Noncommunicable Diseases in The Southwest of Iran, A Region of High Altitude with Distinctive Ethnic Groups: Results of The Shahrekord Cohort Study

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Research article

Keywords: cohort study, noncommunicable diseases, Prospective Epidemiological Research Studies in Iran

DOI: https://doi.org/10.21203/rs.3.rs-76600/v1

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Abstract

Background: Critical inter-provincial differences within Iran in the pattern of noncommunicable diseases (NCDs) and difficulties inherent to the identification of prevention methods to reduce mortality from NCDs have challenged the implementation of the provincial health system plan. The Shahrekord Cohort Study was designed to address these gaps in Chaharmahal and Bakhtiari, a province of high altitude of the southwest of Iran, characterized by its large Bakhtiari population.

Methods: This ongoing cohort, prospective longitudinal study is a unique, rich biobank and a large-scale study conducted for the first time in Chaharmahal and Bakhtiari province in Iran. The study began in 2015, recruited 10075 participants (52.8% female) from both urban and rural (30.2%) areas and participants will be followed up until at least 2035. Diseases and their outcomes are ascertained from clinical examinations, interviews, and linkage with medical records registered in the health system.

Results: Preliminary results indicate that the prevalence of NCDs at baseline was relatively high, for example 10.7% for type 2 diabetes mellitus, 20.2% for hypertension, 14.6% for non-alcoholic fatty liver, 11.4% for thyroid disease, and 5.7%, 0.9% and 1.3% for ischemic heart disease, stroke and myocardial infarction respectively. The mean (standard deviation) of BMI, systolic blood pressure, fasting blood glucose and cholesterol were 27.6 (4.6) kg/m², 115.4 (17.3) mmHg, 96.7 (27.3) mmol/L and 184.1 (42.8) respectively. All NCDs appeared to be more frequent in urban than rural areas, except gastroesophageal reflux (32.3% in rural and 29% in the urban area).

Conclusions: The Shahrekord Cohort Study provides a platform for epidemiological studies that will be useful for a better prevention and management of NCDs in the southwest of Iran.

Background

The World Health Organization (WHO) estimates that more than 36 million people worldwide die annually from noncommunicable diseases (NCDs) (63% of all deaths), and 14 million of these deaths occur before the age of 70. More than 90% of premature deaths from NCDs occur in low- and middle-income countries (1). Reducing the prevalence, incidence, mortality, as well as the costs and burden associated with NCDs, especially cardiovascular disease and cancer, is, therefore, a significant global challenge and priority for public health (2,3). Increased urbanization, industrialization, adoption of modern lifestyles, and rising life expectancy have increased exposure to risk factors and the occurrence of NCDs (4,5). Obtaining a better description and understanding of NCD risk factors and trends in Iran is a priority for the government (5) as it will allow achieving the action plan for the prevention and control of NCDs 2013–2020 set by the WHO (resolution WHA66.10) (6).

Iran is a developing country with a population of over 80 million. In the last two decades, the epidemiological features of health and disease in Iran have changed dramatically due to major variations in demographic indices and health-related social and economic factors (7). These changes have led Iran's health system to give priority to preventing NCDs over-controlling communicable diseases (3,5). Currently,
NCDs impose the most massive burden on Iran's health system so that in 2018, according to WHO reports, 82% of deaths in Iran were caused by NCDs (43% cardiovascular diseases, 16% cancers, and 23% other NCDs) (8). Substantial differences exist between Iran and other Western and Eastern Mediterranean countries in terms of ecological, cultural, and social characteristics. There are also critical inter-provincial differences within Iran in the pattern of health and disease (7). As one of the principal aims of the WHO is to reduce mortality from NCDs worldwide by 25% by 2025, establishing a national and regional plan to control these diseases, and support and conduct research in this region, is a significant public health objective. These WHO prospective goals have, therefore, set the perfect stage for creating high-quality regional documentation to inform decision-making by health system planners and better prevent, control, and manage these fatal diseases (8). Several isolated cohort studies have been previously conducted in Iran to address NCDs in various regions and ethnicities such as the Golestan Cohort Study including Turkmen (9), the Amirkolah Health and Ageing Project in northern Iran [10], the Yazd Health Study in central Iran (11), as well as the Tehran Glucose and Lipid Study in the capital city (12). However, the Prospective Epidemiological Research Studies in IrAN (PERSIAN) is by far the most extensive, multi-center cohort to fulfill this purpose (13). The PERSIAN Cohort started in 2014 in 19 centers, with the aim to include all the major ethnic groups in various regions of Iran including Kurds (14), Turks (15), Fars (16), Tabari (17), and Arabs, among other ethnicities (13). No cohort study was previously conducted in the Bakhtiari ethnicity; therefore, the Shahrekord Cohort Study (SCS), as one of the PERSIAN Cohort Centers, has filled this gap to assess health patterns and risk factors in individuals from the Bakhtiari ethnicity (18).

SCS was therefore conducted to study NCDs in an Iranian province with distinctive environmental, geographical (the highest region above sea level in Iran), and ethnic and social (Bakhtiari) characteristics compared with other Iranian provinces and the rest of the world.

This may have consequences for the appropriate interventions to prevent and manage NCDs in this region. Despite recent efforts to investigate NCDs in Iran (4,9–17), there are currently no comprehensive, population-based and reliable data sources from which to obtain accurate health information in this province so as to better design management plans for improvement of the health care system.

The aims of the SCS study are, therefore: i) to evaluate the prevalence and long-term trends of NCDs and their outcomes, in an Iranian province with unique geographical, ethnic, and socioeconomic characteristics, ii) to investigate associations of environmental and genetic/ethnic factors with the prevalence and incidence of NCDs and their outcomes, iii) to examine the interplay between genetic/ethnic and environmental factors in the aetiology and prevention of NCDs, iv) to provide the basis for various types of epidemiological studies (e.g., social, spatial, molecular epidemiology) and generate scientific evidence that may contribute to improving public health in the CH&B province, v) to provide a research and education platform and a resource for national and international collaboration and to make the research community aware of the existence of large cohorts around the world.

Methods
This population-based prospective cohort study recruited participants from the CH&B province. We used enrolment data in this study and analysed cross-sectional study.

Setting

The Bakhtiari ethnic group mainly lives in Chaharmahal and Bakhtiari (CH&B) province in Iran and has an estimated population of 1.25 million. It is a subgroup of the Iranian Lurs and the genetic background of Bakhtiari people is different from other Lur populations (19). They speak the Bakhtiari dialect. The Bakhtiari have maintained their bloodlines mostly intact over the centuries, largely marrying within their own tribe. Other notable differences with other Iranian ethnic groups include their culture and social and local customs (mourning and weddings), and dietary habits (tiri bread, mountain vegetables, animal oil consumption, traditional dairy products), type of employment (animal husbandry, herding, agriculture, hunting), clothing and apparel (local clothing), and different environmental exposures, such as exposure to sunlight at high altitudes. CH&B province covers an area of 16,421 km$^2$ and is situated in the southwest of Iran, north of the Zagros Mountains, which have the highest average elevation above sea level in Iran; the Shahrekord region is known as the "roof of Iran." Despite its relatively small area (1% of the total area of Iran), CH&B holds 10% of the country's water resources. Because of its mountainous nature and its location where moist Mediterranean air converges, this province has relatively abundant rainfall (18,19). Because of the rare ethnic groups (Bakhtiari), Fars, and Turk living in this region, this cohort is unique in Iran and worldwide (18).

A total of 10075 participants were recruited from the districts of Shahrekord and Ardal, situated in urban (7034 participants) and rural (3041 participants) areas, respectively. The numbers of invited and recruited SCS participants, the area names in these districts and the map of the region are presented on the SCS protocol and website. The formula used for calculating the sample size of the study was described previously in the SCS protocol (18). The inclusion criteria were: being aged between 35 and 70 years at the time of recruitment, having lived in the specified area for at least one year, having completed and signed the informed consent, and having Iranian nationality (i.e., having an Iranian birth certificate and a national identification number) (13,18). People unable to undertake the required questions and measures (e.g., due to disability or mental disorders) were not eligible for the study. The implementation, feasibility, and sampling processes of the SCS were performed in the pre-pilot phase of the study from November 22, 2015, to September 10, 2016. In this phase, the data collection process and biological sample storage capacity were evaluated. Aspects of the regulation of ownership, preservation, and storage of data were also finalized. The pre-pilot phase also allowed i) to evaluate the participants' response rate and the recruitment and training of interviewers, ii) to determine the frequency of participant follow-up contacts, iii) to check the validity of measurements, and iv) to implement effective procedures for bio-sampling and quality control of the collected data. The study protocols were revised accordingly to improve the validity and reliability of the questionnaires and the acceptability of the data collection techniques (13,18). The pilot phase was conducted from October 6, 2016, to December 20, 2016, with the aim to further evaluate the main strengths and weaknesses of the study protocol and participant recruitment process. A total of 1000 participants aged 35–70 years were recruited for this phase. After receiving confirmation from the
quality control team, the main phase, enrolling all participants, started together with the pilot phase on October 6, 2016. The multistage sampling method (stratified proportional cluster sampling) was applied to recruit participants in the SCS in the pilot and main phase. According to the national census statistics, 70% of the CH&B province population lives in urban areas, and 30% live in rural areas, so the urban and rural strata accounted for 70% and 30% of the study sample size, respectively (18). Sampling in urban areas was also carried out using the cluster sampling method. Each of the four areas of Shahrekord county (the capital city of CH&B) was considered as an eligible cluster, and then a specific geographical region of Shahrekord was randomly chosen as the cohort cluster. The population covered by each urban healthcare centers (cluster) were used as sampling weights for recruiting participants from the corresponding (n=77030) health care centers to constitute the final study sample for the urban area (n=7034). For rural areas, the sampling process was as follows: i) nine CH&B counties were considered as eligible clusters, ii) the Ardal county was randomly selected as the cohort cluster, and iii) three of the five rural clusters of the Ardal county were randomly selected for inclusion in the SCS. A total of 3041 participants from these rural areas were recruited based on census-collected information on healthcare coverage provided by the health centers and 'health houses'. The first contact with prospective SCS participants was made through an invitation by phone to eligible people, and this process continued until the required sample size was met. Various initiatives were taken to increase participant enrollment and satisfaction; less than one percent of the people contacted declined to be part of the study and only 20 participants dropped out. Sex- and age-specific proportions of the participants included in the SCS were cross-checked against and found to be in accordance with the national population figures provided by the national census conducted by the Statistical Center of Iran. The distribution of the main sociodemographic characteristics of SCS participants is shown in Table 2.

Measurements

Data collection in SCS used standard PERSIAN cohort questionnaires and protocols (13,18). These questionnaires were used for baseline data collection from 2015 to 2019 and are described in Table 1. In addition to these extensive questionnaires, additional questionnaires unique to SCS were also completed including General Health (22), WHO Quality of Life-BREF (23), Chronic Stressors and Coping Strategies (24), WHO MONICA and the ROSE Angina questionnaire (25), Social Capital (26), Screening Tool for Joint Pain and Musculoskeletal Diseases (27), Health Literacy (28), Oxford Happiness (29), and Oswestry Low Back Pain Disability (30), following SCS protocols (18) in CH&B (Table 1) and additional data unique to SCS were also completed including body composition variables included total body water, body fat mass and percentage, and muscle thickness, which were measured using a body composition analyzer (Tanita, Japan). A spirometry test (pulmonary function test) was performed using the Spirometer device [Spirolab (MIR, Italy)]. An electrocardiography test (ECG) was carried out using an electrocardiogram device (Cardiax®, USA). Physical activity was measured using the general questionnaire and self-reported daily activities were converted to metabolic equivalent rates (METs). Although the validity of these questionnaires was addressed in previous studies (13-15, 18,23,24), SCS's experts further assessed their face validity and approved their use in the pre-pilot phase of the study. In the pre-pilot phase of the SCS, 100 participants completed the questionnaires. The questionnaires had coefficients of Cronbach's alpha
ranging from 82% to 91%, so they were considered to be reliable. A complete description of the questionnaire and information on the selection and training of the interviewers can be found in the SCS protocol (18). The height of participants was measured using a Seca 206 stadiometer. Weights were measured using a Seca analog scale, and standard tape meter was used to measure the participants' wrist, hip, and waist circumferences. Blood pressure and pulse rate measures were obtained using a standard barometer (Richter Japan).

All phases the study and data collection were monitored by a quality control team, including clinicians, a laboratory specialist, two statisticians, and an epidemiologist, under the supervision of the principal investigators.

**Routine (annual) follow-up**

The follow-up process aimed to register new cases of common NCDs and their outcomes, including death, cause of death, and hospital admissions, and to update information on exposures. The SCS focuses primarily on the most common NCDs, including cardiovascular diseases, cancers, and the main endocrine, digestive, hepatic, renal, psychiatric, and respiratory disorders, defined using the International Classification of Diseases 10th version (ICD-10). The annual follow-up of the SCS began in October 2017 and included questionnaires, medical examinations, and linkage with other databases (death, cancer registry). The study follow-up is done on an annual basis through telephone calls and linkage with health databases to identify disease outcomes. More specifically, the follow-up of participants is performed in two forms: an active form including phone interviews and face-to-face interviews (when outcome occurrence), and an inactive form, including self-reports. Identification of outcomes is made through automatic notifications received from the healthcare system and linkage with other health databases such as the National Disease and Health Outcome Registry Systems (13,18). The follow-up is carried out by a team of trained staff under the supervision of an experienced epidemiologist. Outcome assessments, including the cause of death identification, are done by a group of three internal medicine physicians and an experienced epidemiologist. During phone call follow-ups, if an interviewer is not able to gather the requested information, additional phone calls are made during the three consecutive weeks (up to 5 to 6 calls). Additional attempts to collect incomplete data are made during home visits and face-to-face interviews. In rural areas, the data collection process is conducted in local health care units (Health Houses) by health care staff and an experienced epidemiologist. Participants who experience an outcome are invited to undergo an in-person examination. Additional information about the participants' health history is obtained from the Hospital Information System (HIS) and the integrated electronic health system. When a death occurs, the SCS team visits the participant's home and completes an autopsy form. A schematic representation of the phases of the study and the data collection and follow-up process is shown in Figure 1.

**Results**
Of the 10075 participants in the SCS, 5321 (52.8%) were female and 3041 (30.2%) were living in rural areas. The mean age of participants at enrollment was 49.6 years. The proportion of married participants was high (93.8%). While 22.8% of the participants had a bachelor’s degree or higher level of education, 32.7% were illiterate. The main sociodemographic characteristics of participants at baseline are shown in Table 2.

The prevalence of type 2 diabetes mellitus in the SCS was 9.6% and was higher in women (10.7%) than in men (8.8%). The prevalence of hypertension was relatively high and appeared higher in women (20.2%) than in men (13.6%). Non-alcoholic fatty liver disease and thyroid disease were frequent (14.6% and 11.4%, respectively). A history of ischemic heart disease (5.7%), stroke (0.9%), and myocardial infarction (1.3%) was more frequently reported in men than women. All NCDs appeared to be more frequent in urban than rural areas, except gastroesophageal reflux (32.3% in rural and 29% in the urban area) (Table 3). A minority of the participants reported being occasional or regular smokers (15%). The prevalence of overweight and obesity was high (43.5% and 26.9%, respectively). Approximately 57% of the participants had low physical activity levels, particularly women (59%) and participants living in the urban area (66%) (Table 4). The key quantitative physiological variables in terms of mean (standard deviation) were, for BMI: 27.6 (4.6), for systolic blood pressure: 115.4 (17.3) mmHg, for fasting blood glucose: 96.7 (27.3), for total cholesterol: 184.1 (42.8) and for triglyceride: 150.4 (90.5). Additional quantitative variables, such as biochemical and hematological measures are shown in Table 5.

Discussion

The main strength of the study is the collection of a comprehensive set of variables and biological measures in a population including, for the first time, Bakhtiari people (about half of the cohort), and living in the highest-altitude region of Iran. The inclusion of different ethnic groups (Bakhtiari, Fars, and Turk) will allow the comparison of the prevalence and incidence of NCDs across genetic, social, and cultural characteristics of the participants and their interaction with lifestyle and environmental exposures. The SCS biobank provides the infrastructure necessary for the long-term preservation of biological samples (whole blood, blood plasma, hair, nail, and urine), collected in all participants. The SCS, by generating valid and updated information, is also an opportunity for increased cooperation between academic, healthcare and political systems and will permit better planning of health-related programs. It also creates ample opportunities for education and training of students and researchers at the Shahrekord University of Medical Sciences, as well as collaboration with other medical research initiatives such as clinical trials and national and international health research consortia. The SCS study will be limited by the fact that after the enrollment phase, it will not be possible to systematically update the data for measured exposure, in particular for the biological measures. Participants in the SCS were aged 35–70 years at baseline; therefore, it will not be possible to study NCDs in children and young adults, which constitute an essential fraction of the Iranian population. However, after obtaining information in the follow-up process, longitudinal studies and studies of older adults will be possible. Self-reported information on smoking, hookah smoking, alcohol consumption, and intake of drugs may be prone to under-reporting because of the socio-cultural characteristics of the Iranian population.
Abbreviations

NCDs, noncommunicable diseases
WHO, World Health Organization
PERSIAN, Prospective Epidemiological Research Studies in IrAN
CH & B, Chaharmahal and Bakhtiari
M.S., multiple sclerosis
DMFT, Decayed, Missing and Filled Teeth
HIS, Hospital Information System
MOHME, Ministry of Health and Medical Education
MET, metabolic equivalent rates
LDL, low-density lipoproteins
GGT, Gamma-glutamyl transferase
AST, aspartate aminotransferase
ALT, alanine aminotransferase
ALP, alkaline phosphatase
RBC, Red blood cell
WBC, white blood cells

Declarations

Ethics approval and consent to participate: The SCS was approved by the Ministry of Health and Medical Education (approval code: IR.SKUMS.REC.1394.286). All participants provided signed and fingerprinted informed written consent as per the guidelines enforced by the Ethics Committee. The participants can withdraw from the study at any time. Data are stored in an anonymized and confidential database.

Consent for publication: Not applicable.

Availability of data and materials: The SCS data are not open-access, but external investigators may use the data for collaborative projects. Information relative to data access and collaboration can be obtained from the corresponding author Dr. Ali Ahmadi, or at info@persiancohort.com. Suggested projects are first
discussed by SCS principal investigators, and final decision on data sharing for national and international collaborative projects is made by the SCS scientific committee. Further details about the cohort and information relative to data access, collaborative research, and publications can be found at http://persiancohort.com/cohortsites/shahrekord or on the SCS website https://cohort.skums.ac.ir.

Competing interests: None declared.

Funding: This study received financial support from the Deputy of Research and Technology, Ministry of Health and Medical Education of Iran (grant number: 700/12) and from the Shahrekord University of Medical Sciences, Shahrekord, Iran (grant number: 2763 and 1737).

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: AA, HP, MH, SK, AK and MS generated hypotheses for this study. AA, RG, AA and AS performed the laboratory and quality control of field. AA, PAD, AK, SK, RM, HP, and PAD were major contributors to the writing of the manuscript. PAD helped with English language editing of the manuscript. All authors read and approved the final manuscript.

Acknowledgements: The authors would like to thank all interviewers hired for this study. We sincerely thank all the staff who contributed to the design, planning, execution support, and follow-up of the SCS. We appreciate the contribution of the research committee members of the Modeling in Health Research Center, School of Health, Shahrekord University of Medical Sciences, managers, and personnel of health centers in Shahrekord and Ardal. We are grateful to the support from The Iranian Ministry of Health and Medical Education (MOHME) has contributed to the funding used in the PERSIAN Cohort through Grant no. 700/534 and Deputy of Research and Technology of the MOHME and the quality control team of the PERSIAN group involved in the training of participants in the pilot phase.

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**Tables**
| Dimension                       | Number of items | Assessment       | Sample  | Components/ exposures                                                                                                                                 |
|--------------------------------|-----------------|------------------|---------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| General [13, 18]               | 157             | Whole cohort     | 10075   | Age, sex, education, employment status and history, spouse's employment, marital status and number and type of marriages (first-degree or second-degree familial marriage or none); anthropometric measures: weight, height, waist & hip circumference, residence area, domestic and international travels, use of landline and mobile phones, internet access, smoking history; exposure to passive smoking, alcohol consumption, physical activity, sleep duration and quality, daily activities, occupational exposures, cooking and heating fuel, dwelling status, living arrangements, hygiene status of the dwelling and its facilities, drinking water source, history of exposure to animals, agricultural toxins and household pesticides, annual reading rate |
| Nutrition [13]                 | 153             | Whole cohort     | 10075   | Food Frequency Questionnaire (FFQ), including 153 items; dietary habits during the past year and current; food preparation and storage techniques |
| Medical history and examination [13] | 185             | Whole cohort     | 10075   | Current and past medical history, family history of diseases, self-rated health, history of falls and fractures, pain, digestive symptoms, angina, neurologic symptoms, history of transfusion, oral health condition, current use of medications, use of drugs, pulse rate and blood pressure measurement plus complete physical examination. |
| General Health (GHQ12) [22]    | 12              | Subgroup         | 7585    | Psychological distress, social dysfunction, ability to concentrate, sleep deprivation, capable of making decisions, under stress, could not overcome difficulties, enjoying healthy activities, facing up problems, feeling unhappy and depressed, losing confidence, thinking of self as worthless, feeling reasonably happy |
| Quality of Life (WHO-QOL) [23] | 21              | Subgroup         | 7924    | Physical health, mental health, social health, environmental health, self-esteem, interpersonal relationships, sexual activity, social support, home environment, health care, transport, pain, work capacity, mobility, daily activities, leisure activities, financial support, bodily image, security, access to information |
| Dimension                                      | Number of items | Assessment | Sample | Components/ exposures                                                                                                                                 |
|-----------------------------------------------|-----------------|------------|--------|------------------------------------------------------------------------------------------------------------------------------------------------------|
| Chronic stressor and Coping strategies [24]   | 46              | Subgroup   | 6890   | Stress domains consisting of household stress, financial pressure, social relationships, personal and professional conflicts, educational concerns, job security, loss and separation, sexual life, daily life, health concerns, exercising, seeking religious support, focusing on the positive, social distancing, acting out, binge-drinking and binge-eating |
| Modified WHO MONICA [25]                      | 50              | Subgroup   | 7184   | Risk factors and treatment history for coronary heart disease                                                                                          |
| Social capital [26]                           | 44              | Subgroup   | 3080   | Memberships, trust, coherence, ability, value of life, tolerance of diversity, connections, family and friends, neighbors, and work colleagues, community participation, feelings of trust and safety, proactivity |
| Community-oriented program for control of rheumatic diseases [27] | 100             | Subgroup   | 3780   | Work history, pain/tenderness/swelling/stiffness during the last week, functional disability, difficulty in performing specific tasks, treatment and evaluation, pain scale evaluation, history of NSAID/steroid/ DMARD use, disability |
| Health literacy [28]                          | 33              | Subgroup   | 5180   | Access to and understanding of health information sources                                                                                             |
| Happiness [29]                                | 29              | Subgroup   | 1904   | Feeling healthy, feeling attractive, waking up rested, making decisions easily, mentally alert, organized, pleased with self, the cheerful effect on others, happy memories, satisfied with life, feeling happy/joyful, feeling committed and involved |
| Oswestry low back pain [30]                   | 10              | Subgroup   | 4090   | Physical function, role-physical and bodily pain indices, vitality, social function.                                                                  |
Table 2  
Sociodemographic Characteristics of Participants at Baseline of the Shahrekord Cohort Study, by Sex and Residence Area

| Variable                  | Total, N (%) | Sex       | Place of residence | P   | Place of residence | P   |
|---------------------------|--------------|-----------|--------------------|-----|--------------------|-----|
|                           |              | Male (%)  | Female (%)         |     | Urban area (%)     |     |
|                           |              |           |                    |     | Rural area (%)     |     |
| Age group (years)         |              |           |                    |     |                    |     |
| 35–49                     | 5299 (52.6)  | 2398 (50.4) | 2901 (54.5)     | 0.001 | 3770 (53.6) | 1529 (50.3) | 0.001 |
| 40–59                     | 2996 (29.7)  | 1405 (29.6) | 1591 (29.9)     |     | 2091 (29.7)       | 905 (29.8)  |
| 60–70                     | 1780 (17.7)  | 951 (20.0) | 829 (15.6)       |     | 1173 (16.7)       | 607 (20)  |
| Sex                       | 10075 (100)  | 4754 (47.2) | 5321 (52.8)     | -   | 7034 (69.8)       | 3041 (30.2) | -   |
| Ethnicity                 |              |           |                    |     |                    |     |
| Bakhtiari                 | 4869 (48.3)  | 2236 (46.9) | 2643 (49.6)     | 0.001 | 1934 (27.4) | 2945 (96.8) | 0.001 |
| Fars                      | 4102 (40.7)  | 2021 (42.4) | 2088 (39.2)     |     | 4103 (58.2)       | 6 (0.2)    |
| Turk                      | 682 (6.8)    | 349 (7.3)  | 336 (6.3)        |     | 680 (9.6)        | 86 (2.8)   |
| Other                     | 422 (4.2)    | 160 (4/3)  | 262 (4.9)        |     | 336 (4.8)        |     |
| Educational attainment    |              |           |                    |     |                    |     |
| Illiterate                | 3291 (32.7)  | 1001 (21.6) | 2290 (43.7)     | 0.001 | 1335 (19.4) | 1956 (65.6) | 0.001 |
| Primary school            |              |           |                    |     |                    |     |
| Secondary school          | 995 (9.9)    | 560 (12)  | 435 (8.2)        |     | 767 (11.1)       | 228 (7.6)   |
| High school               | 1670 (16.6)  | 924 (19.9) | 749 (14.2)       |     | 1519 (22)        | 151 (5)    |
| Bachelor's degree         | 1878 (18.6)  | 1072 (23.1) | 806 (15.4)     |     | 1821 (26.4)      | 57 (1.9)   |
| Masters / PhD degree      | 423 (4.2)    | 314 (6.8)  | 109 (2.1)        |     | 412 (6.0)       |     |
| Variable          | Total, N (%) | Sex | Place of residence | P  | P  |
|-------------------|--------------|-----|--------------------|----|----|
|                   |              | Male (%) | Female (%) | Urban area (%) | Rural area (%) |
| Marital status    | 169 (1.7)    | 72 (1.5) | 98 (1.8) | 0.001 | 125 (1.8) | 45 (1.5) | 0.001 |
| Single            | 9454 (93.8)  | 4647 (97.7) | 4807 (90.3) | 6672 (94.9) | 2782 (91.5) |
| Married           | 377 (3.7)    | 11 (0.2) | 366 (6.9) | 0.001 | 183 (2.6) | 194 (6.4) |
| Widow             | 75 (0.7)     | 25 (0.5) | 50 (0.9) |
| Divorce           |              | | |
| Employment        | 4720 (46.8)  | 3661 (77) | 1059 (19.9) | 0.001 | 3525 (50.1) | 1195 (39.3) | 0.001 |
| Employed          | 5128 (50.9)  | 955 (20.1) | 4173 (78.4) | 3361 (47.8) | 1767 (58.1) |
| Unemployed        |              | | |
| Health insurance  | 4820 (99.3)  | 2308 (99.1) | 2512 (99.4) | 0.275 | 2959 (98.9) | 1861 (99.9) | <0.001 |
| (yes)             |              | | | | | |

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Table 3
Prevalence of the Main Noncommunicable Diseases (NCD) Self-reported at Baseline of the Shahrekord Cohort Study

| NCD                              | N (%)   | Sex           | P   | Residence Area |   |
|----------------------------------|---------|---------------|-----|----------------|---|
|                                  | Male (%)| Female (%)    |     | Urban (%)       | Rural (%) |
| Type 2 diabetes                  | 968 (9.8)| 408 (8.8)    | 560 (10.7) | 0.002          | 751 (10.9)  |
|                                  |         |              |     |                | 217 (7.2)  |
|                                  |         |              |     |                | < 0.001    |
| Hypertension                     | 1694 (17.1)| 632 (13.6)  | 1062 (20.2) | < 0.001        | 1275 (18.5) |
|                                  |         |              |     |                | 419 (13.9)  |
|                                  |         |              |     |                | < 0.001    |
| Cardiac ischemic disease         | 566 (5.7)| 321 (6.9)    | 245 (4.7)  | < 0.001        | 433 (6.3)   |
|                                  |         |              |     |                | 133 (4.4)   |
|                                  |         |              |     |                | < 0.001    |
| Myocardial infarction            | 127 (1.3)| 100 (2.1)    | 27 (0.5)   | < 0.001        | 111 (1.6)   |
|                                  |         |              |     |                | 16 (0.5)    |
|                                  |         |              |     |                | < 0.001    |
| Stroke                           | 93 (0.9)| 51 (1.1)     | 42 (0.8)   | 0.125          | 65 (0.9)    |
|                                  |         |              |     |                | 28 (0.9)    |
|                                  |         |              |     |                | 0.959      |
| Renal failure                    | 60 (0.6)| 31 (0.7)     | 29 (0.6)   | 0.461          | 48 (0.7)    |
|                                  |         |              |     |                | 12 (0.4)    |
|                                  |         |              |     |                | 0.079      |
| Fatty liver                      | 1476 (14.9)| 542 (11.7)  | 934 (17.8) | < 0.001        | 1231 (17.9) |
|                                  |         |              |     |                | 245 (8.1)   |
|                                  |         |              |     |                | < 0.001    |
| Chronic lung disease             | 410 (4.1)| 183 (3.9)    | 227 (4.3)  | 0.340          | 343 (5.0)   |
|                                  |         |              |     |                | 67 (2.2)    |
|                                  |         |              |     |                | < 0.001    |
| Thyroid disease                  | 1145 (11.6)| 215 (4.6)   | 930 (17.7) | < 0.001        | 976 (14.2)  |
|                                  |         |              |     |                | 169 (5.6)   |
|                                  |         |              |     |                | < 0.001    |
| Kidney stone                     | 2065 (20.8)| 1189 (25.6) | 876 (16.7) | < 0.001        | 1511 (21.9) |
|                                  |         |              |     |                | 554 (18.4)  |
|                                  |         |              |     |                | < 0.001    |
| Rheumatic disease                | 470 (4.7)| 139 (3.0)    | 331 (6.3)  | < 0.001        | 370 (5.4)   |
|                                  |         |              |     |                | 100 (3.3)   |
|                                  |         |              |     |                | < 0.001    |
| Cancer                           | 71 (0.7)| 21 (0.05)    | 50 (1.0)   | 0.003          | 62 (0.9)    |
|                                  |         |              |     |                | 9 (0.3)     |
|                                  |         |              |     |                | 0.001      |
| Gallstone                        | 406 (4.1)| 93 (2.0)     | 313 (6.0)  | < 0.001        | 315 (4.6)   |
|                                  |         |              |     |                | 91 (3.0)    |
|                                  |         |              |     |                | < 0.001    |
| Multiple sclerosis               | 19 (0.2)| 6 (0.1)      | 13 (0.2)   | 0.179          | 17 (0.2)    |
|                                  |         |              |     |                | 2 (0.1)     |
|                                  |         |              |     |                | 0.059      |
| Depression                       | 1610 (16.3)| 432 (9.3)   | 1178 (22.4)| < 0.001        | 1272 (18.4) |
|                                  |         |              |     |                | 338 (11.2)  |
|                                  |         |              |     |                | < 0.001    |
| Gastroesophageal reflux          | 2976 (30.0)| 1229 (26.4) | 1747 (33.2)| < 0.001        | 2003 (29.0) |
|                                  |         |              |     |                | 973 (32.3)  |
|                                  |         |              |     |                | < 0.001    |
Table 4
Prevalence of some NCD Risk Factors at Baseline of the Shahrekord Cohort Study

| Risk factors               | N (%)    | Sex                      | P    | Residence Area    | P    |
|----------------------------|----------|--------------------------|------|-------------------|------|
|                            |          | Male (%)                 | Female (%) |                  |       |
| Tobacco use                |          |                          |      |                   |      |
| Frequent                   | 1275 (12.7) | 1261 (27.1) | 14 (0.3) | 0.001             | 914 (13.3) | 361 (12) | < 0.001 |
| Sometimes                  | 271 (2.7)  | 267 (5.7) | 4 (0.1) |                   | 234 (3.4) | 37 (1.2) |           |
| Use of alcohol (yes)       | 1658 (16.5) | 1562 (33.6) | 96 (1.8) | 0.001             | 1365 (19.8) | 293 (9.7) | < 0.001 |
| Use of hookah (yes)        | 2141 (21.6) | 1680 (36.1) | 461 (8.8) | < 0.001           | 1679 (24.4) | 462 (15.3) | < 0.001 |
| Use of opium (yes)         | 1587 (16.0) | 1472 (31.6) | 115 (2.2) | < 0.001           | 1003 (14.5) | 584 (19.4) | < 0.001 |
| Physical activity (MET)    |          |                          |      |                   |      |
| Low (< 40.4)               | 5744 (57.0) | 2612 (54.9) | 3132 (58.8) | < 0.001           | 4639 (65.9) | 1105 (36.3) | < 0.001 |
| High (≥ 40.4)              | 4331 (43.0) | 2142 (45.1) | 2189 (41.2) |                   | 2395 (34.1) | 1936 (63.7) |           |
| Body mass index            |          |                          |      |                   |      |
| Underweight (< 18.5)       | 123 (1.2)  | 80 (1.7) | 43 (0.8) | < 0.001           | 61 (0.9)  | 62 (2.0) | < 0.001 |
| Normal (18.5–24.9)         | 2781 (27.8) | 1588 (33.8) | 1193 (22.5) |                   | 1706 (24.5) | 1075 (35.5) |           |
| Overweight (25-29.9)       | 4384 (43.8) | 2188 (46.6) | 2196 (41.4) |                   | 3238 (46.5) | 1146 (37.8) |           |
| Obese (≥ 30)               | 2710 (27.1) | 844 (18.0) | 1866 (35.2) |                   | 1964 (28.2) | 746 (24.6) |           |
| Hypercholesterolemia (≥ 240) | 879 (8.9)  | 329 (7.1) | 550 (10.5) | < 0.001           | 710 (10.3) | 169 (5.8) | < 0.001 |
| Hypertriglyceridemia (≥ 150) | 3876 (39.4) | 2147 (46.5) | 1729 (33.1) | < 0.001           | 3225 (46.7) | 651 (22.2) | < 0.001 |
| High LDL                   | 1915 (19.6) | 743 (16.3) | 1172 (22.6) | < 0.001           | 1384 (20.2) | 531 (18.2) | 0.018 |

aMET, metabolic equivalent rates
bhigh blood cholesterol
chigh fasting plasma triglyceride
dLDL, low-density lipoproteins
Table 5
Distribution of the Key Quantitative Physiological Variables measured at Baseline of the Shahrekord Cohort Study.

| Variable                    | Total       | Sex                        | P       | Residence Area | P       |
|-----------------------------|-------------|----------------------------|---------|----------------|---------|
|                             | Total       | Male (%)                   | Female (%) |                 | Urban (%) | Rural (%) |
| Weight (kg)                 | 73.4 ± 13.4 | 77.3 ± 13.4                | 70.0 ± 12.4 | < 0.001         | 75.5 ± 13.0 | 68.7 ± 13.2 | < 0.001 |
| Height (cm)                 | 163.2 ± 9.6 | 170.7 ± 6.7                | 156.5 ± 6.1 | < 0.001         | 164.6 ± 9.5 | 159.9 ± 9.0 | < 0.001 |
| Body mass index (kg/m2)     | 27.6 ± 4.6  | 26.5 ± 4.1                 | 28.6 ± 4.9 | < 0.001         | 27.9 ± 4.5 | 26.9 ± 4.9 | < 0.001 |
| Wrist circumference (cm)    | 17.4 ± 1.4  | 18.0 ± 1.2                 | 16.8 ± 1.3 | < 0.001         | 17.3 ± 1.4 | 17.5 ± 1.4 | < 0.001 |
| Waist circumference (cm)    | 94.8 ± 11.4 | 93.9 ± 10.6                | 95.7 ± 12.0 | < 0.001         | 95.1 ± 10.8 | 94.2 ± 12.6 | 0.001  |
| Hip circumference (cm)      | 101.1 ± 7.9 | 99.7 ± 6.9                 | 102.3 ± 8.6 | < 0.001         | 101.9 ± 7.7 | 99.3 ± 8.2 | < 0.001 |
| Teeth number (n)            | 18.2 ± 9.7  | 17.7 ± 10.0                | 18.7 ± 9.3 | < 0.001         | 19.4 ± 9.9 | 15.6 ± 8.6 | < 0.001 |
| Decayed teeth (n)           | 1.2 ± 2.1   | 1.3 ± 2.4                  | 1.1 ± 1.8 | < 0.001         | 1.3 ± 2.3 | 1.0 ± 1.6 | < 0.001 |
| Missing teeth (n)           | 13.5 ± 9.8  | 14.0 ± 10.2                | 13.0 ± 9.5 | < 0.001         | 12.4 ± 10.0 | 16.0 ± 8.8 | < 0.001 |
| Filled teeth (n)            | 3.4 ± 4.4   | 2.9 ± 4.1                  | 3.8 ± 4.7 | < 0.001         | 4.5 ± 4.7 | 0.8 ± 2.0 | < 0.001 |
| Systolic blood pressure (mmHg) | 115.4 ± 17.3 | 117.9 ± 16.6                | 113.2 ± 17.7 | < 0.001         | 117.0 ± 16.8 | 111.7 ± 17.8 | < 0.001 |
| Diastolic blood pressure (mmHg) | 75.5 ± 10.7 | 77.4 ± 10.6                | 73.9 ± 10.4 | < 0.001         | 76.3 ± 10.8 | 73.8 ± 10.1 | < 0.001 |
| Fasting blood sugar (mmol/L) | 96.7 ± 27.3 | 97.4 ± 26.3                | 96.1 ± 28.1 | 0.019           | 102.0 ± 27.5 | 84.1 ± 22.4 | < 0.001 |
| Hemoglobin (g/dl)           | 14.5 ± 1.6  | 15.6 ± 1.3                 | 13.6 ± 1.3 | < 0.001         | 14.6 ± 1.6 | 14.4 ± 1.6 | < 0.001 |
| Hematocrit (L/L)            | 42.0 ± 4.4  | 44.8 ± 3.5                 | 39.6 ± 3.5 | < 0.001         | 42.3 ± 4.3 | 41.5 ± 4.4 | < 0.001 |

Abbreviations: GGT, Gamma-glutamyl transferase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; RBC, Red blood cell; WBC, white blood cells
| Variable      | Total      | Sex                             | P    | Residence Area | P    |
|---------------|------------|---------------------------------|------|---------------|------|
|               |            | Male (%)                        | Female (%) |                  | Urban (%) | Rural (%) | P    |
| GGT (U/L)     | 27.0 ± 24.6| 32.1 ± 29.0                     | 22.5 ± 19.0 | < 0.001        | 28.4 ± 26.5 | 23.8 ± 19.3 | < 0.001 |
| AST (U/L)     | 19.6 ± 8.8 | 21.2 ± 9.7                      | 18.3 ± 7.5 | < 0.001        | 19.6 ± 9.0 | 19.6 ± 8.1 | 0.981  |
| ALT (U/L)     | 22.0 ± 14.4| 26.3 ± 16.5                     | 18.3 ± 11.1 | < 0.001       | 23.3 ± 15.2 | 19.1 ± 12.0 | < 0.001 |
| ALP (U/L)     | 205.0 ± 65.3| 207.6 ± 66.7                   | 202.7 ± 63.9 | < 0.001       | 206.8 ± 66.6 | 201.0 ± 61.9 | < 0.001 |
| RBC (million/mm3) | 4.8 ± 0.5 | 5.0 ± 0.5                     | 4.5 ± 0.5 | < 0.001       | 4.8 ± 0.5 | 4.7 ± 0.5 | < 0.001 |
| WBC (mm3)     | 6.0 ± 1.5 | 6.2 ± 1.6                      | 5.9 ± 1.4 | < 0.001       | 6.0 ± 1.5 | 6.0 ± 1.5 | 0.195  |

Abbreviations: GGT, Gamma-glutamyl transferase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; RBC, Red blood cell; WBC, white blood cells