaging available in close to 50% of participants.<sup>21</sup> All participants also had selected exome variants genotyped with Illumina HumanExome Beadchip.<sup>22</sup>

**THE EUROPEANS. Study of Health in Pomerania.** After the 1990 German reunification, the SHIP (Study of Health in Pomerania) was commissioned to investigate the prevalence and incidence of risk factors, subclinical and clinical disease, and their complex interactions in the more deprived East Germany.<sup>23,52</sup> SHIP's 4,308 participants had CMR at the 10- and 15-year follow-up examinations; SHIP-TREND's 4,420 participants had CMR at baseline and 10-year follow-up examinations.<sup>23,52</sup> SHIP-NEXT is currently underway, aiming to recruit a further 4,000 participants.<sup>5,23,52</sup> In summary, ~2,000 completed CMR scans across the different SHIP cohorts and >5,000 completed Affymetrix SNP microarray panels are available.<sup>23,52</sup>

**TABLE 3 Summary of Participant Ancestry, Paired Imagenomics Data and Contact Information for Non-European, Non-American Studies**

Study	Participant Information	CMR Details	Other CV Imaging/ Investigations	Genomic Data	Paired Data
Qatar Biobank (QBB) <sup>38,39</sup> <a href="https://www.qphi.org.qa">https://www.qphi.org.qa</a> Contact: <a href="mailto:qphi@qf.org.qa">qphi@qf.org.qa</a>	37,000 by 2023 from target 60,000 permanent residents aged ≥18 y: 85% Qatari nationals, 12% Arabs and 3% non-Arabs	732 whole body MRI scans completed by 2023	BP, 12-lead ECG ETT 3D US carotid, arterial stiffness	25,000 had WGS by 2021; genome libraries were created with TruSeq DNA Nano Kit and sequenced with HiSeq X Ten (Illumina)	All participants with CMR should have linkable WGS
Canadian Alliance for Healthy Hearts and Minds (CAHHM) <sup>40-43</sup> <a href="https://cahnm.mcmaster.ca">https://cahnm.mcmaster.ca</a> Contact: <a href="mailto:Alliance@phri.ca">Alliance@phri.ca</a>	8,580 aged 35-69 y (First Nations cohort aged ≥ 18 y): 80.1% White, 4.2% South Asian, 11% Chinese, 1.3% Black, 3.4% other/mixed	8,258 had CMR (1.5-T or 3.0-T) Standard CMR protocol: bSSFP cine SAX stack Extended CMR protocol: plus bSSFP cine LAX, phase-contrast; LGE; T1 and T2* mapping	BP MRI brain and carotid (3D T1w MPRAGE, 2D FLAIR, TOF), abdomen (visceral fat area and liver fat %)	For example, Ontario Health Study (OHS) subcohort had SNP genotyping (UK Biobank Affymetrix arrays) and WGS (Illumina) For example, CARTaGENE study subcohort had WGS (Illumina NovaSeq platform), WES (Illumina platform) and SNP genotyping (Illumina Infinium Global Screening Array)	Participants with CMR from specific subcohorts will have linkable genomics (eg, up to 3,100 from OHS)
Courtois Cardiovascular Signature Program <sup>44</sup> <a href="https://cvsignature.ca">https://cvsignature.ca</a> Contact: <a href="mailto:ccvs@muhc.mcgill.ca">ccvs@muhc.mcgill.ca</a>	Target 4,000 participants, aged 35 to 79 (1/3 healthy, 1/3 at risk for heart disease, 1/3 known heart disease)	Participants to have CMR (1.5-T) bSSFP cine LAX and SAX stack; T1 and T2 mapping; breathing-enhanced oxygen-sensitive sequence	BP, 12-lead ECG Smartwatch data 6-minute walk test MRI brain and carotid	WGS will be available	All participants will have linkable CMR and WGS
SingHEART Study <sup>45</sup> <a href="https://www.nhcs.com.sg/research-innovation/research-cores/data-digital-technology-ai/singheart">https://www.nhcs.com.sg/research-innovation/research-cores/data-digital-technology-ai/singheart</a> Contact: <a href="mailto:kong.siew.ching@singhealth.com.sg">kong.siew.ching@singhealth.com.sg</a>	>1,000 by December 2021 (target 5,000 aged 21-69 years): 91% Chinese, 3.4% Indian, 3.1 Malay, 2.1% other	Participants to have CMR (1.5-T) bSSFP cine LAX and SAX; 3D LV SAX stack; phase contrast of aortic flow	Subset to have focused echo Most will have CT-CAC BP, 12-lead ECG	WGS will be performed using Illumina HiSeq X at 30X coverage	All participants will have linkable CMR and WGS
Egyptian Collaborative Cardiac Genomics Project (ECCO-GEN) <sup>46</sup> <a href="https://ega-archive.org/dacs/EGAC00001001680">https://ega-archive.org/dacs/EGAC00001001680</a> Contact: <a href="mailto:y.aguib@imperial.ac.uk">y.aguib@imperial.ac.uk</a>	391 by 2020 (target 1,000 healthy volunteers): Exclusively, Egyptian	All to have CMR (1.5-T) bSSFP cine SAX stack; phase-contrast and 4D flow at different aortic levels; T1 mapping and 3D tagging at base, mid and apical level	Echo BP, 12-lead ECG	Targeted 174 genes with reported roles in ICC to be sequenced with Illumina Miseq and Nextseq platforms	All participants should have linkable CMR and targeted gene sequencing

ICC = inherited cardiac conditions; MPRAGE = magnetization-prepared rapid gradient echo; TOF = time of flight; other abbreviations as in Tables 1 and 2.

**Age, Gene/Environment Susceptibility Study.** The AGES (Age, Gene/Environment Susceptibility Study) is an extension of the 1967 Icelandic epidemiological project Reykjavik Study, investigating the genetic contribution to diseases of old age.<sup>24,25</sup> Between 2002 and 2006 5,764 patients were enrolled, undergoing detailed clinical examination, imaging, biochemical phenotyping, and genotyping.<sup>24</sup> A subcohort of ~1,000 had CMRs.<sup>24</sup> The study sets itself apart by leveraging an existing cohort with >40 years of high-quality follow-up data, facilitating a life course analysis to health and disease trajectories.

**Generation R Study.** The Generation R Study is probably the most unique of the presented epidemiological studies. Since recruiting 9,778 pregnant women with expected delivery dates between 2002 and 2006 in Rotterdam, Holland, the study has documented

development and health, particularly of the children, until adulthood.<sup>26,27</sup> Serial whole-body magnetic resonance imaging (MRI) scans with dedicated cardiac sequences and detailed parent and offspring genomic analyses were performed in >7,000 children, providing a unique opportunity to study the hereditary determinants of CV health in the early phases of life.<sup>26,27</sup>

**United Kingdom Biobank.** The UKBB (United Kingdom Biobank) sets itself apart from other population studies through its size, depth, and accessibility. The imaging biobank aims to investigate the etiology of chronic illnesses, including CVD, through detailed phenotyping (eg, multiorgan multimodality imaging) and genotyping.<sup>53</sup> From 2006 to 2010, half a million predominantly White United Kingdom residents 40-69 years of age were recruited, one-fifth of whom are

**FIGURE 2** Imaging Biobanks and Their Available CMR Sequences

	2Ch, 3Ch, 4Ch bSSFP cine	SAX stack bSSFP cine	LGE	Native T1 +/- T2 SAX	Tagging	Flow phase contrast	Thoracic MR angiogram
FHS	✓	✓	×	×	×	×	×
MESA	✓	✓	✓	✓	✓	×	×
JHS	✓	✓	✓	✓	✓	✓	×
DHS	✓	✓	×	×	×	✓	×
SHIP	✓	✓	✓	×	×	×	✓
AGES	✓	✓	✓	×	×	×	×
Gen. R	?	?	?	?	?	?	?
UKBB	✓	✓	×	✓	✓	✓	×
PESA	✓	×	✓	×	×	×	×
NAKO	✓	✓	×	✓	×	×	✓
HCHS	✓	✓	✓	✓	×	✓	×
MyoFit46	✓	✓	✓	✓	✓	✓	×
QBB	?	?	?	?	?	?	?
CAHHM	✓	✓	✓	✓	×	✓	×
Courtois	✓	✓	×	✓	×	×	×
SingHEART	✓	✓	×	×	×	✓	×
ECCO-GEN	×	✓	×	✓	×	✓	×

bSSFP = balanced steady-state free precession; DHS = Dallas Heart Study; FHS = Framingham Heart Study; Gen R = Generation R; HCHS = Hamburg City Health Study; JHS = Jackson Heart Study; LGE = late gadolinium enhancement; MR = magnetic resonance; NAKO = German National Cohort; QBB = Qatar Biobank; SAX = short axis; SHIP = Study of Health in Pomerania; UKBB = UK Biobank; other abbreviations as in [Figure 1](#).

expected to undergo enhanced imaging, including CMR.<sup>6,54</sup> Close to 20 years since the first participant was recruited, the UKBB continues to set milestones with the recent release of WES from 470,000 participants and repeat CMR from 100,000 participants.<sup>28</sup>

**Progression and Early detection of Subclinical Atherosclerosis Study.** The PESA (Progression and Early detection of Subclinical Atherosclerosis) study is uniquely placed to investigate the presence, progression, and prognosis of subclinical atherosclerosis at unprecedented levels.<sup>29,30,55</sup> In brief, >4,000 asymptomatic middle-aged employees from Madrid were recruited between 2010 and 2014 and remain

under follow-up with serial 2-dimensional/3-dimensional vascular ultrasound, CT-CAC, and selectively, sodium-fluoride (NaF)-positron emission tomography (PET), hybrid CV PET-MRI, and CMR.<sup>29,30,55</sup> Already, the study has shown that multiterritory plaque burden and inflammation improve CVD risk prediction beyond CT-CAC.<sup>30</sup>

**German National Cohort.** The NAKO (German National Cohort) represents the largest epidemiological study of chronic disease in Germany by recruiting >200,000 individuals 19-74 years of age across the country from 2014 to 2019.<sup>31,32</sup> With >40,000 participants <40 years of age, NAKO distinguishes

itself from other existing population studies. Participant imagenomics data include CMR scans in 30,861 at baseline and ongoing genotyping of all participants.<sup>31,32</sup> All participants are followed up using a combination of active (self-reported health questionnaires) and passive (eg, linkage to municipal registries) procedures. Another unique aspect of NAKO is that participants are re-invited to the study center every 5 years for re-examination. As such, repeated measurements at 5-year follow-up are available for >137,000 participants, including MRI measurements for >18,000 participants. The 10-year follow-up examination is ongoing with a target of 85,000 participants, including 11,500 with MRI measurements. This combination of follow-up for incident diseases and repeated examinations facilitates the detailed study of subclinical phenotype changes, thus truly reflecting the transition from health to disease.

**Hamburg City Health Study.** By recruiting 45,000 Hamburg residents 45-74 years of age between 2016 and 2022, the HCHS (Hamburg City Health Study) is the largest local population study worldwide.<sup>34</sup> As well as understanding etiology, the study investigates prognostic factors for surviving and living with chronic disease, including CVD.<sup>34</sup> Uniquely, CMR is performed in a subset of the population at increased risk of CVD, atrial fibrillation, and heart failure by disease-specific risk prediction models with a recruitment target of 12,362 participants in addition to a reference cohort of 1,500 other participants.<sup>35</sup> Further participant imagenomics data include genomics, transcriptomics, proteomics, and lipidomics.<sup>34</sup>

**MyoFit46.** MyoFit46 (MRC National Survey of Health and Development) is a CV substudy of 550 participants from the British 1946 initiated MRC (Medical Research Council) NSHD (National Survey of Health and Development); its purpose is to perform detailed electrocardiographic (ECG) imaging with CMR.<sup>36</sup> Strengths include the age homogeneity of participants (all born in the same week in March of 1946) and the well-documented data of participants' life course from early life exposures through traditional cardiometabolic risk to emergent morbidity in the oldest birth cohort in the world with continuous follow-up.<sup>36</sup> The overarching aim is to understand how different life course trajectories affect future CV health.<sup>36</sup> Participant imagenomics data include comprehensive single-magnet high-resolution (3 Tesla) CMR with late gadolinium enhancement (LGE) imaging, stress perfusion, and 4D flow and DNA samples taken at the ages 53, 60-64, and  $\geq 75$  years.<sup>36</sup>

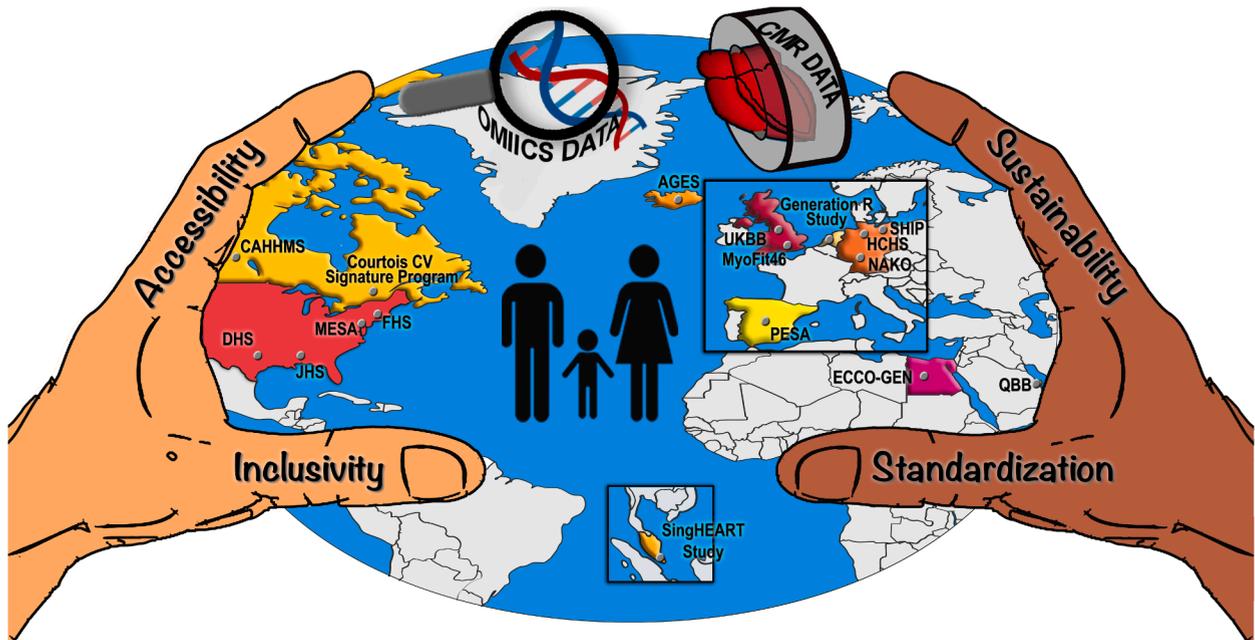
## THE REST OF THE WORLD

**QATAR BIOBANK.** The QBB (Qatar Biobank) aims to recruit 60,000 Qatari nationals and residents for comprehensive baseline phenotyping and long-term health-related outcomes follow-up since 2012.<sup>38,39</sup> The high rate of consanguinity in the Middle Eastern population provides an unrivalled opportunity to investigate disease inheritance.<sup>38,39</sup> The study is also committed to improving the health of its participants by referring those with abnormal investigations to the appropriate health service.<sup>38</sup> By 2023, 37,000 participants were recruited, of whom at least 700 had whole-body MRI and 25,000 had WGS.<sup>38,39</sup>

**Canadian Alliance for Healthy Hearts and Minds.** The CAHHM (Canadian Alliance for Healthy Hearts and Minds) is a pan-Canadian "cohort of cohorts" study that was commissioned in 2013 with 8,850 participants recruited largely from existing population studies, the CanPath (Canadian Partnership for Tomorrow's Health), the PURE (Prospective Urban Rural Evaluation)-Canada cohort, and the MHI (Montreal Health Institute) Biobank, in addition to a new First Nations Cohort.<sup>40</sup> Their collective aim is to better characterize the factors that lead to CVD with a particular emphasis placed on the differential socio-environmental impact on high-risk ethnic groups.<sup>40</sup> A total of 8,258 participants underwent CMR, with a subset having an extended imaging protocol that included phase-contrast, LGE and T1 and T2\* mapping.<sup>41</sup> Genotyping data is available from CanPath's regional cohorts, including the OHS (Ontario Health Study) and CARTaGENE (CaG).<sup>40,42</sup>

**Courtois Cardiovascular Signature Program.** The Canadian Courtois Cardiovascular Signature Program marries the concepts of artificial intelligence (AI)-driven data analysis and personalized medicine. By collecting comprehensive phenotypic data from >4,000 participants 35 to 79 years of age since 2018, the program hopes to define the unique CV signatures of healthy, at-risk, and diseased hearts, respectively.<sup>44</sup> Over 10 years, each participant will undergo WGS and at least 1 CMR scan that includes breathing-enhanced oxygen-sensitive sequences.<sup>44</sup> Importantly, pseudonymized data will be accessible to researchers on application in the trusted research environment, Amazon Web Services Montreal Cloud.<sup>44</sup>

**SingHEART Study.** Initiated in 2015, the SingHEART study is the first Asian population study of its size and depth. Its overarching goal is to characterize the CV health, elucidate ethnic differences, and validate pre-existing biomarkers in healthy volunteers in

**CENTRAL ILLUSTRATION** Global Landscape of Population Studies With Genomics and CMR

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Large population studies with genomics and cardiac magnetic resonance (CMR) data are well-represented in North America and Central Europe and are starting to expand into Asia and Africa. AGES = Age, Gene/Environment Susceptibility Study; CAHMS = Canadian Alliance for Healthy Hearts and Minds; CV = cardiovascular; DHS = Dallas Heart Study; ECCO-GEN = Egyptian Collaborative Cardiac Genomics Project; FHS = Framingham Heart Study; HCHS = Hamburg City Health Study; JHS = Jackson Heart Study; MESA = Multi-Ethnic Study of Atherosclerosis; NAKO = German National Cohort; PESA = Progression of Early Atherosclerosis Study; QBB = Qatar Biobank; SHIP = Study of Health in Pomerania; UKBB = UK Biobank.

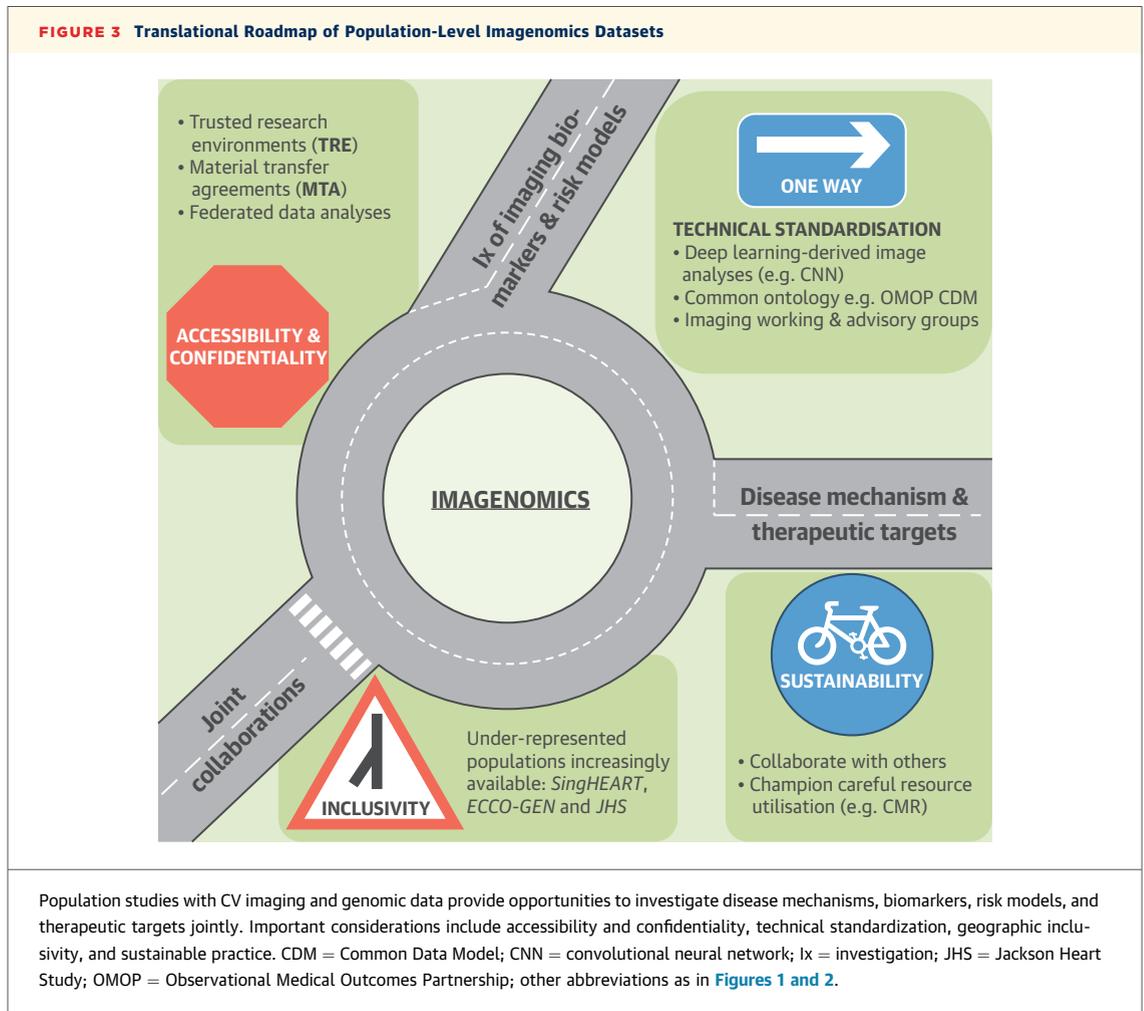
Asia. Targeting 5,000 recruitments, >1,000 have enrolled, undergoing deep phenotyping with CMR, CT-CAC, physical activity from wearables, ambulatory ECG and blood pressure data, and genomic and lipidomic analyses.<sup>45</sup> SingHEART also contributes to the national SG-100K program, in which 100,000 healthy volunteers in Singapore are enrolled for WGS. Importantly, patients include the 3 major ethnic groups in Singapore (Chinese, Malay, and Indian) who consent to 20 years of follow-up and can be recalled for additional phenotyping studies.<sup>45</sup>

**Egyptian Collaborative Cardiac Genomics Project.** African populations remain under-represented and under-studied. To facilitate future African population-level CV and genetic research the ECCO-GEN (Egyptian Collaborative Cardiac Genomics Project) opened in 2015 and seeks to recruit a target 1,000 healthy Egyptian volunteers for comprehensive imagenomics-driven CV phenotyping.<sup>46</sup> The CMR protocol includes a bSSFP cine SAX stack; T1 mapping and 3D tagging at basal, mid, and apical level; as well as phase-contrast sequences and 4D flow at

different levels of the aorta.<sup>46</sup> Participants will also have targeted sequencing of 174 genes with reported roles in inherited cardiac conditions on Illumina Miseq and Nextseq platforms using the TruSight Cardio Sequencing Kit.<sup>46</sup>

## DISCUSSION

To our knowledge, our systematic review is the first to collate population-based biobanks with CMR imaging and genomic data; it has the significant potential to contribute to precision medicine-focused CV research. In total, the 17 presented population studies, spanning 10 countries across 4 continents, recruited close to 1 million participants with multi-level genomics data and with a target >180,000 CMR scans (**Central Illustration**). Each study brings its novelty, be it the life stage, ethnicity, or sheer volume of participants recruited. By collecting comprehensive genotyping and CMR-derived phenotypes, the studies can investigate CVD and health at new levels and scales. We provide a 2-part actionable



guide, describing the challenges and opportunities of participating in CV “big data” research.

**CHALLENGES: BIOBANK INFRASTRUCTURE AND DIRECTIONS.** The foundation of a population-level imaging biobank should be built on the FAIR principles; the data must be findable, accessible, interoperable and reusable ([Figure 3](#)).<sup>56-58</sup> First, these endeavors are dependent on the good will of participants and must comply with appropriate legislation, the GDPR (General Data Protection Regulation) 2016 in Europe and the privacy and security rules under the HIPAA (Health Insurance Portability and Accountability Act) in the United States.<sup>8-10</sup> Data access and sharing procedures must be defined within this legal framework; examples include trusted research environments, material transfer agreements, and federated data analyses structures (eg, DataSHIELD).<sup>56,58-60</sup> Second, large-scale image acquisition and data analysis need to be efficient, accurate, and standardized as we define the ground

truth. Presented opportunities include international imaging working and advisory groups (eg, the European Society of Radiology) and the development of automated machine learning-derived techniques for image reconstruction, segmentation, and tissue characterization (eg, convolutional neural networks).<sup>10,61-64</sup> Third, low- and middle-income countries remain heavily under-represented despite the theoretical wealth of information provided by their profound ethnic and genetic differences, contrasting lifestyle, and environmental exposures. The emergence of, among others, the SingHEART and ECCO-GEN studies is an encouraging sign. Finally, imaging biobanks must address these challenges within a sustainable framework; we must mitigate the thermal, sound pollution, and waste production of our seemingly invisible data centers.<sup>65,66</sup>

**OPPORTUNITIES: A BIOBANK TRANSLATIONAL ROADMAP.** The opportunities provided by CV imagenomics databases are unrivalled. Here, we

describe translational roadmaps to clinical practice and the importance of joint collaborations, clarified by important questions, published examples, and future ideas (Figure 3).

**Disease mechanism and therapeutic targets.** Genomic studies, including GWAS and Mendelian randomization of CMR-derived phenotypes, may identify novel disease mechanisms and therefore targets for pharmaceutical treatment.

1) What are the genetic underpinnings of left ventricular maximum wall thickness (LVMWT)? Aung et al<sup>67</sup> performed a GWAS to investigate the genetic determinants of CMR-quantified LVMWT in the UKBB. The importance of the findings was 2-fold. First, patients with sarcomere-negative hypertrophic cardiomyopathy (HCM) could, in fact, harbor rare variants in novel gene loci implicated in myocardial growth; analysis of downstream protein products may identify novel therapeutic targets. Second, the polygenic heritability of the LVMWT trait suggests that HCM inheritance is not always Mendelian; instead, PRS may improve risk stratification of a proband's family members for disease expression and adverse outcomes. Analyses of other CMR-derived left ventricular phenotypes, including the heterogeneity biomarker, mean absolute deviation of maximum segmental wall thickness may provide further insights into HCM and other cardiomyopathies.<sup>68</sup>

2) What is the clinical and subclinical impact of genetic variants in cardiomyopathy-associated genes? Leveraging the imagenomics data from MESA and UKBB, respectively, Shabani et al<sup>69</sup> and Shah et al<sup>70</sup> demonstrated that common variation in cardiomyopathy susceptibility loci leads to a broad range of CMR- and ECG-detectable markers of cardiomyopathy and arrhythmia in an asymptomatic population. These included ventricular dilatation, myocardial fibrosis, and conduction defects. Beyond further elucidating disease pathogenesis, these findings illustrate the potential but also challenges of population-level genetic testing.<sup>69,70</sup> Similar methodology should be used to describe the penetrance and variable expressivity of particularly arrhythmogenic cardiomyopathy genes on right ventricular structure and function.

**Investigation of imaging-derived biomarkers and risk models.** Robust long-term follow-up of large cohorts, sometimes over generations through electronic health records coupled with detailed baseline phenotyping, using CMR, biological samples, and other clinical tools puts imagenomics databases at the forefront of biomarker and risk model derivation,

validation, and testing. Listed examples have led to biomarkers entering key consensus documents.<sup>71,72</sup>

1) Does CT-CAC predict atherosclerotic CVD? Multiple cohorts performed CT-CAC; however, MESA's landmark studies firmly established CAC as an incremental independent predictor of atherosclerotic events with CAC = 0 conferring very low risk even in the presence traditional risk factors. Pushing the risk stratification boundaries further, PESA aims to quantify vessel wall inflammation as a precursor to plaque formation by using coronary NaF-PET and <sup>18</sup>fluorodeoxy-glucose PET-MRI.<sup>30</sup>

2) Is CMR-feature tracking (FT)-derived strain predictive of adverse events at population level? Chadalavada et al<sup>73</sup> were the first to show the predictive power of CMR-FT-quantified global longitudinal strain for all-cause mortality in a predominantly healthy general population of 45,000 from the UKBB. This marked a significant step in the vetting of CMR strain measurements and set the stage for deep-dive investigations into strain heterogeneity biomarkers, including strain coefficient of variation and mechanical dispersion.<sup>74,75</sup> The fortuitous delineation of extracardiac structures from available CV imaging also provides opportunities to measure skeletal muscle and fat mass as potential biomarkers.

3) Can genomic and imaging biomarkers synergistically improve risk prediction? Building on the legacy of the FHS, which first incorporated "factors of risk" into a 10-year coronary heart disease risk calculator, the addition of imaging biomarkers and PRS should enhance risk prediction models. A recent systematic review by Hosseine et al<sup>76</sup> of AI-optimized PRS only identified 2 studies that combined classical risk factor models with PRS and CV imaging, highlighting significant research opportunities. The challenge resides in integrating high-dimensional heterogeneous datatypes, including clinical information, biochemical results, imaging, and PRS into a parsimonious model. Moving away from traditional statistical methods, machine learning algorithms such as least absolute shrinkage and selection operator regression and random forest models are promising solutions to feature selection.<sup>76</sup>

**Joint collaboration.** Finally, research that combines multiple studies will have greater sample size and heterogeneity, enabling more powerful and robust findings. A good example is the determination of CMR biomarker reference ranges. Leveraging the large UKBB, Petersen et al<sup>77</sup> derived age- and sex-specific reference ranges for standard CMR volumetric indices (eg, left ventricular mass). However,

**HIGHLIGHTS**

- Population studies with genomics and well-protocolized imaging—collectively termed imagenomics—provide unrivalled opportunity to investigate gene-lifestyle-disease interactions.
- Our synthesis of 17 CMR-genomics biobanks identified a target 1 million recruitments with >180,000 available scans.
- Use of personal “big data” should be equitable, standardized, sustainable and protective of participant identity.
- We hope to inspire, guide, and maximize future global collaborative cardiovascular research.

exclusion of participants with comorbidities and/or non-White background meant only 16.2% from >5,000 were available for analyses.<sup>77</sup> To address this limitation, Raisi-Estabragh et al<sup>78</sup> derived 95% prediction intervals, using CMR scans from >9,000 healthy individuals of diverse ethnicities in the Healthy Hearts Consortium. Our 17 identified population studies, whose data is accessible upon application, are tantalizing opportunities to cross-validate findings.

**STUDY LIMITATIONS.** Large population studies with genomics and CMR data are well-represented in North America and Central Europe and are starting to expand into Asia and Africa. We acknowledge that international imaging biobanks published in non-English language published reports may have been missed but contend that our review summarizes the largest and most pertinent population studies to date. Also, we are uncertain if genomic and CV imaging data can be linked in 2 imaging biobanks (ie, QBB and ECCO-GEN) and struggled to identify comprehensive protocols of available genomics data in the newer biobanks. Lastly, several included and many excluded population cohort studies have echocardiography and CT coronary angiography, which provide complementary information about participants' CV health to CMR.

**CONCLUSIONS**

We present a comprehensive synthesis and appraisal of 17 distinct imagenomics biobanks with both CMR and genomics data, accessible upon request to

researchers. In the spirit of the Greek philosopher Aristotle, who once said, “the whole is greater than the sum of its parts,” by sharing and collaborating across the different studies, investigators will contribute more powerful and novel findings to CV research.

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