

## **Cohort profile: AI driven national Platform for CCTA for clinical and industrial applications (APOLLO)**

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## **ABSTRACT**

**Purpose:** Coronary computed tomography angiography (CCTA) is well-established in the diagnostic evaluation and prognostication of coronary artery disease (CAD). The growing burden of CAD in Asia and the emergence of novel CT-based risk markers have necessitated an automatized platform that can efficiently integrate patient data with CCTA findings to provide a patient-tailored and accurate assessment of cardiovascular risk. This study aims to build an artificial intelligence (AI)-driven platform for CAD assessment using CCTA in the context of the multi-ethnic population of Singapore. We aim to conduct a hybrid retrospective-prospective medical records review of patients who underwent CCTA as part of diagnostic work-up for CAD, along with prospective follow-up for a range of listed clinical endpoints. CCTA images will be analyzed at individual sites and by a core laboratory for coronary stenosis grading, Agatston scoring, epicardial adipose tissue and plaque analysis. The images and analyses will also be uploaded to an AI platform for deidentification, analyses, integration, and automated reporting to create precision AI toolkits for each of these parameters.

**Participants:** 4999 patients have been recruited thus far; baseline characteristics have been verified for 1800 of these patients (76% Chinese, 6% Malay, 9% Indian and 9% Other). 44% these 1800 patients were female, with a mean age of  $55 \pm 11$  years, 43% hypertension, 54% dyslipidemia, 16% diabetes and 21% smoking history.

**Findings to date:** The cohort data has been used to develop four AI modules for training, testing, and validation. During the development of each AI module, the data preprocessing standardized the format, resolution, and other relevant attributes of the images.

**Future plans:** We will conduct prospective follow-up on the cohort to track clinical endpoints, such as cardiovascular events, hospitalizations, and mortality. Additionally, we will monitor the long-term impact of the AI-driven platform on patient outcomes and healthcare delivery.

**Trial registration:** ClinicalTrials.gov (Identifier: NCT05509010).

**Keywords:** Computed Tomography Angiography; Coronary Artery Disease; Artificial Intelligence

### **Strengths and limitations of this study**

- APOLLO is a first-in-Asia, AI-driven national platform for CCTA for clinical, and industrial applications in Singapore.
- APOLLO is a hybrid, retrospective-prospective, open-label, observational, multi-centre study. It will involve a retrospective review of patients who underwent CCTA as part of diagnostic work-up for CAD, as well as prospective follow-up for several clinical endpoints.
- The AI-based toolkit will automatize de-identification, identification of coronary stenoses, plaque characterization, as well as quantification of epicardial adipose tissue and coronary artery calcium score.
- This study only included patients from an Asian population. Therefore, additional Western-inclusive population studies are warranted to further validate the findings.

## INTRODUCTION

As in the rest of the world, coronary artery disease (CAD) is a leading cause of death in Asia, and its increasing prevalence portends a significant healthcare and economic burden.<sup>1,2</sup> Coronary computed tomography angiography (CCTA) is now firmly established as an essential modality in the early detection, clinical evaluation, and risk stratification of patients with CAD. This is reflected in guidelines from the National Institute of Clinical Excellence (NICE),<sup>3</sup> as well as European Society of Cardiology (ESC)<sup>4</sup> and American Heart Association (AHA).<sup>5</sup> These recommendations are built on a body of evidence demonstrating that upstream use of CCTA for the diagnosis of CAD improves event-free survival through earlier initiation of guidelines-directed medical therapy,<sup>6</sup> reduces rates of needless cardiac catheterization<sup>7</sup> and facilitates earlier discharge of patients presenting with possible acute coronary syndrome to Accident and Emergency.<sup>8</sup>

CCTA is not only the modality-of-choice for anatomical assessment of the coronary vasculature, but also an essential tool for disease characterization and risk stratification. CT-generated parameters including Agatston score,<sup>9</sup> epicardial adipose tissue (EAT),<sup>10</sup> and plaque characteristics<sup>11</sup> are each of incremental value in this regard. However, uptake of these measurements in routine clinical practice is hampered by the laborious and time-consuming nature of manual quantification. Furthermore, manual determination of these parameters suffers from significant inter-observer variability, reportedly up to 20% even between expert readers.<sup>12</sup> Therefore, there is an unmet need for accurate automatization and streamlining of these parameters to better harness the diagnostic and prognostic utility of CCTA for patients with CAD.

Moreover, whilst several models have been studied and reported, they have been found to be poor predictors of cardiovascular risk in Asian populations. For example, The Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry (CONFIRM) revealed that Asian sites had a three-fold lower-than-expected prevalence of CAD. Similarly, in an observational study Villadsen et al. found ethnic differences in the composition of coronary atherosclerotic plaque between Caucasian and South Asian patients, reporting a significantly lower proportion of non-calcified plaque in the former.<sup>13</sup> Our group has previously studied the performance of the CAD Consortium (CAD2) model in a mixed Asian population in Singapore and found suboptimal discriminative power, though it improved significantly with local calibration.<sup>14</sup> More recently, we evaluated the prognostic utility of both pooled cohort equations (PCEs) and Agatston score in a symptomatic, mixed Asian population. We found that PCE alone provided no discriminative value over random chance, and furthermore, this was not significantly improved after the addition of Agatston scores.<sup>15</sup> Therefore, an automated model must consider these differences for accurate prediction of cardiovascular risk in the mixed Asian population of Singapore. To develop this, a contemporary study of CAD prevalence in Asia is needed.

## **COHORT DESCRIPTION**

### **Patient and public involvement**

Patients and/or the public were not directly involved in the design, or conduct, or reporting, or dissemination plans of this research. The study outcomes will be disseminated through publication in peer-reviewed biomedical, cardiac imaging, and clinical journals, as well as presentations at scientific conferences. This will pave the way for a range of clinical, population health, research, and commercial applications.

### **Cohort objectives**

We aim to build a first-in-Asia, AI-driven national platform for CCTA for clinical, and industrial applications (APOLLO), to create a mixed-ethnic phenotypic registry of CAD in Singapore (**Graphical abstract**). APOLLO will serve a range of clinical, research and industrial purposes. First, as a large, registry, APOLLO stands to offer valuable insights into patient demographics and disease patterns within a highly characterized multi-ethnic Asian population. Second, the development of precision AI toolkits may enable automation of anonymization, reporting, Agatston scoring, EAT and plaque quantification, facilitating integration of these tasks into routine clinical practice. Third, as a de-identified and sharable database, APOLLO will facilitate the calibration and development of Asian-based prediction models whilst expediting the advent of novel medical and device therapies in the Asian context (**Figure 1**).

### **Study type**

APOLLO is a hybrid, retrospective-prospective, open-label, observational, multi-centre study. It will involve a retrospective medical record review of patients who underwent CCTA as part of

diagnostic work-up for CAD, as well as prospective follow-up for several clinical endpoints. Details of the study design are also available on ClinicalTrials.gov (Identifier: NCT05509010).

### **Study population**

There are three hospital sites participating in the creation of APOLLO: National Heart Centre Singapore (NHCS), National University Health System (NUHS) and Tan Tock Seng Hospital (TTSH). These represent the three largest cardiac healthcare systems in the country. Patients who underwent CCTA after 1 January 2007 will be included, with recruitment to be continue until 31 December 2025. The inclusion and exclusion criteria are listed in **Table 1**. Patients aged 21 and above were included. Exclusion criteria include acute coronary syndrome, a body mass index exceeding 40 kg/m<sup>2</sup>, and a history of percutaneous or surgical intervention for CAD. Baseline demographic and clinical characteristics will be obtained from the electronic medical records and case notes, including but not limited to: (1) age, gender, race, socioeconomic status, marital status, (2) comorbidities, (3) laboratory tests, (4) radiological tests, (5) cardiac investigations, (6) cardiac procedures, (7) medication use, (8) chest pain characteristics.

### **CCTA protocol**

CCTA acquisition will be conducted using 6 state-of-the-art CT scanners (Canon, Siemens, GE, Philips) with  $\geq 256$ -detector rows, following image acquisition protocols outlined in the Society of Cardiovascular Computed Tomography (SCCT) guidelines.<sup>16</sup> Medication, as per guidelines, can be administered to moderate heart rate in patients with a heart rate higher than 60 bpm. Sublingual glyceryl trinitrate is administered prior to scanning. The CCTA scans employ a prospective ECG-triggered scanning mode. A tri-phasic injection protocol is applied, involving



contrast injections of approximately 50ml at 5ml/s and 20ml at 3.5ml/s sequentially, followed by a third injection of 30ml saline at 3ml/s.

### **CCTA analysis**

The CCTA images will be analyzed and interpreted both at the clinical site level and at the core laboratory. At the clinical site read, CCTA interpretation will be done in accordance with the 2016 SCCT guidelines.<sup>16</sup> Core lab analysis will be performed at the CardioVascular Systems Imaging and Artificial Intelligence (CVS.AI) research core of NHCS, blinded to the clinical site interpretation. Core lab analyses will include:

- (1) **Coronary stenosis grading:** The assessment focuses on the severity of stenosis and precise localization within the coronary circulation. A crucial aspect involves visually estimating luminal narrowing caused by plaque. Following the SCCT guideline,<sup>16</sup> stenosis is graded across a spectrum, ranging from minimal to total occlusion. Additionally, distinctions between obstructive and non-obstructive categories are made, with the SCCT model guiding the accurate determination of stenosis location.
- (2) **Agatston scoring analysis:** Calcified plaque is evaluated using Agatston scoring programs, aligned with SCCT clinical practical guidelines.<sup>16</sup> Pixels exceeding 130 Hounsfield Units (HU) are identified as indicative of calcium on non-contrast studies.<sup>17</sup> Lesions within each vessel distribution are discerned, and the scoring program generates a comprehensive summed score for each vessel based on area-density (Agatston score) measurements. The total coronary Agatston score aggregates all calcified lesions throughout coronary beds.
- (3) **EAT analysis:** This analysis focuses on the total volume and anatomical locations of EAT and pericardial adipose tissue (PAT), metabolically active fats associated with heightened

cardiovascular disease risk.<sup>18</sup> Quantification on non-contrast CT scans involves meticulous annotation by manually drawing the pericardium. EAT is identified using adipose tissue attenuation references between -190 and -30 HU.<sup>19</sup> Given potential variations in HU values due to CT scan noise and attenuation changes, the final EAT region is verified by an experienced radiologist or cardiologist.

(4) **Plaque analysis:** This facet involves analysis of plaque volume, burden, type, and anatomical locations. Coronary segmentation and analysis are performed for segments with a diameter  $\geq 1.5$  mm, with the SCCT model<sup>16</sup> aiding in precise plaque localization. For each plaque, detailed assessments, including start and end points, area, volume, and plaque burden, and type (non-calcified, calcified, or mixed),<sup>20</sup> are conducted. Additionally, non-calcified plaque is further subclassified into low attenuation plaque (LAP), with HU  $<30$  signifying LAP and  $>30$  signifying non-LAP.

### **Patient outcomes**

Patients whose CCTA data will be utilized for the purpose of this study will also be prospectively followed up till 31 December 2025 for several outcome measures. This will enable prognostic validation of AI-derived measurements. The patient outcomes to be monitored for are as follows:

(1) **Mortality (all-cause and cardiovascular):** Over the course of one to five years from the baseline, the study will examine mortality rates, including both all-cause mortality and mortality specifically attributable to cardiovascular events.

(2) **Major Adverse Cardiovascular Events (MACE):** Besides mortality, the study will assess MACE, including, but not limited to, myocardial infarction, stroke, heart failure, percutaneous/surgical revascularization, and arrhythmias.

(3) **Re-hospitalization:** Another critical aspect of the outcome measures involves evaluating the incidence of re-hospitalization within the one to five-year period from the baseline. This parameter serves as a valuable indicator of the long-term impact of AI interventions on the need for repeated hospital admissions, shedding light on the potential benefits in terms of sustained health outcomes and healthcare resource utilization.

These data will be recorded from hospital medical records as well as national registries in accordance to institution, ministry and national-level regulations. At the institutional level, tracking and extraction of outcomes will be performed by the respective IT teams under PI/study team supervision. The respective institution's Clinical Research Coordinator (CRC) will also track and match outcomes via electronic medical records (EMR). At the national level, matching and tracking of outcome data from national registries (National Registry of Diseases Office; NRDO) will be delegated to NRDO staff. One of the registries to be analysed via NRDO is Singapore Myocardial Infarction Registry (SMIR) for aggregate data.

### **Data sharing**

Data sharing will be through the National University Health System (NUHS)'s DISCOVERY AI platform, a production system that houses centralized anonymization, equitable data access and differential data linkage capabilities.<sup>25</sup> DISCOVERY AI platform processes are summarized in **Figure 2**. Oversight rests with the custodian of a particular database. DISCOVERY AI

incorporates centralized anonymization and data handling measures that are in accordance with the Singapore Personal Data Protection Act (PDPA) 2012,<sup>56</sup> Human Biomedical Research Act 2015,<sup>57</sup> and Human Biomedical Research Regulations 2017.<sup>58</sup> In keeping with PDPA guidelines, all data on board DISCOVERY AI are anonymized by removing protected health identifiers (PHI) such as name, address and identification number. DISCOVERY AI also features proprietary security features, such as data obfuscation and ledger-based access logs.

### **Ethics and dissemination**

The study protocol has been approved by the SingHealth Centralised Institutional Review Board. The project outcomes will be disseminated through publication in peer-reviewed biomedical, cardiac imaging, and clinical journals, as well as presentations at scientific conferences. Patient confidentiality will be maintained by not including any individually identifying information in the publications.

## **FINDINGS TO DATE**

Within 26 months, 4999 subjects have been recruited. Baseline characteristics for 1844 subjects have been verified. These are shown in **Table 2**. The population recruited so far is 44% female, with a mean age of  $55\pm 11$  years. Chinese, Malay, Indian, and other ethnicities make up 76%, 6%, 9% and 9% of the study population, respectively. Over one-half of the total population has lipidaemia (52%), 43% hypertension, 16% diabetes and 21% positive smoking history. All data collected thus far has been anonymized and stored in DISCOVERY AI. Furthermore, the four AI modules are in development using 2,983 CT imaging studies for training, testing and validation. During the development of each AI module, the data pre-processing standardized the format, resolution, and other relevant attributes of the images.

## DISCUSSION

The APOLLO study targets a cohort reflective of the current real-world Asian population undergoing assessment for CAD. Given the growing clinical burden of CAD, a national AI platform to facilitate CCTA analysis is desirable for several reasons. First, as the largest CCTA registry of patients with suspected CAD, APOLLO will provide much needed and highly representative insight into current and emerging states of clinical diagnostic testing in the region. Second, APOLLO aims to enhance the efficiency of CCTA reporting, including analysis of otherwise manually laborious parameters such as plaque characterization and EAT quantification. Third, through robust validation against patient outcomes, APOLLO may enable cardiovascular risk prediction, thus facilitating triage and clinical workflow. Last, but not least, this large, de-identified, and well-characterized patient registry will have a myriad of clinical, research and industrial applications. Recruitment is progressing ahead of schedule, indicating comprehensive and efficient cooperation across Singapore's largest cardiac healthcare institutions.

In a forecast analysis based on 2007 to 2018 data from the Singapore myocardial infarct registry<sup>28</sup> 2025 to 2050, the incidence of acute myocardial infarction (AMI) in Singapore is predicted to rise by 194.4% from 482 to 1418 per 100,000 population.<sup>29</sup> The largest percentage increase in metabolic risk factors within the population with AMI is projected to be overweight/obesity (880.0% increase), followed by hypertension (248.7% increase), diabetes (215.7% increase), hyperlipidemia (205.0% increase), and active/previous smoking (164.8% increase).<sup>28</sup> The number of AMI-related deaths is expected to increase by 294.7% in individuals with overweight/obesity, while mortality is predicted to decrease by 11.7% in hyperlipidemia,

29.9% in hypertension, 32.7% in diabetes and 49.6% in active/previous smokers, from 2025 to 2050.

Similar trends are expected in Asia as the ethnic distribution in Singapore of Chinese, Malay and Indian broadly represent the ethnic distribution of large parts of Asia.<sup>30</sup> The baseline characteristics of the study population recruited thus far suggests notable differences in the prevalence of cardiovascular risk factors from existing study cohorts. For example, as compared to the Danish population studied by Winther et al, our study population appears to have a higher prevalence of both dyslipidemia and diabetes mellitus (52% vs 30% and 16% vs 7%, respectively).<sup>31</sup> Similarly, over one-half of all participants in the SCOT-HEART (Scottish Computed Tomography of the Heart) study were current or former smokers, in contrast to one in five as seen in our local population.<sup>6</sup> Given that most of our study population is of Chinese ethnicity, the prevalence of cardiovascular risk factors is most similar to that noted in the Chinese populations studied by Zhou et al.<sup>32</sup> and Tay et al.,<sup>33</sup> albeit with a markedly higher prevalence of dyslipidemia in the overall cohort. This difference may not be entirely due to a higher prevalence of dyslipidemia in the Indian and Malay patient sub-groups, as prior dyslipidemia studies in Singapore found no significant differences between ethnic sub-groups.<sup>34,35</sup> Instead, it is possible that the higher prevalence of dyslipidemia is a reflection of local dietary and lifestyle factors. Similarly, in comparison to an analysis of CAC incidence and progression in 698 (majority Indian) subjects from the MASALA (Mediators of Atherosclerosis in South Asians Living in America) study, our current study population has half the prevalence of diabetes mellitus.<sup>36</sup> These differences in baseline characteristics from other existing cohorts emphasizes the need for a tailored approach in the creation of an AI-platform for cardiovascular risk prediction.

Furthermore, APOLLO will be the largest study of CCTA-based risk prediction in Asia. The largest studies to date have been from China, most notably that by Zhou et al., comprising 4207 subjects, which demonstrated that a combination of CAC and clinical risk factors offers the greatest utility in identifying the lowest risk group among patients with stable chest pain.<sup>32</sup> Other cohort studies in the Chinese population are generally 2000 patients or fewer.<sup>37-44</sup> Moreover, these studies are limited to identification of functional significant coronary lesions rather than global assessment of CT-based risk markers, as in the APOLLO study design. Similarly, Shiono et al. have previously studied and reported on the 1829 subjects from Japan in the ADVANCE (Assessing Diagnostic Value of Non-invasive FFR<sub>CT</sub> in Coronary Care) registry,<sup>45</sup> whilst in Korea, Yang et al studied 1100 lesions in 643 patients to delineate CCTA markers of functionally obstructive CAD as well as poor vessel-oriented outcomes.<sup>46 47</sup> Therefore, the APOLLO study may not only supersede existing CCTA studies in Asia in terms of sample size, but also in terms of the wealth of CCTA-based information utilized in the risk stratification model.

Data sharing is a common challenge for all healthcare entities with data privacy, consent, ethical use and scalability concerns being the common barriers. Platform solutions to address these at scale include deidentification, anonymization, secured data instances, common data models and federated analysis have been trialed at multiple institutions in Singapore. Examples of this include DISCOVERY AI<sup>25</sup> and Odyssey<sup>48</sup> in two Singapore healthcare clusters which federate data under a common governance mechanism and permits users to share and use data securely. These instances have successfully demonstrated that on-premise cloud instances can support multiple clinical and research groups with inherent safety, scalability and economies of scale. It also permits large scale AI model training using on-premise supercomputing resources



that affords the lowest cost per GPU utilization, if adequately utilized across multiple research groups.

To scale on this successful infrastructure, the Ministry of Health in Singapore and developed a national platform called TRUST,<sup>49</sup> which permits national level data sharing in a secured commercial cloud instance. Issues of cross institution data sharing and access are mediated by a multi stakeholder data access committee. It ensures fair access to specific datasets generated by public entities. The commercial cloud also affords multi-party remote access, larger range of online tools, and on a pay-per use basis which further enhances effective data use.

In summary, APOLLO is the first-of-its-kind, robust, national AI platform for the diagnosis, collection, analysis, interpretation, and automatization of CAD using CCTA. The development of the one-stop AI toolkit may transform the contemporary use of CCTA for the detection of CAD, integrating a range of patient demographics and CT-based risk markers to produce an efficient, accurate and individualized estimation of cardiovascular risk that will be longitudinally validated in a multi-ethnic Asian population. APOLLO also allows for scalability, with the use of a secure, data sharing platform. This may further pave the way for translational impact on the population health, clinical, research and commercial domains in Singapore.

### **Acknowledgement**

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### **Authors' contributions**

LB, MC, LZ contributed to the study design. LB, LT, MSY, and MC contributed in data acquisition. RV contributed to statistical planning. WMH, HKL, ZKL, XHW, EWPT, NZYC

contributed to AI development. KYN contributed to data anonymization and storage. LB, SL and UD drafted the manuscript. LT, MSY, CHS, NWSC, WMH, HKL, RV, KYN, ZKL, XHW, EWPT, NZYC, SYT, MC, and LZ contributed to revising the manuscript. All authors read and approved the final manuscript.

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**Competing interests:** none

**Collaboration:** The APOLLO team invites researchers to contact the corresponding author to request collaboration of any kind.

**Table 1.** Inclusion and exclusion criteria for prospective patient recruitment.

<b>Inclusion criteria</b>
<ul style="list-style-type: none"><li>• Age <math>\geq</math>21 years old</li></ul>
<ul style="list-style-type: none"><li>• Clinically indicated for evaluation by CCTA</li></ul>
<b>Exclusion criteria</b>
<ul style="list-style-type: none"><li>• Known complex congenital heart disease</li></ul>
<ul style="list-style-type: none"><li>• Planned invasive angiography for reasons other than coronary artery disease</li></ul>
<ul style="list-style-type: none"><li>• Non-cardiac illness with life expectancy &lt;2 years</li></ul>
<ul style="list-style-type: none"><li>• Pregnancy</li></ul>
<ul style="list-style-type: none"><li>• Concomitant participation in another clinical trial in which subject is subject to investigational drug or device</li></ul>
<ul style="list-style-type: none"><li>• Cardiac event and/or coronary revascularization (percutaneous coronary intervention and/or coronary artery bypass grafting and/or valvular repair/replacement prior to CCTA</li></ul>
<ul style="list-style-type: none"><li>• Glomerular filtration rate <math>\leq</math>30mL/min</li></ul>
<ul style="list-style-type: none"><li>• Known allergy to iodinated contrast agent</li></ul>
<ul style="list-style-type: none"><li>• Contraindications to beta blockers or nitroglycerin or adenosine</li></ul>

CCTA, coronary computed tomography angiography.

**Table 2.** Baseline characteristics.

	<b>All (n = 1844)</b>	<b>Retrospective (n = 698)</b>	<b>Prospective (n = 1146)</b>
<b>Age, years</b>	55±11	55±11	56±11
<b>Gender, Male/Female</b>	1033/811	412/286	621/525
<b>Height, cm</b>	165±9	164±10	165±9
<b>Weight, kg</b>	70±15	70±15	71±16
<b>Body mass index, kg/m<sup>2</sup></b>	26±5	26±5	26±5
<b>Race</b>			
Chinese, n (%)	1401 (76)	523 (75)	878 (77)
Malay, n (%)	105 (6)	34 (5)	71 (6)
Indian, n (%)	172 (9)	65 (9)	107 (9)
Others, n (%)	166 (9)	76 (11)	90 (8)
<b>Cardiac risk factors</b>			
Hypertension, n (%)	792 (43)	325 (47)	467 (41)
Diabetes, n (%)	300 (16)	102 (15)	198 (17)
Dyslipidemia, n (%)	962 (52)	382 (55)	580 (51)
Family history, n (%)	485 (26)	149 (21)	336 (29)
Smoking, n (%)	390 (21)	117 (17)	273 (24)
Peripheral artery disease, n (%)	5 (0.3)	4 (1)	1 (0.1)
<b>Medication</b>			
Aspirin, n (%)	236 (13)	131 (19)	105 (9)
Thienopyridine, n (%)	63 (3)	42 (6)	21 (2)
Ticagrelor, n (%)	3 (0.2)	1 (0.1)	2 (0.2)
Statin, n (%)	727 (39)	296 (42)	431 (38)
Beta blocker, n (%)	269 (15)	142 (20)	127 (11)
Calcium channel blocker, n (%)	323 (18)	114 (16)	209 (18)
ACE-inhibitor, n (%)	107 (6)	50 (7)	57 (5)
Angiotensin II antagonist, n (%)	241 (13)	86 (12)	155 (14)
Mineralocorticoid antagonist, n (%)	17 (1)	10 (1)	7 (1)
Oral hypoglycemics, n (%)	198 (11)	66 (9)	132 (12)
Insulin, n (%)	32 (2)	13 (2)	19 (2)
<b>Blood test</b>			
Glomerular filtration rate, mL/min	96 (86, 103)	96 (86, 104)	95 (86, 103)
Total cholesterol, mmol/L	4.9 (4.2, 5.7)	5.1 (4.3, 5.7)	4.9 (4.2, 5.6)
High-density cholesterol, mmol/L	1.3 (1.1, 1.6)	1.3 (1.1, 1.5)	1.4 (1.1, 1.6)
Triglycerides, mmol/L	1.3 (1.0, 1.8)	1.3 (0.9, 1.7)	1.3 (1.0, 1.8)
Low-density cholesterol, mmol/L	2.9 (2.2, 3.6)	3.1 (2.4, 3.8)	2.8 (2.2, 3.5)
Hemoglobin, g/dL	14 (13, 15)	14 (13, 15)	14 (13, 15)
Hemoglobin A1c, %	5.9 (5.5, 6.6)	5.8 (5.4, 6.3)	6.0 (5.6, 6.8)

## **Figure legends**

**Figure 1.** Workflow of the APOLLO platform. CT images are first anonymized and uploaded into APOLLO's database. The images are then processed using AI engines and results uploaded into the database again. A summary report will be generated and presented to the end user. CAD: coronary artery disease; AI: artificial intelligence; EAT: epicardial adipose tissue; CVD: cardiovascular disease.

**Figure 2.** DISCOVERY AI tribrid platform processes. Clinical and research data processed by various production AI modules to make predicted clinical warnings on the electronic health record system. AI: artificial intelligence; ICU: intensive care unit; EPIC: an American private held healthcare software company; I2B2: informatics for integrating biology & the bedside; SDSD: surgical data systems directorate dataset; SPH: School of Public Health.

**Graphical abstract.** APOLLO Study Design. Integration of risk markers derived from coronary CT angiography together with patient demographics, cardiovascular risk factors, medications, laboratory findings and survival data. Coronary CT angiography parameters will include characterization of coronary artery lesion, epicardial adipose tissue and coronary artery calcium score. To generate a sharable database for clinical, research and industrial purposes. AI: artificial intelligence; CAD: coronary artery disease; CT: computed tomography.

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