Study Protocol

CARDIAC RESEARCH

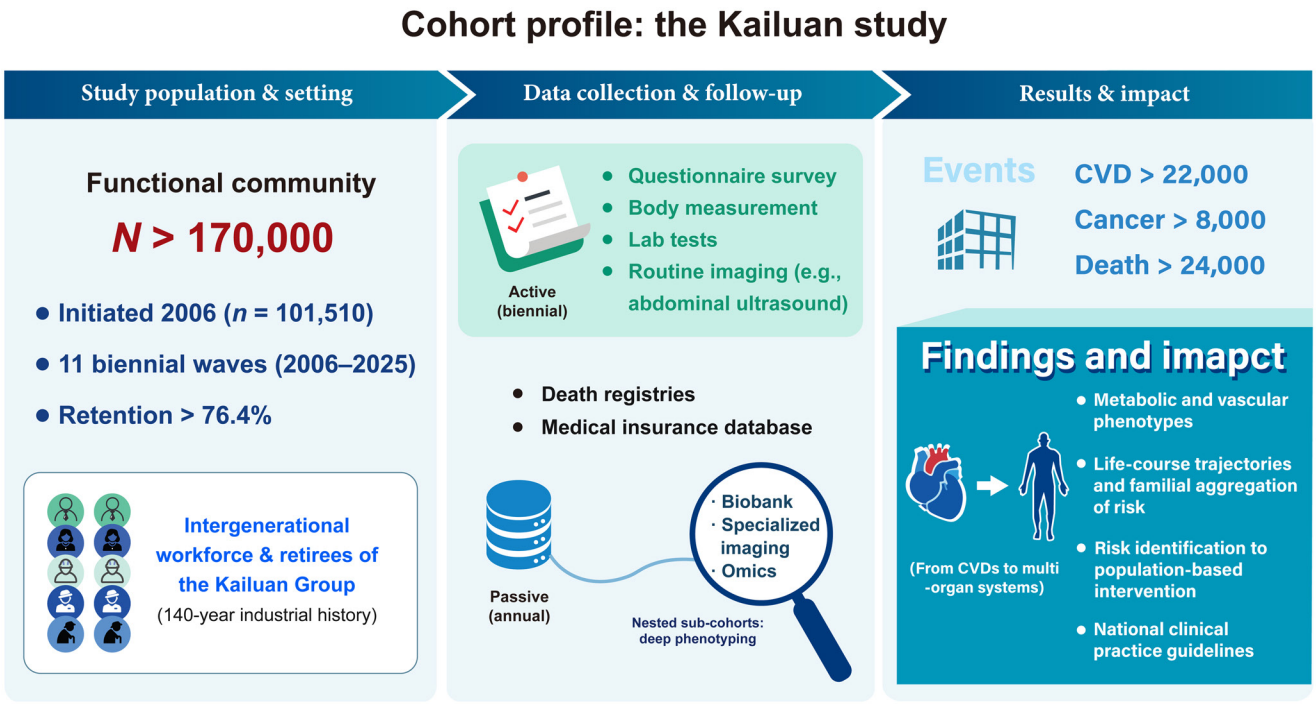
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# Cohort profile

## The Kailuan study

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### Graphical abstract




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**Abstract**

**Purpose:** The Kailuan study was established to investigate the life-course natural history of noncommunicable diseases, identify key risk factors and biomarkers, and elucidate the underlying pathological pathways. Ultimately, this study aims to provide a real-world evidence platform for evaluating health interventions and tailored health management.

**Participants:** Initiated in 2006 in Tangshan, China, this prospective dynamic cohort is embedded within the Kailuan Group, a large industrial functional community with an integrated healthcare system. At baseline, 101,510 adults (aged 18–98 years) were enrolled, and biennial rolling recruitment expanded the cohort to over 170,000 participants. Follow-up is conducted by linking biennial standardized health examinations with annual medical insurance databases and death registries.

**Findings to date:** As of December 2023, the study has captured over 22,000 cardiovascular events, 8,000 cancers, and 24,000 deaths. Research has shifted from cardiovascular to multisystemic diseases, identifying longitudinal risk trajectories, the temporal ordering of metabolic dysfunction, and the life-course impact of early-life and occupational exposures. Furthermore, the embedded healthcare setting of the cohort supports the evaluation of real-world prevention and management strategies.

**Future plans:** Ongoing follow-up will integrate multiomics, advanced imaging, and digital phenotyping to support life-course and multimorbidity research. Using artificial intelligence-driven approaches and causal inference frameworks, this study will develop integrated health models for whole-life-cycle-based management and disease control.

**Registration:** The cohort was registered in the Chinese Clinical Trial Registry (ChiCTR-TNRC-11001489 and ChiCTR2000029767).

**Key words:** cohort study, Kailuan study, life-course epidemiology, multimorbidity, noncommunicable diseases

## 1. Introduction

The global health landscape has shifted from a predominance of infectious diseases to noncommunicable diseases (NCDs), which now account for 91% of all deaths in China.[1] Driven by rapid population aging, urbanization, and evolving lifestyle patterns, China's NCD burden is characterized by its high prevalence, significant disability, and emergence of "multimorbidity".[2] In response to this global health imperative, numerous large-scale population-based cohort studies have been conducted since the mid-20th century. These studies, characterized by long-term follow-up, are designed to identify the etiological and associated risk factors for NCDs, generating evidence crucial for prevention, early detection, and effective management. Landmark examples of these efforts include the Framingham Heart Study[3] and the UK Biobank.[4]

In the early 21st century, China established several large-scale population-based studies, including the China Kadoorie Biobank Study[5] and the China Multicenter Collaborative Study of Cardiovascular Epidemiology,[6] among others. These initiatives have provided critical insights into the complex interplay between genetic, environmental, and lifestyle factors in the development of chronic diseases in the Chinese population. For instance, the China-PAR (Prediction for Atherosclerotic Cardiovascular Disease Risk in China) was developed and is widely used to identify high-risk populations for atherosclerotic cardiovascular disease (CVD).[6] However, such traditional risk models predominantly rely on static baseline variables, potentially limiting their precision in identifying individuals with complex metabolic dysregulations.[7] NCDs are systemic disorders driven by chronic, dynamic, cross-organ signaling.[8] The complexity of these dynamic biological processes necessitates the use of high-quality, long-term prospective cohorts, which the Kailuan study was explicitly designed to include.

Initiated in 2006, the Kailuan study is a prospective longitudinal platform integrated within the "functional community" of the Kailuan Group in Tangshan, China. With over 170,000 participants and systematic follow-up, the study integrates longitudinal data from multiple sources, including (1) biennial questionnaires, physical examinations, and laboratory tests; (2) comprehensive clinical and medical insurance records for the ascertainment of endpoints including CVD, cancers, and mortality; (3) a "secondary reimbursement" registry that captures clinical records for care sought outside the Kailuan network; and (4) unique contextual information, including longitudinal occupational histories and historical exposures such as the 1976 Tangshan Earthquake and the Great Chinese Famine.

This integrated foundation has facilitated a series of nested subcohort studies, including (1) a family-based cohort of over 10,000 parent-offspring pairs to unravel transgenerational and early-life determinants of chronic diseases; (2) advanced physiological phenotyping substudies that quantify system-level pathophysiology via vascular function (e.g., brachial-ankle pulse wave velocity [baPWV])[9] and multimodality medical imaging; and (3) pharmaco-epidemiological studies integrated with medical insurance data to evaluate the real-world effectiveness of pharmaceutical interventions.[10]

By synthesizing these multisystemic and multimodal data, the Kailuan study was designed to identify the key

risk factors and core biomarkers of NCDs and to characterize their dynamic trajectories over the life course. This platform facilitates nested subcohort studies that clarify the underlying pathological pathways and multiorgan interactions. Furthermore, by integrating long-term follow-up with a stable healthcare system, the Kailuan study provides a foundation for evaluating population-level prevention and health management strategies using a quasi-experimental and real-world study design.

Here, we summarize the cohort profile of the Kailuan study, detailing its description, findings to date, and future expectations as a cornerstone of health management.

## 2. Cohort description

### 2.1. Study design and setting

The primary objective of the Kailuan study was to characterize the life-course natural history of NCDs and identify their risk factors. Initially, in 2006, this ongoing prospective dynamic cohort study was established in Tangshan, Hebei Province, Northern China. The study employed a rolling enrollment design, recruiting employees (including active workers and retirees) of the Kailuan (Group) Co., Ltd. during their biennial standardized health examinations. The Kailuan Group, with a history spanning over 140 years, encompasses diverse industries, ranging from coal production and chemical industries to modern logistics and financial services, which are supported by a comprehensive healthcare network of 11 integrated hospitals. This infrastructure ensures a sustainable population base and provides a rich historical context for long-term observations. Furthermore, the study allows for the nested evaluation of clinical and public health interventions in a real-world setting.

This study was approved by the Ethics Committee of the Kailuan General Hospital in 2006 (No. 2006-5) and 2008 (No. 2008-1), which is responsible for ethical issues in scientific research across the 11 Kailuan Group-affiliated hospitals. All research procedures were conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants at baseline and during follow-up.

This long-term longitudinal project was documented through sequential registrations in the Chinese Clinical Trial Registry. The initial baseline cycle (2006–2007) was registered as an observational cohort (ChiCTR-TNRC-11001489). In response to the study's dynamic rolling enrollment and the broadened objectives of evaluating health education strategies in real-world settings, a subsequent registration was established for the expansion phase (Kailuan II, 2008 onwards; ChiCTR2000029767). Furthermore, the primary outcome, originally limited to cardiovascular and cerebrovascular diseases, was extended to include other NCDs. This dual registration indicates the study's evolution into a comprehensive platform for etiological research and health evaluations.

### 2.2. Study participants

Baseline enrollment was conducted between 2006 and 2007. The target population comprised all 153,901 registered employees of the Kailuan Group. All employees were invited to undergo free and comprehensive health examinations at 11 affiliated hospitals. The inclusion criteria were as follows: (1) age ≥ 18 years, (2) provision of written informed consent, and (3) completion of a face-to-face questionnaire interview regarding demographics and lifestyle. Of the eligible population, 52,391 individuals did not participate due to refusal, absence during the examination window, or critical illness. Consequently, 101,510 participants (81,005 men and 20,505 women) completed the survey, yielding a response rate of 66.0%.

Utilizing a dynamic cohort design, this study implemented a rolling recruitment strategy in subsequent biennial waves. Employees who missed the baseline survey or newly hired employees became eligible for enrollment. This strategy significantly expanded the cohort size, with 71,348 participants recruited across seven additional waves between 2008 and 2022. This sample size ensures the statistical power necessary to investigate the etiological determinants of NCDs. The detailed enrollment figures for each wave are presented in Table 1.

### 2.3. Follow-up and attrition

Participant follow-up employed a combination of active and passive methods. Active follow-up was conducted biennially, consisting of standardized questionnaires, physical examinations, and laboratory assessments administered by trained physicians or nurses. To date, the Kailuan study has completed nine waves of health checkups (2006–2025), with data cleaning for the ninth wave currently ongoing and the 10th wave initiated in 2025. Passive follow-up was performed annually via data linkage with local vital statistics registries, the Tangshan Medical Insurance System, and the Kailuan Group Medical Insurance Information System, ensuring coverage of all study participants.

Retention rates remained robust owing to the stability of the functional community. As of 2020–2022, the cumulative loss to follow-up for the initial 2006–2007 subcohort was 5.7%. The primary reasons for attrition included mortality and loss of contact due to termination of employment, with a cumulative retention rate of 76.4%. The detailed participant flow, including the number of invitees, participants, and retention rates for each wave, is shown in Table 1.

### 2.4. Measurements

Data collection at baseline and subsequent follow-ups included comprehensive questionnaires, physical examinations, laboratory tests, and imaging assessments. A detailed summary of the variables collected at each wave is provided in Table 2.

**Table 1**

**Participants' involvement and retention across eight waves of the Kailuan study.**

| Enrollment cycle | Invitees (a) | Actual enrollees (b) | Response rate (c, %) | New enrollees (d) | Cumulative withdrawal (e, %) | Cumulative deceased (g, %) | Retention from baseline (f, %) |
|---|---|---|---|---|---|---|---|
| 2006–2007 | 153,901 | 101,510 | 66.0 | 101,510 | 1438 (5.7) | 18,199 (17.9) | 81,873 (76.4) |
| 2008–2009 | 146,919 | 101,133 | 68.8 | 25,337 | 555 (5.3) | 2251 (8.9) | 22,531 (85.8) |
| 2010–2011 | 147,537 | 92,967 | 63.0 | 10,519 | 704 (4.1) | 929 (8.8) | 8886 (87.1) |
| 2012–2013 | 152,558 | 109,018 | 71.5 | 17,120 | 843 (10.0) | 696 (4.1) | 15,581 (85.9) |
| 2014–2015 | 149,698 | 99,939 | 66.8 | 8466 | 612 (17.2) | 239 (2.8) | 7615 (80.0) |
| 2016–2017 | 145,855 | 89,759 | 61.5 | 3566 | 164 (3.6) | 100 (2.8) | 3302 (93.6) |
| 2018–2019 | 142,016 | 80,413 | 56.6 | 4606 | 194 (11.2) | 29 (0.6) | 4383 (88.2) |
| 2020–2022 | 140,611 | 67,203 | 47.8 | 1734 | -* | - | - |

Percentages for withdrawal, death, and retention are calculated using new enrollees (d) as the denominator for each row, ensuring that each enrollment cycle is tracked as an independent subcohort. Invitees (a): Total number of eligible individuals invited for clinical examination during each cycle. Actual Enrollees (b): The total number of participants who completed the examination in that cycle, consisting of both returning participants and new recruits. Response rate (c, %): Actual Enrollees (b)/Invitees (a) × 100%. New enrollees (d): Participants recruited into the cohort for the first time during a specific cycle. Cumulative withdrawal (e, %): Number and percentage of participants lost to follow-up primarily by termination of employment, which precludes passive follow-up through company records. Retention (f, %): Number and percentage of the original enrollment cycle (d) still active in the study.

*While the follow-up data for the 8th cycle (2020–2022) have been completed, the final processing of cumulative withdrawal and mortality proportions for this period is currently in progress. Furthermore, data cleaning for the ninth cycle (2023–2025) is underway, and the tenth wave of follow-up, initiated in 2025, is presently ongoing.

**Table 2**

**Summary of measurements in the Kailuan Cohort.**

| Measurements | Variables |
|---|---|
| Questionnaire | |
| Demographic characteristics | ID, age, sex, date of birth, ethnicity, current marital status, educational level, household income. |
| Occupation and working conditions | Type of work, exposure to dust and other chemicals. |
| Lifestyle habits | Frequency and average quantity for smoking, alcohol intake, physical activity, sedentary behavior, and tea consumption. |
| Personal and family health history | Hypertension, diabetes, hyperlipidemia, myocardial infarction, stroke, malignant tumor, infection, and other diseases. |
| Medical drugs and adherence behaviors | Use of antihypertensive drugs, hypoglycemic drugs, lipid-lowering drugs, antiplatelet agents, and anticoagulants, including drug name, type, start and end dates, dosage, and other relevant information. |
| Sleep-related events | Insomnia, daytime sleepiness, snoring, and sleeping duration. |
| Dietary habits* | Self-reported semiquantitative FFQ with 33 food items and 7 condiments, covering staples, vegetables, meats, fruits, beverages, alcohol, and seasonings. |
| Life events* | Tangshan earthquake and trauma exposure survey. |
| Parental and offspring survey* | Diseases and health exposures of parents and offspring. |
| Women's pregnancy and fertility survey* | Pregnancy and childbirth-related information, including gestational age, pregnancy-related diseases, delivery date, menstrual history, obstetric history, etc. |
| Cognitive function survey* | Cognitive function and other brain health estimation |
| Physical examination | |
| Anthropometric measurements | Weight, height, waist circumference, hip circumference, neck circumference*. |
| Physiological measurements | Blood pressure, heart rate, and electrocardiography (including a 24-h dynamic electrocardiogram for specialized population), brachial-ankle pulse wave velocity*. |
| Laboratory tests | |
| Blood test | Complete blood count (red blood cell count, hemoglobin, white blood cell count, neutrophil count, lymphocyte count, platelet count, etc.), fasting blood glucose, serum lipid panel (total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol), hepatic function (albumin, globulin, total bilirubin, direct bilirubin, alanine transaminase, and gamma-glutamyl transferase*, etc.), kidney function (uric acid, urea, serum creatinine, etc.), high-sensitivity C-reactive protein, and biomarkers of hepatitis virus infection. Serum electrolytes ($Na^+$, $K^+$) |
| Urinalysis | Proteinuria, urine specific gravity, and urinary creatinine*, and urine pH* |
| Blood metals* | Calcium, copper, iron, magnesium, manganese, selenium, and zinc. |
| Gut microbiota* | |
| Imaging | Abdominal ultrasound, chest X-ray, carotid artery ultrasound, brain computed tomography scans*, magnetic resonance imaging*, and ocular fundus photography (Visual acuity, tonometry, slit lamp-assisted biomicroscope)* |
| Outcomes | Incident cardiovascular vascular disease (myocardial infarction, atrial fibrillation, percutaneous coronary intervention, and coronary artery bypass grafting, ischemic stroke, hemorrhagic stroke), cancer, and death |

*For specialized survey only.

### 2.5. Questionnaire survey

Face-to-face interviews were conducted with the participants. The core data included sociodemographic characteristics, occupational and working conditions, lifestyle habits, personal and family health statuses, medical drug use and related behaviors, and sleep characteristics. In specific waves, supplementary modules were administered to capture additional data on dietary habits, significant life events, parental and offspring surveys, and reproductive surveys (Table 2).

### 2.6. Physical examination

Anthropometric and clinical measurements were performed following standardized operating procedures (Table 2). Essential physical examinations included measurements of body weight, height, waist circumference, hip circumference, blood pressure (BP), and electrocardiography. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, with the participants wearing light clothing and no shoes. Waist circumference was measured at the midpoint between the lower rib margins and the iliac crest. BP was assessed using a calibrated mercury sphygmomanometer or a validated electronic device on the left arm after the participant had rested in a seated position for at least 5 min. Three readings were taken at 1-min intervals, and the average was recorded. A standard 12-lead electrocardiogram was recorded for all participants in each wave to detect arrhythmias and ischemic changes.

### 2.7. Laboratory tests

Fasting venous blood samples (8–10 h fasting) and midstream urine samples were collected at each wave. Measurements included complete blood count, fasting blood glucose, serum lipid profile, liver function tests, and hepatitis virus infection biomarker detection. Urine samples were used for standard urinalysis and protein electrophoresis. All laboratory analyses were conducted using commercially available reagents approved for clinical use and performed in accordance with the national standards for laboratory testing and quality control. Standardized operating procedures, calibrated instruments, and routine internal quality control were consistently applied, together with regular participation in external quality assessment programs to ensure the accuracy, consistency, and comparability of biochemical measurements across survey waves. Additionally, several specialized examinations, such as blood metal levels, were conducted within specific nested substudies.[11] Details are shown in Table 2.

### 2.8. Imaging examination

Abdominal ultrasound (assessing the liver, gall bladder, spleen, pancreas, and kidneys) was performed on all participants. Subsets of the cohort underwent specialized imaging, including carotid artery ultrasound, chest radiography, BaPWV, brain magnetic resonance imaging (MRI), and ocular fundus photography. Specifically, BaPWV measurements were implemented starting with the 2010 survey to evaluate arterial wall stiffness and vascular health,[12] with over 36,000 individuals to date. Within the multimodality medical imaging substudy, participants underwent serial imaging assessments every 2–4 years, including brain MRI, retinal fundus photography, fundus optical coherence tomography, and ultrasonography of the internal carotid artery.[13] Depending on the modality, the sample sizes ranged from 3,000 (brain MRI) to 23,600 (carotid ultrasonography). These participants were recruited primarily based on their availability and participation in the longitudinal follow-up waves at 11 integrated hospitals. Ophthalmological examinations (involving over 1,000 participants), including visual acuity, tonometry, slit lamp-assisted biomicroscopy of the anterior segment of the eye, and optical low-coherence reflectometry, were further detailed in the Kailuan Diabetic Retinopathy Study.[14]

### 2.9. Outcome ascertainment

The primary outcomes, initially limited to CVD, have been expanded to other NCDs (ChiCTR2000029767), including cancer and all-cause mortality. Through December 2023, outcome events were ascertained using three complementary sources: the hospital discharge register, the municipal and corporate medical insurance system, and biennial face-to-face interviews. CVD events included myocardial infarction, atrial fibrillation, heart failure, coronary revascularization procedures (percutaneous coronary intervention or coronary artery bypass grafting), ischemic stroke, and hemorrhagic stroke.

Outcomes were defined according to the standard diagnostic criteria. Myocardial infarction was determined using the World Health Organization's Multinational Monitoring of Trends and Determinants in CVD criteria.[15] Heart failure diagnosis followed the European Society of Cardiology guidelines and was confirmed by cardiologists.[16] Stroke was diagnosed according to the World Health Organization criteria and confirmed by neuroimaging tests.[17] Cancer diagnosis was primarily based on pathological and MRI findings, where available. Outcomes were coded using the International Classification of Diseases, 10th Revision (Appendix Table S1, Supplemental Digital Content, https://links.lww.com/CARES/A18). To ensure data quality, a panel of experienced clinical experts, including neurologists, cardiologists, oncologists, and imaging specialists, reviewed the medical records and verified all the diagnoses. Death data were linked annually to municipal death registration centers and the participants' local residential records. Additionally, the status of hypertension, diabetes, and chronic kidney disease was updated through biennial interviews and clinical examinations.

Biospecimens were collected during the follow-up surveys of selected subcohorts. For each subcohort study, independent ethical approval was obtained from the Ethics Committee of the Kailuan General Hospital, and all participants provided study-specific written informed consent that included explicit authorization for the long-term preservation of their samples. Fasting venous blood and midstream urine samples were obtained. All samples were processed within 4 h. Blood samples were processed and aliquoted into plasma, serum, and whole blood, and all specimens were stored at –80°C for long-term storage.

### 2.10. Quality control and data management

Quality control was implemented at all stages.[18] During the study design phase, questionnaires were developed by epidemiologists. Before data collection, all medical staff received standardized training in interviewing and physical examination protocols. During the data collection phase, uniform procedures were enforced across all survey sites to ensure accuracy and consistency. Identical instrument brands and models were used for the anthropometric and clinical assessments. Laboratory assays followed uniform operating protocols.

Data management utilized an Oracle Database system to ensure integrity throughout the data life cycle. For cancer outcomes, cases were recorded and verified using CanReg 4 software (International Agency for Research on Cancer). Data underwent logical checks for consistency and plausible value ranges to identify errors before being uploaded.

The original paper questionnaires were securely archived in the Department of Cardiology at the Kailuan General Hospital. Data security and participant confidentiality were maintained by the designated staff in compliance with institutional and national regulations. The electronic database was housed on air-gapped computers (physically isolated from the Internet) to prevent unauthorized access, with routine backups performed on encrypted external hard drives to ensure data preservation.

## 3. Findings to date

### 3.1. Cohort characteristics

The baseline characteristics of the study participants are presented in Table 3. The mean age across the different survey waves ranged from 51.3 to 55.4 years. The cohort was predominantly male (over 70%), reflecting the occupational nature of the coal mining and heavy industry sectors from which the population was recruited. During the follow-up period, an upward trend was observed in the prevalence of several cardiometabolic risk factors, specifically body mass index, diabetes, hypertension, dyslipidemia, and physical inactivity. The annual average incidence rates of CVD, cancer, and all-cause death were 1,027.02, 366.18, and 1,064.11 per 100,000 person-years (PYs), respectively (Table 4).

The Kailuan study evolved from a cardiovascular-focused observational cohort to a comprehensive platform for understanding the etiology of NCDs. The findings focused on the transition from subclinical markers to clinical events throughout the lifespan. By October 2025, the cohort contributed to over 1,000 scholarly publications addressing the etiology, progression, and prevention of NCDs.

### 3.2. Metabolic and vascular phenotypes

This study demonstrated that the metabolic systemic consequences extend beyond the traditional atherosclerotic pathophysiology. A landmark finding established obesity as an independent risk factor for cardiac conduction block, a discovery recognized as one of the top 10 cardiovascular advances in China in 2023. This association was particularly pronounced in older adults and those with preexisting diabetes, suggesting that obesity exacerbates the aging conduction system.[19]

Longitudinal analysis indicated that arterial stiffness acted as both a dynamic mediator and modifiable precursor in the cardiometabolic disease continuum. Evidence confirmed a temporal sequence in which elevated arterial stiffness preceded and predicted incident diabetes, establishing a unidirectional relationship between baseline baPWV and future glycemic levels.[12] This vascular progression was driven by the transition from a "metabolically healthy obese" to an "unhealthy obese" phenotype[20] and by increased insulin resistance.[21] Intensive BP control was found to result in significantly greater reductions in baPWV compared with standard therapy in older hypertensive patients.[22]

Research on metabolic dysfunction-associated steatotic liver disease (MASLD) found that MASLD increased the risk of extrahepatic malignancies, including thyroid, lung, and kidney cancers.[23] Furthermore, cohort data highlighted the "lean MASLD" paradox. Individuals with lean MASLD may face a higher risk of specific adverse outcomes than their overweight or obese counterparts.[24,25] Additionally, the study linked metabolic dysregulation to subclinical markers of accelerated brain aging, including neuroimaging signatures of cerebral small vessel disease, brain structure, and cognitive decline.[26–28]

### 3.3. Life-course trajectories and familial aggregation of risk

A life-course epidemiology framework was established to elucidate how health risks are programmed during sensitive developmental periods and accumulate in adulthood. Research demonstrated that fetal or childhood exposure to the Great Chinese Famine was associated with an increased risk of midlife intracerebral hemorrhage[29] and adult cancer.[30] Similarly, prenatal exposure to the 1976 Tangshan earthquake was linked to elevated serum uric acid levels in adulthood.[31]

**Table 3**

**Characteristics of participants in the Kailuan study.**

| Variables | 2006–2007 (*N* = 101,510) | 2008–2009 (*N* = 101,133) | 2010–2011 (*N* = 92,967) | 2012–2013 (*N* = 109,018) | 2014–2015 (*N* = 99,939) | 2016–2017 (*N* = 89,759) | 2018–2019 (*N* = 80,413) | 2020–2022 (*N* = 67,203) |
|---|---|---|---|---|---|---|---|---|
| Age, year | 51.3 ± 12.6 | 50.8 ± 12.9 | 51.3 ± 13.2 | 51.1 ± 13.9 | 51.4 ± 14.4 | 53.0 ± 14.1 | 53.2 ± 14.8 | 55.4 ± 14.1 |
| Men | 81,005 (79.8) | 79,187 (78.3) | 72,514 (78.0) | 85,909 (78.8) | 79,222 (79.3) | 70,575 (78.6) | 61,974 (77.1) | 52,787 (78.5) |
| Smoking | 40,909 (40.3) | 44,498 (44.0) | 36,071 (38.8) | 36,017 (33.1) | 39,512 (39.5) | 27,231 (30.3) | 24,105 (30.0) | 19,797 (29.5) |
| Drinking | 40,924 (41.3) | 45,206 (44.7) | 33,003 (35.5) | 32,715 (30.9) | 10,493 (10.5)* | 12,745 (14.2)* | 12,544 (15.6)* | 12,902 (19.2)* |
| Physical activity | 15,937 (15.7) | 19,518 (19.3) | 13,480 (14.5) | 10,706 (10.1) | 4,597 (4.6)* | 16,964 (18.9)* | -† | -† |
| BMI, kg/m$^2$ | 25.0 ± 3.5 | 24.9 ± 3.4 | 25.1 ± 3.4 | 25.0 ± 3.4 | 24.9 ± 3.4 | 25.0 ± 3.5 | 25.4 ± 3.5 | 25.3 ± 3.5 |
| FBG, mmol/L | 5.5 ± 1.7 | 5.6 ± 1.8 | 5.6 ± 1.8 | 5.7 ± 2.1 | 5.8 ± 2.1 | 5.9 ± 2.4 | 5.9 ± 2.3 | 6.1 ± 2.2 |
| SBP, mmHg | 131.1 ± 21.1 | 130.8 ± 20.9 | 130.5 ± 19.7 | 129.8 ± 19.3 | 135.4 ± 19.9 | 136.7 ± 19.4 | 136.5 ± 18.8 | 140.4 ± 19.6 |
| DBP, mmHg | 83.5 ± 11.8 | 84.4 ± 11.7 | 84.2 ± 11.0 | 83.4 ± 10.6 | 81.8 ± 10.9 | 81.1 ± 10.6 | 81.8 ± 11.0 | 83.2 ± 11.1 |
| LDL-C, mmol/L | 2.3 ± 0.9 | 2.6 ± 1.2 | 2.6 ± 1.0 | 2.5 ± 1.0 | 2.9 ± 1.2 | 2.9 ± 1.1 | 3.0 ± 1.3 | 3.1 ± 1.3 |
| HDL-C, mmol/L | 1.5 ± 0.4 | 1.5 ± 0.5 | 1.5 ± 0.5 | 1.4 ± 0.6 | 1.4 ± 0.6 | 1.5 ± 0.8 | 1.4 ± 0.6 | 1.4 ± 0.6 |
| TG, mmol/L | 1.3 (0.9–1.9) | 1.3 (0.9–1.9) | 1.3 (0.9–1.9) | 1.2 (0.9–1.9) | 1.3 (0.9–1.9) | 1.4 (1.0–2.6) | 1.3 (0.9–2.0) | 1.4 (1.0–2.1) |
| TC, mmol/L | 5.0 ± 1.1 | 5.0 ± 1.4 | 5.0 ± 1.3 | 5.0 ± 1.5 | 5.2 ± 1.5 | 4.6 ± 2.1 | 5.1 ± 1.7 | 5.3 ± 1.8 |
| hs-CRP, mg/L | 0.8 (0.3–2.2) | 1.5 (0.8–3.2) | 1.0 (0.5–2.5) | 1.0 (0.4–2.2) | 1.0 (0.5–2.2) | 0.9 (0.3–2.5) | 1.0 (0.4–2.2) | 1.3 (0.7–2.6) |
| ALT, U/L | 18.0 (13.0–25.0) | 18.0 (13.0–25.3) | 18.0 (13.0–25.0) | 19.0 (14.0–27.0) | 20.0 (14.0–28.0) | 19.0 (14.0–27.0) | 19.0 (14.0–27.0) | 21.0 (15.0–29.0) |
| Hypertension | 44,664 (44.0) | 46,117 (45.6) | 40,905 (44.0) | 44,260 (40.6) | 39,534 (39.6) | 38,989 (43.4) | 34,103 (42.4) | 33,731 (50.2) |
| Diabetes | 9,440 (9.3) | 10,720 (10.6) | 9,576 (10.3) | 12,168 (11.2) | 11,355 (11.4) | 11,477 (12.8) | 10,748 (13.4) | 10,948 (16.3) |
| Dyslipidemia | 32,483 (32.0) | 31,250 (30.9) | 28,727 (30.9) | 39,288 (36.0) | 37,554 (37.6) | 38,648 (43.1) | 30,253 (37.6) | 29,835 (44.4) |

Data are presented as mean ± standard deviation, number (%), or median (interquartile range). Missing data were managed via complete-case analysis. Smoking was defined as having smoked for more than 6 months in one's lifetime. Dinking was defined as an individual who had consumed any type of alcoholic beverage in the past year (current drinker) or who had consumed alcohol previously but had abstained in the year preceding the survey (former drinker). Physical activity was defined as exercising ≥ 3 times/week and ≥ 30 min/time. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, a self-reported history of hypertension, or current use of antihypertensive medications. Diabetes was defined as a fasting plasma glucose level ≥ 7.0 mmol/L, a self-reported history of diabetes, or current use of insulin or oral hypoglycemic agents. Dyslipidemia was defined as having one or more of the following: total cholesterol ≥ 6.2 mmol/L, low-density lipoprotein cholesterol ≥ 4.1 mmol/L, high-density lipoprotein cholesterol < 1.0 mmol/L, triglycerides ≥ 2.3 mmol/L, a self-reported history of dyslipidemia, or current use of lipid-lowering drugs.

ALT = alanine transaminase; BMI = body mass index; DBP = diastolic blood pressure; FBG = fasting blood glucose; HDL-C = high-density lipoprotein cholesterol; hs-CRP = high-sensitivity C-reactive protein; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure; TC = total cholesterol; TG = triglyceride.

*Breaks in the series were caused by changes in the questionnaire's structure.

†Data unavailable.

Beyond early development, this study revealed that an earlier onset of metabolic dysfunction significantly increased the cumulative biological burden. Each 10-year decrease in age at type 2 diabetes onset was observed to be associated with a 24% increase in cardiovascular risk and a 31% increase in all-cause mortality.[32] Notably, diabetes was identified as the most potent clinical predictor of premature CVD.[33] Each 10-year decrease in the age of MASLD onset was associated with an 11% increase in overall cancer risk.[34] Multifaceted investigations of metabolic dynamics, including trajectories, variations, and cumulative exposure, further confirmed these associations across cardiovascular, renal, oncological outcomes, and mortality.[35–40]

Finally, this life-course perspective extends across multiple generations. Research within the parent-offspring subcohort demonstrated that parental arterial stiffness independently predicts increased arterial stiffness in offspring.[9] By synthesizing evidence on developmental programming and the long-term consequences of early-onset metabolic dysfunction, this study established a multitiered foundation for life-course-based prevention.

### 3.4. From risk identification to population-based intervention

This study moved beyond risk factor identification toward the implementation and evaluation of real-world

**Table 4**

**Major events and annual average incidence rate in the Kailuan study.**

| Outcome | Total events | Total PYs | Incidence rate (per 100,000 PYs) |
|---|---|---|---|
| All-cause of death | 24,915 | 2,341,391.24 | 1,064.11 |
| Cardiovascular disease | 22,637 | 2,204,138.91 | 1,027.02 |
| Cancer | 8,440 | 2,304,850.40 | 366.18 |

Events, PYs, and incidence rates are calculated based on all available follow-up data from the date of initial enrollment through December 31, 2023, for all participants.

PYs = person-years.

interventions. Specific lifestyle behaviors and environmental exposures, including their integration, such as the dietary approaches to stop hypertension[41] and adherence to Life's Essential 8,[42,43] were consistently associated with a reduced risk of NCDs and improved survival.

The study also provided real-world evidence of the effectiveness of established clinical interventions, such as statin therapy[10,44,45] and structured hypertension management programs.[22,46–48] Most importantly, the comprehensive evaluation of a workplace-based hypertension management program implemented within the Kailuan Group.[46,49] This program, which integrated regular BP monitoring, free antihypertensive medications, and individualized health consultations, was associated with significantly lower BP levels and reduced risks of major adverse cardiovascular events and all-cause mortality among the participating employees. Economic modeling further confirmed that this workplace program was highly cost-effective compared with routine care.[49]

Evidence from the Kailuan study has provided empirical evidence for clinical decision-making both domestically and internationally. As of 2026, findings from this cohort have been cited by 162 clinical practice guidelines and expert consensus statements, including 151 international and 11 domestic documents. For example, data on CVD risk factors and BP assessment from the cohort have been incorporated into clinical consensus statements and guidelines published by the European Society of Cardiology,[50,51] the American Heart Association/American College of Cardiology,[52] and the Chinese Society of Cardiology.[53,54]

### 3.5. Innovative research directions

The Kailuan cohort serves as a dynamic platform for exploring novel biomarkers and concepts. It was instrumental in investigating biological age metrics as predictors of mortality and CVD risk,[55,56] developing deep learning methods for analyzing retinal vessel morphology as potential biomarkers for cognitive decline,[57] and evaluating the role of the exposome in brain health.[58] These ongoing investigations highlight the potential of this cohort to contribute to cutting-edge research.

## 4. Strengths and limitations

The Kailuan Cohort has several strengths. The primary advantage is the exceptional stability afforded by the "closed loop" nature of the Kailuan functional community. While many large-scale cohorts are limited by significant loss to follow-up due to migration, the Kailuan structure ensures near-complete long-term observation through consistent employment, stable residence, and a centralized corporate healthcare system. Data integrity is reinforced by a combination of biennial active health examinations and annual passive surveillance via comprehensive medical insurance linkages. Notably, the integration of "secondary reimbursement" data serves as a key addition, capturing clinical endpoints for care sought outside the parent network and effectively minimizing ascertainment bias.

Second, the cohort's 140-year institutional history allows for the retrospective ascertainment of high-impact historical exposures (e.g., the 1976 Tangshan Earthquake[31] and the Great Chinese Famine[29,30]) that are often unavailable in newer cohorts. Furthermore, the parent-offspring subcohort of over 10,000 families provides an opportunity to examine intergenerational health determinants and familial disease aggregation, adding a genetic and epigenetic dimension to the epidemiological findings.

Third, this specific demographic and institutional composition enhances the internal validity of etiological research, which is the primary objective of the Kailuan study. Broad occupational diversity within a unified socioeconomic and geographic setting allows for robust internal comparisons. By comparing various workers (from underground miners to office administrators) in the same conglomerate, this study design effectively minimizes confounding factors from unmeasured socioeconomic and environmental variables. This internal consistency strengthens the validity of the findings and provides a more reliable platform for identifying the biological and lifestyle determinants of NCDs.

Despite its strengths, the study has several limitations. First, the cohort is rooted in an industrial setting and is predominantly male, which may limit the direct generalizability of the findings to women or the broader population. However, the absolute sample size of over 20,000 female participants per examination cycle provides the statistical power necessary to rigorously address sex in the analytical framework: either as a confounder controlled through multivariable adjustment or as an effect modifier explored via robust sex-stratified analyses. Furthermore, the Kailuan Group serves as a microcosm of society. The baseline prevalence of major chronic conditions (e.g., hypertension: about 44% and diabetes: about 10%) and the incidence rates of key outcomes (e.g., annual average incidence rate of all-cause mortality: 1,064/100,000 PYs, CVD: 1,027/100,000 PYs, and cancer: 366/100,000 PYs) align closely with national statistics for the general Chinese population.[59–62]

Second, as is common in large-scale epidemiological studies, certain lifestyle and dietary data were collected using self-reported questionnaires, which are susceptible to recall bias. However, this was minimized by standardized face-to-face questionnaire interviews conducted by trained staff, rather than self-administered surveys.

Third, although the cohort has integrated advanced biomarkers, multiomics, and multimodality imaging, these assessments are currently restricted to specific subcohorts because of logistical and financial constraints. Consequently, analyses involving these high-dimensional data may have lower statistical power than the main cohort findings. Expanding the scope of these advanced phenotypes to larger, more representative samples remains a key strategic priority.

The Kailuan study is committed to maximizing the utility of its data ecosystem by applying advanced analytical

techniques, including artificial intelligence and machine learning. By integrating longitudinal data with multiomics data, multimodal medical imaging, and digital phenotyping metrics from wearable devices, this study aims to transcend traditional risk factor identification. Future research should focus on decoding multimorbidity trajectories and elucidating the complex multiorgan systemic interactions driving cardiometabolic, renal, hepatic, oncological, and skeletal diseases, as well as neurodegenerative and sensory disorders affecting the brain and eyes.

The study will prioritize the development of novel biomarker panels and multimodal predictive models. Using robust causal inference frameworks, such as target trial emulation, this study will quantitatively assess how precise modifications of lifestyle and clinical risk factors can reduce the disease burden. Ultimately, the cohort will envision developing a comprehensive "large health model" for the entire life cycle management.

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## Ethical statement

This study was approved by the Institutional Review Board (IRB) of Kailuan General Hospital (Approval Nos. 2006-5; 2008-1). Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki. The project was registered in the Chinese Clinical Trial Registry (ChiCTR-TNRC-11001489 and ChiCTR2000029767).

## Conflicts of interest

The authors have no conflicts of interest to disclose.

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## Data availability statement

The Kailuan study data are available to qualified investigators whose research proposals align with the study objectives and data-sharing policies. Access to the data requires a collaborative research agreement with the Kailuan study team. Inquiries regarding data access should be directed to Prof Shouling Wu.

## Author contributions

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**Approved the submission of the final version of the protocol**: All authors.

## AI statement

The authors used AI solely to polish language and improve readability and clarity. The authors have reviewed and revised all AI-modified content and take full and sole responsibility for the accuracy, originality, and integrity of the final manuscript.

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