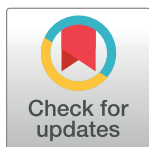RESEARCH ARTICLE

# Cohort profile of a prospective cohort study among middle-aged community-dwellers in rural Vietnam: The Khánh Hòa Cardiovascular Study

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**Data Availability Statement:** The data supporting the findings of this study are not publicly available due to privacy concerns and the potential for participant identification. Given the sensitive nature of the collected data, including detailed personal health information, lifestyle habits, and early-life experiences, combined with the publication of specific study locations, there is a heightened risk of participant identification. This restriction is in accordance with the decisions made by the Research Ethics Committees at the National Center

## Abstract

Disease burden associated with cardiovascular diseases (CVDs) in low- and middle-income countries has been on an increasing trend in the past decades. Despite the worldwide genetic, cultural, and environmental variations in determinants of CVDs, few studies have attempted the identification of risk factors of CVDs in low- and middle-income countries. This article aims to introduce the Khánh Hòa Cardiovascular Study, a prospective cohort study among middle-aged community dwellers in rural Khánh Hòa, Vietnam. A total of 3000 individuals, aged 40–60 years at baseline, participated in the baseline survey conducted from June 2019 to June 2020 and will be followed up for the subsequent 10 years. The base-line survey collected information on sociodemographic variables, disease history, lifestyle, social environment, and mental health via questionnaires, physical examinations, and bio-chemical measurements. Information on the incidence of severe health outcomes (i.e., mortality, CVDs, and cancer) has been and will be collected using a study-specific disease registry. Results showed that the prevalences of excess body weight (body mass index $\geq 25$ kg/m$^2$), hypertension, diabetes mellitus, and dyslipidemia were 25.9%, 39.6%, 10.2%, and 45.1%, respectively. Furthermore, by March 2023, 21 participants had died, including 5 CVD deaths and 12 cancer deaths. Moreover, we recorded 22 and 31 cases of nonfatal CVDs and cancer, respectively. These results suggest that many rural residents in Vietnam have high cardiometabolic risk, and underscore the importance of advancing research to identify risk factors and prevent the onset of serious health events.

## Introduction

Cardiovascular diseases (CVD) are the leading cause of mortality worldwide [1,2], and the World Health Organization (WHO) estimates showed for approximately 17.9 million CVD-

related deaths, which comprised 31% of all global deaths, in 2019 [1]. As an attempt to mitigate the CVD-associated disease burden, numerous epidemiological studies investigated risk factors of CVD, including behavioral risk factors (e.g., smoking, physical inactivity, and unhealthy diet), clinical risk factors (e.g., hypertension, diabetes, and dyslipidemia) [2,3], and social determinants [4].

In contrast to high-income countries (HIC) that have reported robust evidence, low- and middle-income countries (LMIC) have reported limited epidemiological evidence, possibly because of insufficient research-related human capacity and funding [5]. Given the genetic, cultural, and environmental variations in the determinants of CVD that exist worldwide, this underrepresentation of LMICs in CVD research has resulted in an incomplete understanding of the epidemiology of CVD [6]. Moreover, compared to HICs, LMICs have been more disproportionately burdened with CVDs and account for more than 80% of all CVD deaths [7]. Thus, effective strategies to prevent and reduce the CVD-associated disease burden in LMICs will help improve global health.

Vietnam has experienced rapid economic growth since the introduction of a market-oriented policy in 1986 [8], and the gross domestic product per capita has been estimated to increase from USD706 to USD4320 during the period between 1986 and 2023 [9]. Although this economic growth has extended life expectancy at birth from 69.09 years, in 1986, to 75.77 years, in 2023 [10], the prevalence and incidence of noncommunicable diseases (NCD), including CVD, has also increased. Cerebrovascular and ischemic heart disease are the leading causes of premature mortality in Vietnam [11]. Despite this, epidemiological data remain scarce, and we are not aware of any prospective cohort study that has investigated these diseases in Vietnam.

This article aims to describe the Khánh Hòa Cardiovascular Study (KHCS), in which we aim to identify CVD determinants in the Vietnamese context, to enable better-informed strategic planning to mitigate the CVD-associated disease burden and the related morbidity and mortality in the country. This article provides an overview of the collected data and summarizes the main results published to date.

## Methods

### Cohort, study design, and study population

The KHCS is a collaborative effort of the Pasteur Institute in Nha Trang (PINT), Vietnam, a national research institute under the Vietnamese Ministry of Health with expertise in infectious diseases, epidemiology, and vaccine development (http://www.pasteur-nhatrang.org.vn/en/), and the National Center for Global Health and Medicine, Japan (NCGM), known for research on infectious and immunological diseases, diabetes, and metabolic diseases as well as advanced medical care, international medical collaboration, and training initiatives (https://www.ncgm.go.jp/en/index.html). Initially focused on infectious diseases, this collaboration has expanded since 2018 to include research and initiatives on NCDs in response to the escalating CVD- and NCD-associated disease burden in Vietnam.

The KHCS was designed as a prospective cohort study and was conducted in the Cam Lâm district, Khánh Hòa Province, located on the south-central coast of Vietnam (Fig 1); the study sites are in a suburban area, which is situated approximately 35 km from Nha Trang, the provincial capital. The primary industries in the district include agriculture, aquaculture, forestry, and manufacturing. The region has a tropical savanna climate, with annual average temperature and precipitation of 26.5˚C and 1768 mm, respectively [12].

We selected eight of 14 communes in the district because of their proximity to Nha Trang with the aim of following up the study cohort for an extended period. Participants aged 40 to

**Fig 1. The map of the study location.** Source of the GeoJSON files: Vietnam: https://data.opendevelopmentmekong.net/dataset/vietnam-province-iso-codes; Cambodia: https://data.opendevelopmentcambodia.net/dataset/administrative-boundaries-of-cambodia-2014; Laos: https://data.laos.opendevelopmentmekong.net/dataset/laos-administrative-boundaries-country-province-and-district; Thailand: https://data.humdata.org/dataset/cod-ab-tha; and China: https://data.humdata.org/dataset/geoboundaries-admin-boundaries-for-china. The files for Vietnam, Cambodia, and Laos are licensed under the CC BY-SA 4.0, the file for Thailand is licensed under the CC-BY-IGO, and the file for China is licensed under the CC BY 4.0 and the ODC-ODbL.

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**Table 1. Selection of Study Participants in the Baseline Survey of Khánh Hòa Cardiovascular Study, Vietnam (2019–2020).**

| | Commune | | | | | | | | Pilot Survey[b] | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | D | E | F | G | H | | |
| **Villages[a]** | 3 | 3 | 16 | 8 | 7 | 4 | 4 | 8 | | |
| **Selected villages** | 3 | 2 | 9 | 1 | 4 | 2 | 2 | 2 | | |
| **Individuals aged 40–59 years in the residents' registry in the selected villages** | 913 | 837 | 1283 | 677 | 913 | 1543 | 950 | 970 | - | - |
| **Candidate participants listed initially by the Commune Health Centers[c]** | 469 | 523 | 428 | 366 | 449 | 469 | 474 | 419 | - | - |
| **Participants, n** | 381 | 387 | 317 | 328 | 393 | 374 | 400 | 353 | 67 | 3000 |
| **Population coverage rate (%)[d]** | 41.7 | 46.2 | 24.7 | 48.4 | 43.0 | 24.2 | 42.1 | 36.4 | - | - |

[a] A village is a residential unit within a commune.

[b] The pilot survey, conducted in June 2019, included 100 participants aged 30–59 from the eight villages in Commune D. In the main survey, we used data from 81 individuals aged 40–59, with 14 participants from the village where we recruited for the main survey (the number is included in the column for Commune D) and the remaining 67 from the other seven villages.

[c] Candidate participants listed initially by the Community Health Centers (CHCs) were those identified by CHCs as residents who could participate in the study.

[d] The population coverage rate was calculated as the number of participants divided by the number of registered individuals aged 40–59 years, regardless of the eligibility criteria.

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59 years were chosen to focus on a population at higher risk for developing CVD, which tends to increase in incidence during middle age. This approach ensures a sufficient number of cases during the observation period, enabling a more robust analysis of associated risk factors. Furthermore, by examining a wide range of CVD risk factors during middle age rather than later in life, we aim to identify risk factors that are essential for early interventions to best minimize the disease burden associated with CVD.

Each commune health center aimed to recruit approximately 400 participants, continuing recruitment efforts until the sample size reached 3,000 (i.e., convenience sampling) (Table 1). The exclusion criteria were as follows: institutionalized individuals, those who were unable to provide informed consent, those who had a plan to move out of the community within 1 year, pregnant women or those who gave birth within 1 year, and those who had a history CVD events.

The specific recruitment procedure involved the following steps: Commune health centers have access to the residents' registry, which is regularly updated by the local government, and this enabled the initial identification of households with residents aged 40–59 years. Staff members from these commune health centers selected a village (i.e., a residential unit within a commune) and visited each household to verify the eligibility and willingness of individuals in this age group to participate in the survey. If they did not recruit a sufficient number of candidates, they selected another village and repeated the process until the required number of candidate participants was attained. Candidate participants were approached with invitation letters delivered in person to participate in the survey until the target sample size of 3000 was reached.

All participants provided written informed consent before study participation and were informed that they could withdraw their consent at any time. The research ethics committees of the NCGM (approval number: NCGM-G-003172-03) and the PINT (02/2019/HDDD-IPN) approved this study.

## Baseline survey

The baseline survey commenced, in June 2019, with a pilot phase, during which the number of participants was limited to 25 per day for training purposes; the main survey was conducted

from November 2019 to June 2020. Participants were instructed to visit the commune health center corresponding to their place of residence during the morning hours, after fasting for at least 8 hours before the sample collection. Individuals who did not adhere to the fasting protocol, specifically by consuming breakfast, were instructed to return on different days to ensure compliance with the essential fasting requirements for the study. Anthropometry, blood samples for biochemical measurements, and sociodemographic and lifestyle parameters were collected during face-to-face interviews, as described below.

**Questionnaire survey.** The study questionnaire was developed by referring to the WHO STEP Survey [13], although other questions deemed essential for capturing various health determinants in the Vietnamese context, for a more comprehensive questionnaire, were added. The information collected from the baseline survey is presented in Table 2.

Sociodemographic variables included age, sex, marital status, insurance number, educational attainment, job category, household income, and household assets. Participants were asked to choose one of the response options for education (i.e., did not go to school; less than primary school; primary school; junior high school; high school; university; and attained further education) and job categories (i.e., government employee; non-government employee; self-employed; farmer or fisherman; homemaker; other; and unemployed), respectively. To calculate an equivalized income value, household income per capita was estimated based on

**Table 2. Summary of items collected in the baseline survey of the Khánh Hòa cardiovascular study, Vietnam (2019–2020).**

| Items | Description | Specific instruments |
|---|---|---|
| **Sociodemographics** | • Age, sex, ethnicity, and marital status, insurance number<br>•Educational attainment, occupation, household income, and household assets | • Based on the WHO STEP Survey [13] |
| **Lifestyle** | • Smoking status or passive smoking<br>•Alcohol consumption<br>•Physical activity<br>•Sleep duration | • Based on the WHO STEP Survey [13] |
| **Diet** | • Vegetable and fruit<br>•Rice, noodles, and bread<br>•Meat consumption, fish consumption, and soy<br>•Milk, yogurt, and cheese<br>•Sweetened beverages, coffee, and tea (green tea and other tea)<br>•Sodium consumption<br>•Frequency of skipping breakfast, eating outside, and eating alone | • Information on vegetable and fruit consumption and sodium consumption were retrieved using questions employed in the WHO STEP Survey [13]<br>•Information on the other food items were collected using food-frequency questionnaires [14,15]. |
| **Social environment** | • Social capital (structural and cognitive social capital)<br>•Childhood socioeconomic status<br>•Parental absence before age 15 | • Questions on social capital were retrieved from the Adapted Social Capital Assessment Tool (SASCAT) [16]. |
| **Medical characteristics** | • Disease history and treatment status (hypertension, diabetes, and dyslipidemia)<br>•Family history of cancer and CVD | • Information on disease history and treatment status (hypertension, diabetes, and dyslipidemia) were collected using questions of the WHO STEP Survey [13]. |
| **Physical examination** | • Height, weight, and waist circumference<br>•Blood pressure | |
| **Biochemical measurement** | • Total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride<br>•Insulin, glucose, and glycated hemoglobin<br>•Uric acid<br>•High-sensitivity C-reactive protein | |
| **Mental health** | • Depressive symptoms | • The Center for Epidemiological Scale-Depression [17] |

CVD: Cardiovascular diseases; WHO: World Health Organization.

responses regarding monthly household income and the number of household members. Household assets were assessed by asking about the possession of several items in households (e.g., cars, motorbikes, television, and mobile phones).

Lifestyle-related variables included smoking status, alcohol consumption, physical activity, fruit and vegetable consumption, consumption of other selected food items (e.g., rice, bread, noodles, meat, coffee, and tea), and sleep duration (hours). Questions on smoking status, alcohol consumption, and fruit and vegetable consumption were derived from the STEP survey questionnaire [13]. For other dietary components, we employed the methodology from previous research that used food-frequency questionnaires [14,15]. Specifically, we asked them to provide their consumption frequency (i.e., the number of days per week and the number of times per day) and choose one of three response options for the consumption amount, which were based on a comparison with standard amounts illustrated on the show cards (i.e., smaller, equivalent, and larger). The list of food items was determined after group discussions with the PINT and CHC staff members who were familiar with the local diet.

We asked the participants questions regarding their social environment, including social capital (cognitive and structural social capital) based on a previously validated questionnaire [16], self-reported childhood socioeconomic status with five response options (i.e., high; upper-middle; middle; lower-middle; low), and parental absence in childhood, for which we ascertained the causes (i.e., death, divorce, and parents' out-migration to other locations) and timing (i.e., before 3 years of age, or after 3 years to before 15 years of age).

Information on the history of hypertension, diabetes, dyslipidemia, cancer, and diseases of the circulatory system was collected via a questionnaire. Furthermore, participants were asked about their family history of hypertension, diabetes, dyslipidemia, cancer, and CVD. Depressive symptoms were assessed using the 11-item Center for Epidemiological Scale-Depression [17].

**Physical examination and biochemical measurement.** Experienced staff members from PINT, who had previously conducted physical measurements in other surveys, used a digital scale (Tania, HD-661, Tokyo, Japan) and a portable stadiometer to measure body height and weight to the nearest 0.1 cm and 0.1 kg, respectively. Measurements were taken with the participants wearing light clothing and without shoes. Body mass index (BMI) was calculated by multiplying the weight (kg) by the height squared ($m^2$). Waist circumference measurements were taken using a tape measure placed over the light clothing worn by the participants, and the waist-to-height ratio (WHtR) was then calculated by dividing the waist circumference (cm) by height (cm) [18,19].

With the participants seated and their left arm held at heart level, blood pressure was measured twice using an electric sphygmomanometer (Omron, HEM1020, Tokyo, Japan). Prior to the first measurement, participants were instructed to relax in a seated position for at least 5 min, and was increase to 20 min for those who arrived at the venue by bicycle. The mean systolic and diastolic blood pressures were calculated using two measurements. A mean systolic blood pressure ≥140 mmHg, a mean diastolic blood pressure ≥90 mmHg, or the self-reported use of antihypertensive medication were all considered indicative of hypertension.

Blood samples were collected through venipuncture, centrifuged at the study sites, and transported at temperatures below 4˚C to the PINT laboratory. Fasting blood samples were used to measure insulin, glucose, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), and C-reactive protein (CRP) using the Cobas 8000 (Roche, Switzerland), whereas the HbA1c was determined using the HLC-723 G8 high-performance liquid chromatography system (Tosoh Bioscience, Japan). These devices pass annual accuracy inspections that are conducted by the governmental regulatory departments.

Definitions of general obesity [20], hypertension [21], diabetes and prediabetes [22], dyslipidemia and metabolic syndrome [23], and elevated CRP levels [24] were adopted from previous studies and are detailed in S1 Table.

## Follow-up of study participants

We conducted follow-ups with the participants at 1- to 2-year intervals, for a maximum duration of 10 years. CHC staff used the participants' identification numbers to search for information on mortality and health outcomes in the electronic databases (*Phần mềm thống kê y tế* for mortality records, and *Phần mềm khám chữa bệnh BHYT* and *HIS.ONE* for health events). All mortality cases within the area are reported to the Commune People's Committee and documented in the system and in a death register, referred to as "*A6*," at the commune health center. The medical database included records of insured individuals treated at core hospitals in the area. CHC staff members collected data on diagnosed health events from the medical database (e.g., specific disease names and associated ICD codes) without considering specific case definitions, and detailed information on these is presented in Table 3. Subsequently, researchers at the PINT and NCGM extracted health events that matched our case definitions. For individuals without insurance or insurance numbers as well as those whose information was not available in the database, we also conducted telephonic surveys. Household visits were conducted to verify specific documents, such as medical certificates for individuals who self-reported severe health outcomes but lacked the corresponding information in the database. Information on the causes of death and severe health outcomes was coded according to the International Classification of Diseases, 10th Edition (ICD-10), and recorded in a study-specific registry.

We verified the participants' residence in the commune by checking the database, conducting telephonic interviews, and conducting household visits. Additionally, CHC staff, who reside in close-knit communes, were familiar with the participants' addresses. If a participant relocated during the follow-up period, the date of relocation that was determined based on information from knowledgeable individuals was used as the cutoff date. If the date of relocation was unknown, the last follow-up date was used to censor individuals.

## Second survey (KHCS II)

In addition to the follow-up disease registry, a second health survey has been planned for 2023/2024 with the same participants to collect information on anthropometry, biochemical

**Table 3. Definitions of severe health outcomes in the Khánh Hòa cardiovascular study, Vietnam (2019–2030).**

| Health outcomes | Specific diseases listed in the International Classification of Diseases 10th revision (ICD-10) |
|---|---|
| Mortality | N/A |
| Cardiovascular diseases | • Ischemic heart diseases except angina pectoris (I21–I25)<br>• Cardiac arrest (I46)<br>• Atrial fibrillation and heart failure (I48–I50)<br>• Cerebrovascular diseases (I60–I69)<br>• Aortic aneurysm and dissection, and other aneurysms (I71–I72) |
| Neoplasm | • All cancers (malignant neoplasm: C00–C96)[a]<br>• In situ neoplasm / Benign neoplasms / Neoplasms of uncertain or unknown behavior (D00–D48) |

ICD: International Classification of Disease.

[a]Information on the other forms of neoplasms (D00–D48) were considered.

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measurements, and questionnaires. This follow-up study would allow us to identify the incidence of minor diseases that cannot be comprehensively calculated using data extracted from the disease registry (e.g., hypertension, diabetes, and depressive symptoms).

## Results

### Baseline information about the cohort

Information collected from the baseline survey is presented in Table 4. Female participants accounted for 61.3% of the cohort. The mean age (standard deviation [SD]) was 49.9 [5.5] years, and was similar among the sexes (men: 50.2 [SD 5.5] years; women: 49.7 [SD 5.5] years). Almost 90% of the participants were married, and approximately 60% of the participants had attained at least a junior high school education (equivalent to 9 years of formal education), with a higher proportion of those among men (68.5%) than women (53.9%). The proportion of farmers/fishers was higher among men (40.5%) compared with women (21.7%). Approximately four-fifths of the participants were insured (78.3%).

We found that 20.5% of all participants were current smokers, although the majority were men, which indicated a higher smoking prevalence in men (52.2%) than in women (0.4%). Similarly, men reported drinking alcohol more than women (72.1% vs. 2.7%). The median daily cooked rice consumption was 840 g (interquartile range [IQR] = 630–1260 g), with higher consumption among men (median = 1260 g) than in women (median = 630 g). Most participants did not drink coffee or green tea.

The mean [SD] of BMI was 23.2 kg/m$^2$ [3.0] and the corresponding WHtR was 0.520 [0.054]. The prevalence of hypertension was 39.6% in the study cohort, with a higher prevalence in men (48.1%) than in women (34.3%). Approximately 10% of the participants had diabetes while the corresponding figure for prediabetes was 46.7%. Dyslipidemia was observed in nearly half of the participants (45.1%). After excluding those with CRP ≥10 mg/L, who were judged to have acute inflammation (n = 58), 13.0% of the participants had elevated CRP (≥3 mg/L) levels.

### Analyses using the baseline information

Using the baseline data, we examined the following associations: parental absence during childhood with depressive symptoms [25], metabolic syndrome [26], and body weight categories (i.e., excess body weight and underweight) [27]; social capital with depressive symptoms [28]; meat consumption with diabetes [29]; tea consumption with diabetes [30]; eating speed with abdominal obesity [31]; physical activity with hypertension [32]; and socioeconomic status with antihypertensive medication among those with hypertension [33].

### Disease registry

As of March 2023, 21 participants were recorded in our study-specific registry as deceased, including 5 CVD-related and 12 cancer-related deaths. Furthermore, we registered 22 and 31 cases of nonfatal CVD and cancer events, respectively. Six participants left the study area and were lost to followup. Table 5 presents a comprehensive list of the health events registered in our study.

## Discussion

In this article, we describe the data collected in the baseline survey of the KHCS–a prospective cohort study aimed at exploring CVD determinants in the Vietnamese context. We discovered that our study participants were highly burdened with cardiometabolic risk factors, which

**Table 4. Summary of selected variables collected in the baseline survey of the Khánh Hòa cardiovascular study, Vietnam (2019–2020), shown by sex.**

| Variables | | All participants (n = 3000) | Male (n = 1160) | Female (n = 1840) |
|---|---|---|---|---|
| **Sociodemographic** | | | | |
| Age | in years, mean [SD] | 49.9 [5.5] | 50.2 [5.5] | 49.7[5.5] |
| Marital status | Currently married, n (%) | 2691 (89.7) | 1114 (96.0) | 1577 (85.7) |
| Education | Secondary school or higher, n (%) | 1785 (59.5) | 794 (68.4) | 991 (53.9) |
| Occupation | Farmer/fisherman, n (%) | 870 (29.0) | 470 (40.5) | 400 (21.7) |
| Household income | in 10,000 VND, median (IQR)[a] | 422.1 (264.6–577.4) | 447.2 (288.7–626.1) | 404.1 (250–577.4) |
| **Lifestyle-related** | | | | |
| Smoking status | Current smokers, n (%) | 614 (20.5) | 606 (52.2) | 8 (0.4) |
| Alcohol | Current drinkers, n (%) | 886 (29.5) | 836 (72.1) | 50 (2.7) |
| Physical activity | Total METs·min/week, median (IQR) | 8400 (3980–13440) | 9600 (5040–13440) | 7840 (3360–13200) |
| Sleeping hours | <7 hours, n (%)[b] | 657 (21.9) | 197 (17.0) | 460 (25.0) |
| Rice consumption | g, median (IQR) | 840 (630–1260) | 1260 (840–1260) | 630 (420–840) |
| Noodle | g, median (IQR) | 81.4 (27.1–135.7) | 81.4 (54.3–135.7) | 81.4 (27.1–135.7) |
| Bread | Pieces, median (IQR) | 0 (0–2) | 0 (0–2) | 1 (0–2) |
| Meat consumption | g, median (IQR) | 82.9 (42.9–142.9) | 108.6 (57.1–194.3) | 68.6 (35.7–117.1) |
| Vegetable | Servings, median (IQR)[c] | 1 (1–2) | 1 (1–2) | 1 (1–2) |
| Fruit | Servings, median (IQR)[c] | 0.5 (0.21–1.00) | 0.43 (0.14–1.00) | 0.5 (0.29–1.00) |
| Sweetened beverage | Cans, median (IQR) | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) | 0.0 (0.0–0.0) |
| Coffee | Cups, median (IQR)[d] | 0.0 (0.0–0.86) | 0.43 (0.0–1.0) | 0.0 (0.0–0.3) |
| Green tea | Cups, median (IQR)[e] | 0.0 (0.0–0.14) | 0.0 (0.0–3.0) | 0.0 (0.0–0.0) |
| **Social environment** | | | | |
| Social capital | Social participation, n (%) | 1125 (37.5) | 405 (34.9) | 720 (39.1) |
| Childhood SES | Low SES at age 15, n (%) | 1947 (64.9) | 738 (63.6) | 1209 (65.7) |
| Parental absence | Parental absence before age 15, n (%) | 636 (21.2) | 235 (20.3) | 401 (21.8) |
| **Health-related** | | | | |
| Body mass index | Mean [SD] | 23.2 [3.0] | 22.9 [3.1] | 23.4 [2.9] |
| Waist-to-height ratio | Mean [SD] | 0.520 [0.054] | 0.510 [0.053] | 0.526 [0.053] |
| Excess body weight | BMI ≥25.0 kg/m², n (%) | 778 (25.9) | 285 (24.6) | 493 (26.8) |
| Hypertension | n (%) | 1189 (39.6) | 558 (48.1) | 631 (34.3) |
| Systolic blood pressure | Mean [SD] | 130.9 [19.1] | 133.8 [19.3] | 129.1 [18.7] |
| Diastolic blood pressure | Mean [SD] | 83.9 [12.1] | 87.4 [12.5] | 81.7 [11.4] |
| Diabetes | n (%) | 307 (10.2) | 122 (10.5) | 185 (10.1) |
| Prediabetes | n (%) | 1401 (46.7) | 565 (48.7) | 836 (45.4) |
| Fasting plasma glucose | Mean [SD] | 99.9 [26.7] | 101.4 [26.0] | 99.0 [27.1] |
| HbA1c | Mean [SD] | 5.8 [1.0] | 5.8 [0.9] | 5.8 [1.0] |
| Dyslipidemia | n (%) | 1352 (45.1) | 592 (51.0) | 760 (41.3) |
| Total cholesterol | Mean [SD] | 198.7 [40.3] | 194.4 [40.1] | 201.5 [40.1] |
| Triglycerides | Mean [SD] | 174.0 [133.7] | 212.5 [176.9] | 149.8 [88.8] |
| Low-density lipoprotein cholesterol | Mean [SD] | 126.2 [35.9] | 116.9 [34.6] | 132.0 [35.4] |
| High-density lipoprotein cholesterol | Mean [SD] | 51.4 [12.9] | 49.8 [14.2] | 52.3 [11.9] |
| Metabolic syndrome | n (%) | 1151 (38.4) | 424 (36.6) | 727 (39.5) |
| Subclinical inflammation | C-reactive protein 3.0–9.9 mg/L, n (%)[6] | 381 (13.0) | 130 (11.5) | 251 (13.9) |

(*Continued*)

**Table 4.** (Continued)

| Variables | | All participants (n = 3000) | Male (n = 1160) | Female (n = 1840) |
|---|---|---|---|---|
| C-reactive protein | Mean [SD] | 1.6 [1.5] | 1.5 [1.5] | 1.6 [1.6] |

BMI, body mass index; IQR, interquartile range; MET, metabolic equivalents; SD, standard deviation; VND: Vietnamese Dong.

[a]Household income was estimated based on the responses from a participant who represented the given household. This information was available for 2967 individuals.

[b]The sum of nighttime sleep and naps. The information was available for 2999 individuals (1159 men and 1840 women).

[c]Results are shown in terms of one serving shown in a show card (125 mL or 1/2 cup).

[d]Results are shown in terms of one serving depicted in a show card (40 mL)

[e]Results are shown in terms of one serving depicted in a show card (65 mL).

[f]Participants with CRP ≥10 mg/L, defined as acute inflammation, and were excluded; thus, 2942 participants (1130 men and 1812 women) were included.

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conferred a high risk for CVD or other major NCDs. The majority of those who smoked and consumed alcohol were men, whereas these unhealthy behaviors were uncommon among women, which should be considered in subsequent research.

The WHO STEP survey [34], which was conducted among individuals aged 18–69 years in all 63 provinces and cities of Vietnam, reported a similar prevalence of hypertension and excess body weight as in our study. Although the age categories used in the report to summarize the findings do not match the age group of the present study cohort, when we used the publicly available STEP Survey data for comparison and calculated the prevalence for the same age category (i.e., 40–60 years), the prevalences of hypertension were 35.6% and 25.0% and of excess body weight (BMI ≥25 kg/m$^2$) were 17.2% and 23.9% among men and women,

**Table 5. Fatal and non-fatal health events registered in the Khánh Hòa cardiovascular study as of March 2023.**

| Health events | ICD-10 code | Specific diseases | Fatal cases, n | Non-fatal cases, n |
|---|---|---|---|---|
| CVD | I21–I25 | Ischemic heart diseases except angina pectoris | 1 | 9 |
| | I46 | Cardiac arrest | 0 | 0 |
| | I48–I50 | Atrial fibrillation and heart failure | 0 | 2 |
| | I60–I69 | Cerebrovascular diseases | 4 | 11 |
| | I71–I72 | Aortic aneurysm and dissection and other aneurysms | 0 | 0 |
| | - | Subtotal | 5 | 22 |
| Neoplasm | C00–C14 | Malignant neoplasms of lip, oral cavity and pharynx | 0 | 1 |
| | C15–C26 | Malignant neoplasms of digestive organs | 7 | 9 |
| | C30–C39 | Malignant neoplasms of respiratory and intrathoracic organs | 2 | 3 |
| | C45–C49 | Malignant neoplasms of mesothelial and soft tissue | 1 | 1 |
| | C50 | Malignant neoplasm of breast | 1 | 7 |
| | C51–C58 | Malignant neoplasms of female genital organs | 0 | 1 |
| | C69–C72 | Malignant neoplasms of eye, brain and other parts of central nervous system | 0 | 1 |
| | C73–C75 | Malignant neoplasms of thyroid and other endocrine glands | 0 | 6 |
| | C81–C96 | Malignant neoplasms, stated or presumed to be primary, of lymphoid, haematopoietic and related tissue | 1 | 2 |
| | D00–D48 | In situ neoplasm / Benign neoplasms / Neoplasms of uncertain or unknown behaviour | 1 | 7 |
| | - | Subtotal | 13 | 38 |
| Other causes | A41 | Sepsis | 1 | - |
| | - | Unknown | 2 | - |
| - | - | Total | 21 | 61 |

CVD: Cardiovascular diseases; ICD-10: International Classification of Diseases 10th Revision.

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respectively. Although these values were lower than those reported in our survey, these comparative results suggest that our study population and the general population in Vietnam have a high cardiovascular risk (S2 Table). Thus, the evidence from this study group could potentially contribute to improved public health initiatives in Vietnam.

Furthermore, our baseline results also suggest that there are also several concerning aspects as regards health-related lifestyle habits, particularly among men. For example, the prevalence of smoking among males was particularly high, with the prevalence of smoking being 52.2%, which was equivalent to the figure reported in a study using the STEP survey questionnaire in Vietnam [35]. Given that smoking has health effects [36,37], the high smoking rate in Vietnam suggests the possibility of various health problems arising from both active and secondhand smoke. Quitting smoking can reduce the risk of several health outcomes [38–40], and thus, necessary measures should be taken. In addition, the prevalence of current alcohol drinkers among men was high (72.1%), which warrants attention because the evidence has increasingly shown a lack of support for a beneficial health effect of low- to moderate-alcohol consumption [41,42].

Using cross-sectional data collected from the baseline survey, we have identified similarities and differences in the determinants of health between Vietnam and countries where prior studies have been conducted. Our finding that meat consumption is positively associated with diabetes [43,44] and that individuals with higher social capital exhibit fewer depressive symptoms [45,46] are consistent with previously reported results. However, the positive association found between green tea consumption and diabetes observed in our dataset [30] differed from previous studies that reported inverse associations [47,48]. Regarding physical activity and hypertension, our study reported an inverse association with occupational physical activity but not with leisure-time physical activity, which has often been linked with a reduction in hypertension risk in previous studies [49,50]. Additionally, when we examined the association with parental absence, we found a significant association with low body weight but not with metabolic syndrome, although adverse childhood experiences in general have been suggested to result in metabolic abnormalities [51]. These findings suggest the need for epidemiological research that accounts for possible differences in the effects of health determinants.

Currently, we do not have a sufficient number of negative health events for the survival analysis. Therefore, we plan to conduct a longitudinal survival analysis after a maximum follow-up period of 10 years. Moreover, we are scheduling the second round of the KHCS survey inviting the same individuals in 2023 and 2024. During this, we intend to collect blood samples and questionnaire data again. As the disease registration system is unsuitable for capturing the onset of less severe health conditions (e.g., diabetes, hypertension, and depressive symptoms) in locations with limited access to medical services, we plan to define the onset of these conditions using data collected in the second wave of the study. Additionally, the research topics examined earlier using cross-sectional data will be re-evaluated longitudinally. Accordingly, we aim to produce high-quality epidemiological evidence that reflects the Vietnamese context.

This study has several strengths, including its focus on a rural population in a low-to-middle-income country, which enhances its contribution to epidemiological research by providing valuable insights into health outcomes in underrepresented and underserved communities. However, this study also has several limitations. First, as participants of this study were not selected via a random sampling procedure and did not fully represent the general Vietnamese population, or even inhabitants of the Khánh Hòa Province, caution should be exercised when generalizing the findings to other populations. Heterogeneity in the characteristics across the study communes may exist, which should be accounted for when conducting analyses. For example, using multilevel models can help accommodate variations within and between communes. Second, this study was observational in nature, and exposures were not randomly

assigned; factors determining exposures might influence health outcomes (i.e., unmeasured confounding). Third, some exposure information was self-reported, which introduced the possibility of recall and social desirability biases. Fourth, although we used a validated questionnaire to measure physical activity, the estimates were deemed quite high, which might have resulted from exaggerated responses. A similar limitation was reported in a previous study that examined the reliability of the GPAQ in Vietnam, which highlighted that estimates from Vietnam were particularly exaggerated among those who lived in rural areas [52]. Fifth, the results of the cross-sectional analysis cannot deny the possibility of reverse causation; therefore, caution is required when interpreting the findings. Future longitudinal studies should address these limitations. Sixth, although the disease registry system combines not only local medical databases but also telephonic confirmation with individuals, family members, and household visits to ensure that no case was missed, we cannot rule out the possibility that the capture rate might be lower than expected in HICs.

## Conclusions

The KHCS is a prospective cohort study among 3000 rural residents in Khánh Hòa Province, Vietnam. We conducted a baseline survey to collect information on anthropometry, biochemical measurements, lifestyle parameters, and social determinants of health. With the outcome information collected in the disease registry and the second health survey (KHCS II), this study group will produce robust evidence that would facilitate the effort to combat the CVD- and NCD-associated disease burden in Vietnam.

## Supporting information

**S1 Table. Specific criteria used to define health outcomes in the Khánh Hòa cardiovascular study, Vietnam.**
(DOCX)

**S2 Table. Prevalence of selected health-related outcomes ascertained from the STEP survey data.**
(DOCX)

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