

BMJ Open Lifestyle, genomic types and non-communicable diseases in Korea: a protocol for the Korean Medicine Daejeon Citizen Cohort study (KDCC)

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ABSTRACT

Introduction Non-communicable diseases (NCDs) are the leading cause of death worldwide, including in Korea; thus, customised techniques for chronic disease management for the prevention, early diagnosis and treatment of NCDs are crucial. The Korean Medicine Daejeon Citizen Cohort (KDCC) study has been tasked with developing precise health promotion model for preventing and managing chronic diseases that considers individual traits, lifestyle factors and clinical data based on traditional Korean medicine.

Methods and analysis The KDCC study is a prospective cohort study of the community-based population in Korea. This study will sample 2000 adults aged 30–55 years in Daejeon area using stratified cluster sampling. The baseline survey began in 2017 and was completed in 2019, and follow-up surveys will be conducted three times every 2 years until 2025. In follow-ups, factors related to cardiovascular disease, metabolic syndrome and relevant diseases, as well as respondents' health status information, will be examined via questionnaire surveys and health examinations.

Discussion The KDCC study will investigate the effects of an interaction of Korean medicine type with genome based, lifestyle and various clinical information on chronic diseases and individuals' health status using longitudinal epidemiological data. These findings are expected to inform the development of tailored health promotion programmes based on precision Korean medicine.

Trial registration number KCT0004297.

INTRODUCTION

Non-communicable diseases (NCDs), which include cardiovascular disease (CVD), diabetes, chronic respiratory diseases and cancer, are the leading cause of death worldwide, accounting for about 70% of all deaths.¹ Although national numbers vary according to the economy of each country, premature death caused by NCDs is consistently on the rise and has increased from 31.6 million in 2000 to 40.5 million in 2016²; further, premature death caused by CVD is high—about 31% of all global deaths.^{3,4} Prevention

Strengths and limitations of this study

- The Korean Medicine Daejeon Citizen Cohort (KDCC) study is the first prospective cohort study to assess the causal relationships among Korean medicine types, lifestyle factors and chronic diseases.
- This study will present crucial results to clarify the biological features of Korean medicine types.
- Detailed clinical data will be collected, biological resources will be used and enhanced genomic analysis techniques will be employed to inform the clinical applicability of Korean medicine.
- KDCC longitudinal data will be used to develop a health promotion model for the prevention of chronic diseases based on Korean medicine types.
- Limitations of this study include the possibility of selection bias—owing to voluntary participation—and ungeneralisable findings—owing to participants being recruited from one region.

through lifestyle adjustment and control of risk factors is the key for NCDs, and diverse studies are underway to develop customised chronic disease management technologies, such as programmes for early diagnosis and treatment.^{5,6}

In recent years, there have been attempts—primarily centred on precision medicine—to develop customised disease management by thoroughly examining individual traits and various external factors based on developments of genomic technology.⁷ Research concerning precision medicine is focused on cancer in the near term; however, the long-term aim is to develop knowledge applicable to a wide range of health issues and diseases, including chronic diseases, such as diabetes mellitus and CVD,⁷ and chronic disease management incorporating precision medicine will be realised in the near future.

In traditional Korean medicine (KM), individualised disease treatment and health management consider KM types, such as

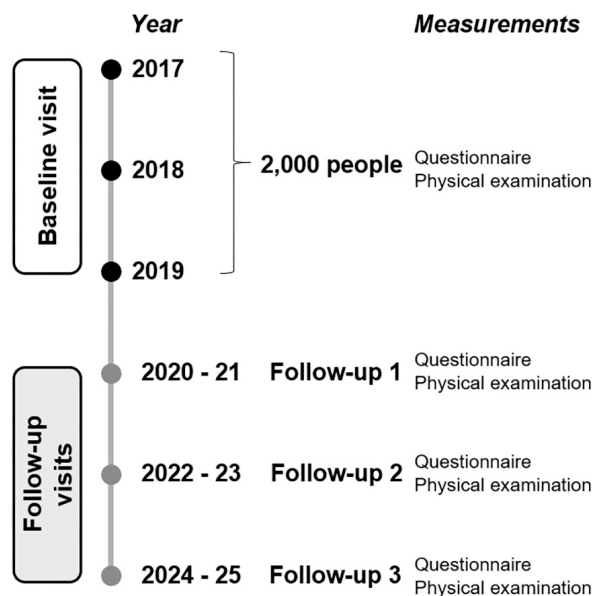


Figure 1 Flow of the Korean Medicine Daejeon Citizen Cohort study.

constitution types and cold–heat patterns. Multiple studies have found that constitution is an independent risk factor for chronic diseases, such as metabolic syndrome,⁸ hypertension,^{9 10} diabetes mellitus¹¹ and CVD¹²; and several studies have confirmed the efficacy of several Korean medical treatment techniques in the management of chronic diseases. With constitution and cold–heat found to be heritable by family^{13 14} and twin^{15 16} studies, there is active ongoing research on heredity indices, such as whole genome studies.

Here, we describe the design of the Korean Medicine Daejeon Citizen Cohort (KDCC) study, a prospective community-based cohort in Korea. The study has been planned to develop precise health promotion model for the prevention and treatment of chronic diseases, and it considers individual lifestyles and clinical data based on an analysis of individual genomic characteristics with reference to previous cross-sectional studies.

OBJECTIVES

The aim of the KDCC study is to develop a precise prevention and treatment model for chronic diseases that considers lifestyles and clinical data based on individual KM types as interpreted with the genome. The specific objectives for this cohort are as follows:

1. Establish a sustainable KM cohort.
2. Develop a genome-based diagnostic technology using KM types, such as constitution types and cold–heat patterns.
3. Identify the important factors of lifestyle related to chronic disease and health-related quality of life (HRQOL) according to the KM type.
4. Propose a health promotion model for the prevention and treatment of chronic diseases and for improving

the HRQOL that considers KM types and individual traits.

METHODS AND ANALYSIS

Study design and setting

The KDCC is a prospective cohort study based in a region of South Korea. This cohort study is being conducted over a 9-year period between 2017 and 2025, with 2000 adults aged 30–55 years living in Daejeon. Participants will visit the hospital four times for study purposes: for the baseline study (2017–2019) and for three follow-ups every 2 years (2020–2025). The study schedule is summarised in [figure 1](#). Stratified cluster sampling was used to obtain the sample. The entire 30–55 years adult population in Daejeon was set as the population,¹⁷ which was clustered according to region (five administrative districts called ‘Gu’ based on the address of residence), sex (male or female) and age (30–39 years, 40–49 years and 50–55 years). The sample was extracted based on the target sample size and the probability proportion of the population in each cluster.

This study is conducted in a joint collaboration among the Korea Institute of Oriental Medicine, Gallup Korea and Korean Medicine Hospital of Daejeon University. All information will be acquired by well-trained expert interviewers and researchers. The questionnaire consists of items concerning general characteristics, disease history, lifestyle, HRQOL and KM clinical information. An expert interviewers at Gallup Korea will conduct face-to-face interviews, using a structured questionnaire, to obtain said information. Health examinations include physical examination and laboratory tests, such as anthropometric measurements, cardiovascular function, body composition and blood tests (for details, see [tables 1 and 2](#)). All health examinations will be performed at the Korean Medicine Hospital of Daejeon University.

Study population

Participants were recruited between June 2017 and December 2019. Eligible individuals were identified by key members of researchers, who were trained regarding the inclusion/exclusion criteria and the procedures involved in recruitment. We examined preliminary suitability based on participants’ self-reported information. Potential participants visited the hospital to have their suitability further checked by the medical staff through a detailed examination. Medical staff individually interviewed participants for about 20 min to explain the cohort study and determine participants’ suitability.

The inclusion criteria are as follows: (1) men and women aged 30–55 years, (2) residents of Daejeon and (3) individuals who provided informed consent. However, (1) individuals diagnosed with cancer (malignant tumour) or CVD (myocardial infarction, angina, stroke/apoplexy); (2) individuals deemed to have difficulty following study instructions, such as having difficulty completing and understanding the questionnaire and (3)

Table 1 Health questionnaire and physical examination in the Korean Medicine Daejeon Citizen Cohort study

Classification	Measures and instruments
General characteristics	(Questionnaire) Sociodemographic information, smoking, drinking
Medical history	(Questionnaire) Disease history, family history, menstrual history
Lifestyle	(Questionnaire) Sleep, amount of activity, diet (dietary pattern, nutrition index, food frequency questionnaire)
Health-related quality of life	(Questionnaire) Health-related quality of life, psychological stress
Korean medical information	(Questionnaire) Constitution, cold-heat, sub-health status (Mibyeong) (Measurement) Facial image, body temperature, iris testing
Anthropometric measurements	(Measurement) Height, weight, waist/hip circumference, grip strength (hand)
Cardiovascular function	(Device) Blood pressure/pulse, pulse wave, heart rate variability
Body composition	(Device) Body composition analysis

individuals determined by the researcher to be inappropriate to participate in this study were excluded.

Baseline and follow-up visits

This study is currently planned as a 9-year study. Cohort registration and baseline surveys, which began in June 2017, were completed in December 2019. On conclusion of registration, follow-up surveys will be performed three times from 2020 to 2025 in 2-year intervals (first follow-up, 2020–2021; second follow-up, 2022–2023 and third

follow-up, 2024–2025). During the follow-ups, a questionnaire survey will be administered, and health examinations will be performed including all items collected at baseline (table 3). To minimise follow-up losses, participants will be contacted via phone and mail. If the first phone call attempt fails, additional calls will be made on other days and at other times for up to five times. We plan to update any changes to addresses and contact numbers and to maintain awareness among participants by providing them with study explanations. Further, we plan to send out a study newsletter and thank-you cards periodically.

Table 2 Blood tests and human biological materials in the Korean Medicine Daejeon Citizen Cohort study

Classification	Measures
Complete blood count	White blood cells, red blood cells, haemoglobin, hematocrit, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, red cell distribution width, platelet count, Eosinophil count
Renal panel	Blood urea nitrogen, creatinine
Liver function test	Total protein, albumin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, total bilirubin, direct bilirubin, r-GTP
Lipid profile	Total cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol
Glucose metabolism	Glucose, HbA1C, insulin
Thyroid function	TSH, T4, T3
Inflammation	High sensitivity C reactive protein,
Others	Calcium
Human biological materials	Blood: DNA, serum, peripheral blood mononuclear cell

HbA1C, hemoglobin A1c; r-GTP, gamma-glutamyl transpeptidase; T3, triiodothyronine ; T4, thyroxine; TSH, thyroid-stimulating hormone.

Table 3 Details and procedures of the baseline study visit and follow-up periods

Classification	Follow-up period			
	Baseline	2 years	4 years	6 years
Participant enrolment	X	–	–	–
Informed consent	X	X	X	X
General characteristics	X	X	X	X
Medical history	X	X	X	X
Lifestyle	X	X	X	X
Health-related quality of life	X	X	X	X
Korean medical information	X	X	X	X
Anthropometric measurements	X	X	X	X
Cardiovascular function	X	X	X	X
Body composition	X	X	X	X
Blood test	X	X	X	X
Biological materials	X	X	X	X

Outcome events

The primary outcome in this study is new onset of CVD, such as myocardial infarction, angina, or stroke, during participation; and the endpoint is either death from CVD or the conclusion of the study period. The secondary outcome is the onset of chronic diseases, such as metabolic syndrome, hypertension, diabetes mellitus, obesity and dyslipidaemia. Finally, we plan to examine the characteristics of risk factors related to changes in subjective health status, such as HRQOL. When the standardised, structured questionnaire identifies a potential outcome event, physicians and appropriate specialists will verify and adjudicate the information.

Within the legally allowed range, the diagnosis of myocardial infarction, angina and stroke will be determined by direct follow-up through participant recontact as well as indirect tracking using medical insurance and official statistical record of death linkage based on International Classification of Disease 10th revision. Furthermore, the secondary outcomes are defined as follows based on the international guidelines for the diagnosis of each disease: metabolic syndrome is defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III),¹⁸ hypertension is defined according to the Joint National Committee,^{19 20} diabetes mellitus is defined according to the American Diabetes Association,²¹ obesity is defined by WHO Asia-Pacific Guideline²² and Korean Society for the Study of Obesity,²³ and dyslipidaemia is defined according to the NCEP-ATP III.¹⁸

Sample size calculations

To assess the suitability of the suggested sample size ($n=2000$), we considered various genetic models and disease incidences. This is because identifying significant biomarkers for KM types is one of the important goals of this study. We explored the appropriate sample size according to the Allelic model, dominant model, codominant model and recessive model, which are used in Genome-Wide Association Studies (GWAS) with the incidence of chronic disease set to 20% and ORs between genotype and disease set to 1.3, 1.5, 2 and 2.5.²⁴ Power and alpha were set to 80% and 5%, respectively, and the ratio of the disease group to normal group was set to 1:4, with minor allele frequency of 5% and complete linkage disequilibrium (D') equal to one. We confirmed that about 300–500 patients are needed for the genotype OR for chronic disease to increase by two or more. Thus, based on the incidence of disease and statistical power in this study, we set the sample size to 2000.

Measurement and instruments

General information and medical history

As general attributes, sociodemographic characteristics such as sex, age, occupation, education, marital status, number of hours worked and family income are surveyed.

For smoking, the following questions are asked: 'Have you smoked more than 100 cigarettes in your entire life?'

and 'Do you currently smoke?' Participants are then classified according to their smoking status (ie, currently smoking, smoked in the past and non-smoker), and the age they first started smoking and the period of smoking are further investigated. In addition, for drinking, the following questions are asked: 'Have you consumed alcohol in the past?' and 'Do you currently drink alcohol?' Participants are then classified according to their drinking status (ie, currently drinking, drank in the past and non-drinker) and the total period of drinking as well as average frequency of drinking for the past year and the amount of drinking per incidence according to the type of a drink (unrefined rice wine, refined rice wine, wine, soju, beer, liquor, etc) are further investigated.

For medical history, about 40 diseases are listed, and the status of each of these diseases is investigated based on a hospital diagnosis, along with family history of the diseases. For female participants, information about menstrual status is collected.

KM clinical information

To classify the KM types of individuals, constitution types and cold–heat patterns are examined. Constitution types and cold–heat patterns can be assessed using a previously validated questionnaire with established classification criteria and can be used to classify individual KM types. To assess constitution, the simplified Korea Sasang Constitution Diagnostic Questionnaire comprising 15 questions on body type (one question on physical trait, six questions on personality traits, and eight questions on physiological symptoms) are administered.^{25 26} Cold–heat patterns are assessed using two types of tools. First, the Cold-Heat Pattern Identification, which consists of eight items for cold pattern and seven items for heat pattern, is used to assess daily symptoms.²⁷ The Cronbach's alpha coefficients representing internal consistency are 0.79 (cold) and 0.83 (heat).^{27 28} Then, the seven-item Short Form Cold/Heat Questionnaire (SF-CHQ), which can identify the traits of specific parts of the body, such as the hands, feet, and abdomen and cold–heat sensitivity, is used. The correlation coefficient for test–retest reliability for the SF-CHQ was 0.609, and classification accuracy against expert classification was 74.5%.²⁹

Subhealth status is assessed using a Mibyeong questionnaire. The Mibyeong questionnaire evaluates an individual's subhealth status based on subjective symptoms, and it consists of 21 items regarding the persistence of, discomfort from, and recovery from seven conditions (fatigue, pain, sleep, indigestion, anxiety, depression and anger) after rest. Based on the total score on the Mibyeong questionnaire, individuals are classified into healthy, mild Mibyeong and severe Mibyeong.^{30 31}

The colour and texture of the face are important indicators of health in KM. Thus, we collected facial photographs of the cohort (using a Nikon DSLR D5100 with 50mm lens), and per the standard operating procedure, distance, lighting and posture were controlled during the photographing.³² The front and side of the faces

are photographed using a facial imaging programme with participants going without make-up as much as possible. Further, as one of the methods to assess cold-heat patterns, body surface temperature (using an IRIS-XP, Medcore, Seoul, Korea) and iris images (using a Camscope Pro, Sometech, Seoul, Korea) are taken.

Lifestyle

In this study, we observe sleep, physical activity and diet pattern as lifestyle variables. The components of sleep status, sleep duration and sleep quality, is investigated using the Korean Pittsburgh Sleep Quality Index (PSQI).^{33 34} The PSQI measures sleep quality and disturbances during the previous month using 19 items that assess a broad range of domains related to sleep quality.³⁴ These items are combined to form seven component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Each component score has a range of 0–3, and the sum of the seven components yields a global score ranging from 0 to 21, with the higher scores indicating more severe sleep complaints.

Physical activity is assessed using the Korean Global Physical Activity Questionnaire (GPAQ) developed by WHO.^{35 36} The GPAQ can assess the amount of physical activity by domain, such as work-related activity, activity when moving to another location and leisure activity. It also measures the intensity levels of physical activity by converting it to a metabolic equivalent task—commonly used in the analysis of physical activity.

Diet is assessed using three questionnaires: dietary behaviours, nutrition quotient (NQ) and the Food Frequency Questionnaire (FFQ). For dietary behaviours, meal frequency (average frequency, specific frequency of breakfast, lunch and dinner), meal regularity, meal speed and frequency of overeating/snacking/dining out are surveyed. NQ, a questionnaire developed by the Korea Nutrition and Health Society, consists of items about intake of 12 major food groups and nine diet behaviours. The NQ questionnaire can be used to assess adults' meal quality and nutrition intake status, and the questionnaire and scoring method have been validated.³⁷ The FFQ assesses the average frequency of food intake in the past year, and we will use a modified version based on the items in the 2011 Korea Health and Nutrition Examination Survey.^{38 39}

HRQOL and stress

HRQOL is assessed using the SF-12 version 2 and EuroQoL 5-dimension (EQ-5D). The SF-12 is a 12-item scale that assesses overall HRQOL based on physical and mental health status.⁴⁰ It contains eight categories (physical functioning, physical role restriction, pain, general health, mental health, emotional role restriction, social functioning and vitality), and their scores are used to calculate the physical component summary-12 (PCS) and mental component summary-12 (MCS) scores. The

PCS and MCS are scored from 0 to 100 per a norm-based scoring algorithm, and a higher score indicates a better HRQOL. The EQ-5D was developed by the EQ Group as a generic measure of HRQOL.^{41 42} This tool assesses health status in five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with three levels (no problems, some or moderate problems and extreme problems), which was called EQ-5D index, and 100 mm Visual Analogue Scales (EQ-5D VAS) with vertical lines. EQ-5D index provides an estimate of the health summary score by applying a formula that attaches specific values to each level in each dimension. EQ-5D index scores are calculated using a time trade-off valuation set that pertains to the Korean population.³⁰ The total score ranges from 0 to 1, with a lower score indicating a poorer health status. EQ-5D VAS scores range from worst (0) to optimum health (100). Both the SF-12 and EQ-5D assess the overall HRQOL, but a comparison of the two scales shows that EQ-5D can be used for economic assessment (quality-adjusted life year) but has a ceiling effect. Thus, the two questionnaires are combined for various purposes, such as health status evaluation.⁴³

Psychological stress is assessed using the 18-item Psychological Well-being Index-SF (PWI-SF).⁴⁴ Each item on PWI-SF is rated on a four-point scale from 0 (always true) to 3 (never true), and the total score ranges from 0 to 54, with a higher score indicating a higher level of stress.

Anthropometric measurements

Anthropometry is taken by trained personnel with participants wearing only light underwear. Body height (in cm) and weight (in kg) is measured with the measuring station BSM370 and Inbody 770 (Biospace), and waist and hip circumference (both in cm) are taken with a tape measure (Hoechstmass-Rollfix, Germany) according to WHO guidelines. For grip strength, a hand dynamometer (TKK 5401, Takei Scientific Instruments, Niigata, Japan) is used to measure maximum strength in the right and left hands. Body circumferences and grip strength are each measured twice.

Cardiovascular function assessment

For cardiovascular function assessment, blood pressure, pulse rate, pulse wave and heart rate variability are measured with the participant sitting down and after 5–10 min of rest. Blood pressure and pulse rate are measured twice using an automatic blood pressure cuff (FT-500R PLUS, Jawon medica, Korea). The second measurement is taken 5 min after the first measurement in the same position, and if there is a significant difference between the first and second measurements (eg, ≥ 5 –10 mm Hg), a third measurement is taken. Pulse wave is measured with a DMP-1000 (Daeyomedi, Korea) using the tonometry method, where pressure is measured while compressing the left radial artery (vascular area). Pulse waves show the features of a pulse, circulation resistance and vascular anomaly. Heart rate variability is measured with the SA6000P (Medcore) for 5 min after attaching

ECG sensors on the right and left wrists and left ankle. The level of autonomic nervous system function is assessed using low frequency and high frequency values computed based on an algorithm.

Body composition

We assess body composition by measuring bioimpedance with the InBody 770 (Biospace) and along six frequencies (1 kHz, 5 kHz, 50 kHz, 250 kHz, 500 kHz and 1 MHz) at five locations: right arm, left arm, trunk, right leg and left leg. The manufacturer recommends that participants stand barefoot on the electrodes and while holding the hand electrodes wearing light clothing and no accessories. Arms and legs should not contact any other parts of the body and should instead be spread. Bioimpedance analysis allows non-invasive, easy and an inexpensive assessment of body composition and is applicable to a wide range of subjects.

Blood test and human resources

A venous blood sample (about 22.5 mL) is taken in the morning following overnight fasting. Thirty minutes after collection, the sample is centrifuged for 10 min at 3450 rpm, and all samples are transported to the Seoul Clinical Laboratories (Seoul, Korea) within 24 hours. As shown in table 2, the blood test includes complete blood count, kidney and liver function, lipid profile, glucose metabolism, thyroid function and inflammatory marker. Further, for a genomic study, DNA, serum and peripheral blood mononuclear cell are collected and are stored at -80°C per the standard procedure until use.

Data analysis

The detailed data analysis plan for genomic research and clinical epidemiology research in this study is as follows. For genomic research, heritability in KM types including constitution types and cold-heat pattern has been reported in previous family^{13 14} and twin^{15 16} studies. In this study, using the GWAS-convolutional neural network, an improvement on the existing GWAS analysis method,⁴⁵ KM types of the cohort participants will be predicted. For the clinical epidemiology analysis, using previous studies on lifestyle factors such as sleep, physical activity, eating habit, smoking and drinking,^{46 47} we will divide responses as healthy and unhealthy lifestyle based on a clustering phenomenon, and the factors influencing CVD, metabolic syndrome and relevant diseases will be analysed according to KM types deduced from genomic research.

In addition, we will perform a variety of analyses conducted in cohort studies. To estimate cumulative risk of primary and secondary outcomes, the study will employ Kaplan-Meier analysis. Adjustments for covariates will be made prior to the follow-up period where Cox proportional hazard models will estimate the risk of experiencing any of the primary or secondary outcomes. We will also conduct cross-sectional analysis. Categorical variables will be compared using χ^2 tests, while continuous

variables will be compared using the Student's t-test and the analysis of variance. In case of skewed distributions which cannot be normalised corresponding, non-parametric tests will be used.

Data management and protection

All data collected in this cohort study are managed and stored by the Korean Medicine Data Center (KDC) of the Korean Institute of Oriental Medicine. All data are electronically managed using the KDC electronic data capture (EDC) system, a secure, web-based application that allows for data instruments to be created, data quality to be monitored and data analysis to be completed (<https://ecrf.kiom.re.kr/>). The KDC EDC system has restricted physical access; data are stored under coded filenames, and the network has secure password access restricted to a limited number of people. All researchers will be trained in data entry by the KDC administrator and must demonstrate proficiency with mock patients and data entry before being granted access to data collection forms. All records containing personal health information will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. Deidentified data may be used for future analysis and publication.

Ethics and dissemination

All participants will provide written informed consent and consent to the collection of human biological materials. All participants are informed that they can withdraw their consent to participate at any point. There are no anticipated physical, social, legal or economic risks associated with the study. There is minimal risk of breach of confidentiality. No vulnerable populations are specifically targeted in this study. Results from this study will be disseminated at regional and international conferences and in peer-reviewed journals.

Researchers' training and cooperation

The primary investigator has extensive training and experience in clinical research and relevant bioethics. The researchers will include a team of primary investigator that have extensive qualifications and expertise to lead the study. All study staff, including interviewers and medical staff who collect the data, are trained and routinely re-educated about the ethical conduct of human subject research. Further, researchers from various disciplines will cooperate to develop a cohort study protocol, manage and conduct the research, and analyse clinical and genomic data. The researchers in this study hold regular meetings to discuss the study design, progress and clinical issues; and they also participate in theoretical and practical training sessions. All research processes including participant recruitment, obtaining consent and data collection follow the standard operating procedure.

Patient and public involvement

There was no patient or public involvement in this study as it describes a study protocol.

DISCUSSION

This protocol describes the design and method of the KDCC study in detail. The KDCC study aims to assess genomic-based KM types, lifestyle and chronic disease status in middle-aged residents of Daejeon, Korea, through a series of long-term follow-up examinations. In this study, we focus on discovering biomarkers that define the KM types of an individual based on the genome in the short term. In the long term, we aim to examine how the associations between chronic disease and HRQOL vary across different patterns of the KM types. Ultimately, this study will evaluate the impact of the varying lifestyle according to KM types on chronic disease and health status, and will discover a genetic marker for KM types, such as constitution types and cold–heat patterns, based on genomic analysis to develop a technique for predicting them.

This study has several strengths. First, it is a long-term cohort study. Thus, the study will gather important data to assess the causal relationships among KM types, lifestyle and chronic disease. Second, it is the first KM-centred prospective cohort study. Hence, various clinical data and genomic data obtained in this study could be used as evidence to support the clinical value of traditional Korean precision medicine. Third, this study sheds light on genomic-based KM types. Whereas prior research relied on expert-dependent studies or questionnaire-based studies, this study will perform a genomic analysis and thus can produce more objective results than prior studies that used genomic analysis, as well as presenting key results to understand the biological features of KM types. Fourth, the questionnaires are administered via a face-to-face interview; thus, it will produce more accurate information than self-reported data by using standardised methods. Finally, the KDCC is implemented by a multidisciplinary research team comprising experts in traditional KM, genetics, statistics and epidemiology. The combination of diverse perspectives and expertise among team will enable novel and original research into health management using traditional Korean precision medicine. Despite these strengths, the greatest limitations of this study are the possibility of selection bias owing to voluntary participation and the limitation of the generalisability of the findings to the Korean adult population, as the participants were sampled from one region.

The KDCC study is expected to present key evidence and model for the development of traditional Korean precision medicine by examining the impact of the interaction among KM types, lifestyle factors and various clinical information on chronic disease and health status. Moreover, our data could be used as foundational data for further research. Currently, we plan to conduct this study on 2000 people for a minimum of 9 years; however, we hope to increase the sample size and extend the follow-up period depending on the availability of resources.

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Contributors YB, B-NS and SL made substantial contributions to the conception and design of this protocol. YB, B-NS and KJ critically read and revised this manuscript. SL and HY approved this final version for submission. All authors agree to be accountable for the future integrity of this study.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval All aspects of this study, including written informed consent, data collection and photo acquisition, were approved by the Institutional Review Board of the Dunsan Korean Medicine Hospital of Daejeon University (no. DJDSKH-17-BM-12) and the Korea Institute of Oriental Medicine Institutional Review Board (no. I-1703/002–002).

Provenance and peer review Not commissioned; externally peer reviewed.

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