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ORIGINAL ARTICLE

Pars cohort study of non-communicable diseases in Iran: protocol and preliminary results

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Abstract
Objectives The pars cohort study (PCS) is a 10-year cohort study aiming to investigate the burden and the major risk factors of non-communicable diseases, and to establish a setting to launch interventions for prevention of these diseases and controlling their risk factors.
Methods All inhabitants of Valashahr district in South of Iran, aged 40–75 years, were invited to undergo interviews and physical examination, and to provide biological samples. A total of 9264 invitees accepted to participate in the study (95 % participation rate) and were recruited from 2012 to 2014. Active follow-up was also carried out after 12 months.
Results About 46 % of participants were male and 54 % were female. About 14.0 % of the participants were current smokers and 8.4 % were ever opium users. The prevalence of overweight and obesity were 37.3 and 18.2 %, respectively. The prevalence of hypertension was 26.9 %. A total of 49 participants died during a median follow-up of one year.
Conclusions PCS with its large scale and wealth of socio-economic and medical data can be a unique platform for studying the etiology of non-communicable diseases and effective interventions in Iran.

Keywords Non-communicable diseases · Risk factors · Cohort studies · Epidemiology · Iran

Introduction

Worldwide, based on the report of the global burden of disease (GBD) study, non-communicable diseases (NCDs) comprised 57 % of all deaths in 1990, which increased to 70 % in 2013 (GBD Collaborators 2015a). Ischemic heart disease and cerebrovascular accidents were the top causes of death across the globe in 2013. The share of NCDs in

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global disability (in terms of years of life lost due to disability) has also increased from 76 % in 1990 to 82 % in 2013 (GBD Collaborators 2015a, b; Fitzmaurice et al. 2015; Murray et al. 2015).

In Iran as well, ischemic heart disease was the first cause and stroke was the 5th cause of death in 2013. Overall, 292 thousand deaths have occurred in Iran in 2013, out of which about 46 % were caused by circulatory diseases and about 17 % by cancers. There is a sharp increase in prevalent cases from 1990 to 2013 (GBD Collaborators 2015a, b; Fitzmaurice et al. 2015; Murray et al. 2015).

At sub-national level, however, there are scarce population-based studies on prevalence of main NCDs and their risk factors. Apart from the cross-sectional prevalence, investigating the trend and prognosis of NCDs and their risk factors is mandatory as well. It can only be done within the setting of prospective studies. Population-based longitudinal studies are not numerous in Iran (Azizi et al. 2000; Gharipour et al. 2015; Najafipour et al. 2012; Rabiei et al. 2009). The results of these studies revealed a high prevalence of CVDs and metabolic diseases in both urban and rural settings. The major risk factors of CVDs were unhealthy diet, overweight and obesity, high blood pressure, high blood glucose, and high cholesterol. A high prevalence of metabolic syndrome was reported among adult participants in these studies.

Golestan cohort study (GCS) is by far the largest prospective study in the entire country and even in the Middle East region. A total of 50,045 participants from rural and urban areas in the province of Golestan have been recruited from 2004 to 2008. The details have been described elsewhere (Pourshams et al. 2010). The methods and instruments used in this study have been validated and the feasibility and reliability have been extensively investigated in a comprehensive pilot study (Abnet et al. 2004; Khademi et al. 2010; Malekshah et al. 2006). The GCS was originally designed to investigate upper gastrointestinal cancers in the Northeast of Iran, in which the rates were considerably high (Islami et al. 2004; Kamangar et al. 2007; Pourshams et al. 2005). Numerous publications showed the main risk factors of cancers in the province of Golestan (Etemadi et al. 2013; Hashemian et al. 2015; Islami et al. 2009a, b; Khademi et al. 2012; Malekzadeh et al. 2013b; Nasrollahzadeh et al. 2008; Shakeri et al. 2012, 2013a, b; Zamani et al. 2013). However, later results indicated a high burden of CVDs, diabetes, chronic kidney disease, and their risk factors in the area (Bahrami et al. 2006; Etemadi et al. 2014; Garg et al. 2015; Golozar et al. 2011; Islami et al. 2013; Malekzadeh et al. 2013a; Najafi et al. 2010, 2012; Sepanlou et al. 2015a, b). The results demonstrate that over 80 % of all deaths in GCS are due to NCDs, out of which 46 % is due to CVDs and 14 % due to cancers (Fig. 1, unpublished data). Subsequently, several interventional studies for prevention and control of CVDs and their risk factors have been designed and conducted in the setting of GCS. The main intervention investigated in GCS is the effectiveness of a fixed-dose pharmacotherapy (Polypill) in the prevention of CVDs. (Majed and Moradmand Badie 2011; Malekzadeh et al. 2010; Ostovaneh et al. 2014).

To the best of our knowledge, no population-based prospective study on NCDs has been established in the South of Iran so far. Pars cohort study (PCS) was established in 2012. The methods of baseline data definition and collection, and follow-up methods have been largely adopted from GCS. Similarly, interventional studies are designed to investigate the cost-effectiveness of Polypill and the predictive performance of clinical and imaging risk scores. Pars cohort study can be a platform for further nested case–control studies and trials and also for strengthening the research network in the area.

Methods

PCS was developed by the joint collaboration of research teams from Non-Communicable Disease Research Center (NCDRC) in Shiraz University of Medical Sciences (SUMS) and Digestive Diseases Research Institute (DDRI) in Tehran University of Medical Sciences.

The study protocol and the informed consent used for this investigation were approved by the ethical review committees of DDRI and the SUMS. The informed consent form was completed and signed in the presence of other visitors (third party). These forms and the questionnaires are kept in a secure and safe place. The questionnaires are also available with the online version of the article.

The project was operated by a 13-member team in pars cohort study center (PCSC), including general practitioners, nurses, and nutritionists to work on the food frequency questionnaire (FFQ), lab technicians, data entry team, and receptionists in Valashahr and the nearby villages, in southern Fars Province starting in fall, 2012.

Participants

The district of Valashahr has an area of 1650 km^2 and over 40,000 inhabitants mainly of Fars or Azari ethnicities and sparsely of other ethnicities. The district consists of five counties and the city of Valashahr. There are five health centers in the area supervising 31 health houses and covering a total of 93 villages. Each health house is staffed by two community health workers named “Behvarz”. These community health workers were originally responsible for vaccination, family planning, and primary health care mainly for communicable diseases. Behvarz are basically

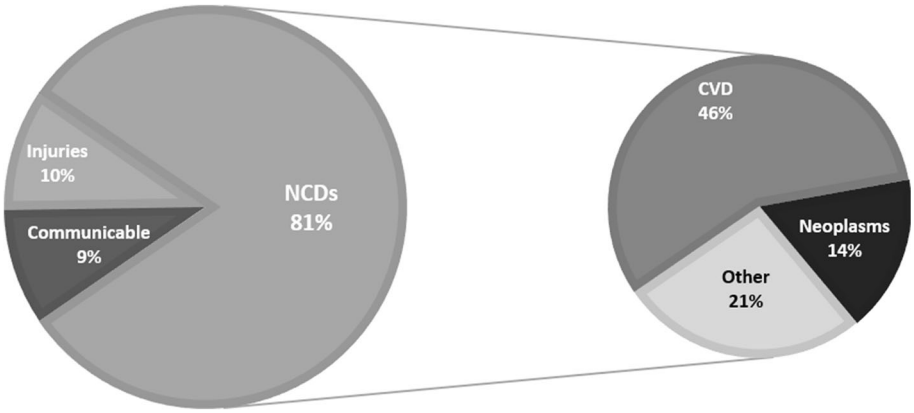

Fig. 1 Deaths by cause in Golestan Cohort Study from 2005 to the end of 2014. *NCD* non-communicable disease, *CVD* cardiovascular disease

responsible for completion of the vital horoscope, which is a data source designed to record and display vital events such as births and deaths and family planning within the area covered by the health house and health centers. Behvarz conduct a census in the catchment area of the health house and the final data are recorded in the vital horoscope chart and finally entered into a computerized database and transferred to the Ministry of Health in Tehran. As Behvarz are native, acquainted with residents and can communicate effectively with them, they were the best choice for the conduct of this study. All Behvarz were trained to participate in the implementation of this study and the follow-up.

The sample of this study consisted of all eligible people, both healthy and those with any kind of disease, in the city of Valashahr and the nearby villages. First, the list of participants with their home and cell phone numbers were acquired through 31 health houses and health centers in the region. Then, based on the catchment area of health houses, the district was divided into sub-regions. In the villages, Behvarz', who had been trained for the project, contacted all eligible household members and thoroughly explained the purpose and procedure of the study to them. Likewise, an expert local health professional contacted all eligible household members aged between $\geq$40 and $\leq$75 in Valashahr and thoroughly explained the purpose and procedure of the study to them. As the staffs were native residents, people knew them and discussed any issue that might cause ambiguity.

All residents of the district between 40 and 75 years old were contacted over the phone and invited. Totally 9721 residents were invited among whom, a total of 9264 subjects (95 %) referred to the pars cohort study center (PCSC) for interview and limited physical examination, and provided biological samples. The response rate was higher among the rural inhabitants (around 97 %), which is explained by the proximity of their workplace to their residence in agricultural occupations, and their flexible working hours. The only exclusion criteria for participants who accepted the invitation and referred to PCSC were unwillingness to participate after the process of the study was explained or being a temporary resident. However, no one needed to be excluded.

Recruitment took place at the PCSC that was established for this project in Valashar, in close contact with the 31 health houses in the region. Every day 20 participants were invited to attend the PCSC early in the morning for the tests. They were informed on the previous day through telephone, cell phone or by the Behvarz' in the health houses. Participants were asked to fast for about 12 h preceding their attendance in the center. The center indeed provided a van and a driver, to either take the team to places where the participants had difficulty attending the center or to bring the participants to the center for tests, however the farthest place was only 40 km away from the center and the participants themselves willingly wanted to attend the center, there was no need to use the van.

Before enrolment of the invited participants, their identity was verified by checking their identity cards by the receptionist and a signed written consent was obtained. In case the participant was illiterate, the study was explained again and they could have the opportunity to observe the enrolment procedure in the PCSC, and to participate in the study if they were willing. A personal cohort identification card and a unique code were assigned to each participant.

Data entry was completed by expert computer operators, who were trained to appropriately use the software designed for the study.

Selected demographic characteristics of the study population are reported in Table 1. A total of 9264 participants were ultimately recruited in PCS. The sample constitutes of 4276 men (46.2 %) and 4988 women (53.8 %). The mean age among the total sample, men, and women were 52.6 $\pm$ 9.7, 52.7 $\pm$ 9.9, and 52.6 $\pm$ 9.5 years, respectively. A total of 8212 participants (88.6 %) were married, 56.3 % were Fars, 38.8 % were Azari, and 49.0 % were illiterate.

Table 1 Summary statistics for demographic characteristics and life style of participants in Pars Cohort Study, Pars province, Iran, 2014

	Total	Men	Women	*p* value
	9264 (100 %)	4276 (46.2 %)	4988 (53.8 %)	
Age range				
40–49	4218 (45.5)	1933 (45.2)	2285 (45.8)	0.451
50–59	2810 (30.3)	1354 (31.7)	1456 (29.2)	
60+	2236 (24.2)	989 (23.1)	1247 (25.0)	
Marital status				
Married	8212 (88.6)	4174 (97.6)	4038 (81.0)	<0.001
Non-married	1052 (11.4)	102 (2.4)	950 (19.0)	
Ethnicity				
Fars	5217 (56.3)	2368 (55.4)	2849 (57.1)	0.130
Turk	3596 (38.8)	1697 (39.7)	1899 (38.1)	
Other	451 (4.9)	211 (4.9)	240 (4.8)	
Education				
Illiterate	4545 (49.0)	1340 (31.3)	3205 (64.2)	<0.001
≤5 years	2731 (29.5)	1188 (27.8)	1543 (30.9)	
6–8 years	974 (10.5)	811 (19.0)	163 (3.3)	
High school	733 (7.9)	674 (15.8)	59 (1.2)	
University	281 (3.1)	263 (6.1)	18 (0.4)	
Wealth score				
Quintile 1	2176 (23.5)	864 (20.2)	1312 (26.3)	<0.001
Quintile 2	1562 (16.9)	689 (16.1)	873 (17.5)	
Quintile 3	2004 (21.6)	920 (21.5)	1084 (21.7)	
Quintile 4	1657 (17.9)	816 (19.1)	841 (16.9)	
Quintile 5	1865 (20.1)	987 (23.1)	878 (17.6)	
Physical activity				
Low	3061 (33.0)	1035 (24.2)	2026 (40.6)	<0.001
Medium	3056 (33.0)	1173 (27.4)	1883 (37.8)	
High	3147 (34.0)	2068 (48.4)	1079 (21.6)	
Smoking (now)				
No	7967 (86.0)	3014 (70.5)	4953 (99.3)	<0.001
Yes	1297 (14.0)	1262 (29.5)	35 (0.7)	
Tobacco (ever)				
No	7346 (79.3)	2403 (56.2)	4943 (99.1)	<0.001
Yes	1918 (20.7)	1873 (43.8)	45 (0.9)	
Opium use (ever)				
No	8490 (91.6)	3534 (82.6)	4956 (99.4)	<0.001
Yes	774 (8.4)	742 (17.4)	32 (0.6)	
Alcohol use (ever)				
No	9068 (97.9)	4110 (96.1)	4958 (99.4)	<0.001
Yes	196 (2.1)	166 (3.9)	30 (0.6)	

Follow-up

We have planned to continue the follow-up of PCS for at least 10 years from 2012. The follow-up form is completed for all participants annually. This form includes 40 items including the unique identification code, name, contact information of the participants (and two of his family members or close friends), migration, vital status, and history of disease incidence and/or hospitalization. The follow-up is carried out actively by calling the participants through telephone. If the participants are not accessible after 7 attempts, the Behvarz' in rural areas and the PCS team in urban areas visit the participants at their home.

After successful contact, the follow-up form will be completed through conversation over the phone, in which the vital status, the occurrence of any major disease, or hospitalization will be recorded. Participants are also questioned about their probable intent for changing their address or emigration in near future.

If a participant dies, the PCS team visits the participant's home and completes a verbal autopsy form. This form has been already validated in GCS with the overall multi-rater agreement across four reviews of 0.84 (95 % CI: 0.78–0.89) (Khademi et al. 2010). The form includes 25 items, which refer to the cause of death according to the respondents' report about signs and symptoms. In case other medical documents are available, including hospital reports or any paraclinical medical documents regarding diagnostic or therapeutic procedures, all will be scanned and filed.

If the participant is alive and reports occurrence of any major disease or hospitalization, the documents are likewise gathered and filed.

Three types of outcomes are assessed in PCS: death, hospitalization, and occurrence of major diseases (CVDs and cancers). For case confirmation, two separate internists independently review the existing documents and allocate an ICD-10 code and date of occurrence or death to each participant. If the two codes differ, a third more senior internist reviews the documents and makes a final diagnosis.

Data collection

The three categories of data collection included: (1) self-reported data, which was recorded using structured general and food frequency questionnaires (FFQ); (2) limited Physical examination; (3) biological samples (blood, urine, hair and nail) collection;

Bio-specimen collection

After the enrolment, based on the specified checklist, the following samples were taken: Blood samples (15 ml), Urine samples (4 ml), hair and a nail sample

Blood drawing was carried out using EDTA-Tube and clot 9 ml (Venoject tube). We used Auto analyzer, model BT1500, and the kits made by Pars Azmoon Company (Iran) to measure blood biochemical parameters including fasting blood sugar (FBS), total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), Alanine Aminotransferase (ALT), Asparagine Aminotransferase (AST), Alkaline Phosphatase, Gamma Glutamyl Transpeptidase, urea, and creatinine. The standards established by the company were indeed strictly followed. To measure complete blood count (CBC), we used a cell counter device (Nihon Kohden, model Alpha cell-tac made in Japan).

10 ml of each blood sample was centrifuged and separated into buffy coat, plasma, serum and red blood cells, stored in color-coded 1.8 ml tubes at –70 °C for further supplementary tests. 3 ml of blood serum and 4 ml of the urine were also stored at −20 °C. The hair and nail samples were stored at room temperature with a unique code for each participant.

Self-reported data

After the biosamples collection, the participants were given a simple breakfast. Having had the breakfast, participants were invited for interview. Interviewers were local physicians and well trained nurses and in the case of dietary interviews, nutritionists who were trained for this purpose. The interview was conducted in the local Persian language for Fars participants and in Azari language for Turks. It took about 1 h for every participant to complete all of the questionnaires.

The general questionnaire included 187 items. These included the identity information such as name and contact information of the participant and his or her family members and friends. The structured questionnaire was used to collect the following data:

Demographic: sex, age, residence, ethnicity, marital status, education, socio-economic status.
Life style: physical activity, tobacco smoking, opium consumption, alcohol consumption, oral health.
Disease history: heart disease, stroke, hypertension, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, liver disease, tuberculosis, malaria, mental diseases, musculoskeletal disease, surgery, blood transfusion.
Family history
Medication history: antihypertensive, glucose and lipid lowering medications, aspirin, antibiotics, mental, etc.
Food frequency Questionnaire: the food frequency questionnaire also included 183 items and was completed by nutrition assistants asking the participants relevant questions on their diet and eating habits. To make the participants understand the questions well and provide more accurate and precise answers, the assistants made use of food albums, and some scales such as cups, different types of spoons, matchboxes and 10 × 10 sheets of cardboard (Malekshah et al. 2006).

Physical examination

Physicians and nurses did the physical exam. The physical examination included anthropometric measurements (height, weight, waist, and hip), checking systolic and diastolic blood pressure, measurement of pulse rate, and oral examination. The blood pressure was measured in

sitting position after 5 min of rest. Measurement was carried out twice from each arm with an interval of about 2 min. Finally, a pictogram was used to record the body shape perceived by the participants at years 15 and 30 and at the present time. Physical examination was completed based on standards of Golestan Cohort Study (Pourshams et al. 2010) which is itself based on World Health Organization STEPwise approach to NCD risk factor surveillance (WHO 2004).

In the end, pamphlets about prevention of cardiovascular disorders, diabetes, cancers, and other chronic diseases were given to all participants. A copy of the lab test report was ready to be given to participants and if there was any important abnormality in lab results, participants were referred to their family physician. Additionally, all participants were instructed to report or refer to PCSC in case a major disease develops.

Access to data

Information about the study design, ongoing sub-studies and relevant future publications can be accessible at www.sums.ac.ir. Proposals are welcome and should be submitted to R.M. (malek@ams.ac.ir). Proposals will be discussed in the steering committee, which consists of principal investigators and other experts.

Results

Demographic and life style determinants are demonstrated in Table 1, anthropometric indices and blood pressure in Table 2, past medical history in Table 3, and metabolic syndrome and its components in Table 4.

A total of 1297 participants (14.0 %) were current smokers, 1918 (20.7 %) ever smokers, 774 (8.4 %) ever opium users, and 196 (2.1 %) ever alcohol users. The mean BMI was 25.9 ± 4.7 kg/m^2. About 37.3 % of participants are overweight and 18.2 % are obese. Mean SBP was 112.0 ± 19.0 and mean DBP was 73.5 ± 11.9 mmHg. A total of 2489 participants (26.9 %) were hypertensive in its classical definition (SBP/DBP ≥ 140/90 mmHg or being under treatment for hypertension). However, the prevalence of hypertension based on self-report was 16.3 %. The prevalence of heart disease and stroke were 10.4 and 1.8 %, respectively. The prevalence of metabolic syndrome was 26.4 and 25.7 % based on the definition of Adult Treatment Panel III (ATP III) and International Diabetes Federation (IDF), respectively.

In comparing men and women, men were more probable to be married, had higher education, were wealthier, were physically more active, smoked and used opium and alcohol more frequently, were leaner, and had lower SBP than women. The prevalence of self-reported hypertension, diabetes, heart disease, and metabolic syndrome were lower in men while there was no difference in the prevalence of stroke and cancers.

The mortality follow-up data are demonstrated in Table 5. Overall, 49 participants have died during the median follow-up duration of one and a half years. Myocardial infarction accounts for almost half of the deaths. Next are cerebrovascular accidents, colorectal cancer, stomach cancer, and traffic accidents. The number of deaths in men is over double that in women.

Discussion

What is already known and what this study adds

Iran is experiencing an era of demographic, epidemiologic, socio-economic, life style, and dietary transition.

Table 2 Anthropometric indices and blood pressure in participants of Pars Cohort Study, Pars province, Iran, 2014

	Total	Men	Women	*p* value
Mean BMI (SD)	25.9 (4.7)	24.4 (4.1)	27.1 (4.8)	<0.001
BMI number (%)				
Underweight	725 (7.9)	504 (11.8)	221 (4.4)	<0.001
Normal	3376 (36.6)	1938 (45.5)	1438 (29.0)	
Overweight	3442 (37.3)	1428 (33.6)	2014 (40.6)	
Obese	1675 (18.2)	386 (9.1)	1289 (26.0)	
Mean SBP (SD) mmHg	112.0 (19.0)	111.5 (17.9)	112.4 (19.9)	0.033
Mean DBP (SD) mmHg	73.5 (11.9)	73.7 (11.7)	73.3 (12.0)	0.066
Hypertension number (%)				
No	6775 (73.1)	3350 (78.3)	3425 (68.7)	<0.001
Yes	2489 (26.9)	926 (21.7)	1563 (31.3)	

BMI body mass index in kg/(m^2), *SD* standard deviation

Table 3 Past medical history in participants of Pars Cohort Study, Pars province, Iran, 2014

	Total	Men	Women	*p* value
Hypertension				
No	7751 (83.7)	3853 (90.1)	3898 (78.1)	<0.001
Yes	1513 (16.3)	423 (9.9)	1090 (21.9)	
Diabetes				
No	8390 (90.6)	4003 (93.6)	4387 (88.0)	<0.001
Yes	874 (9.4)	273 (6.4)	601 (12.0)	
Heart disease				
No	8303 (89.6)	3872 (90.5)	4431 (88.8)	0.007
Yes	961 (10.4)	404 (9.5)	557 (11.2)	
Stroke				
No	9098 (98.2)	4201 (98.2)	4897 (98.2)	0.799
Yes	166 (1.8)	75 (1.8)	91 (1.8)	
Cancer				
No	9157 (98.8)	4221 (98.7)	4936 (99.0)	0.274
Yes	107 (1.2)	55 (1.3)	52 (1.0)	

Prospective studies are the best types to investigate and follow these transitions and their impacts on health. The unprecedented population-based pars cohort study (PCS) with its large scale, high response rate, high quality data collection methods, and precise follow-up, in an area with multiple ethnicities, cultures, and socio-economic status in a developing country provides the setting for studying etiologies of NCDs and facilitates experimental studies on prevention and control. The biobank generated in this study makes future studies on biomarkers and genetic susceptibility possible. The results of the study will help policy makers to design and implement cost-effective service packages within the setting of primary health care network in Iran, which can serve as an example for neighboring countries.

The initial results of PCS demonstrate the danger of an epidemic of NCDs and their risk factors among Iranians and especially among women. Unhealthy life style including physical inactivity, smoking, opium and alcohol use is very common in this area of Iran. Unlike the high prevalence of smoking and opium and alcohol use among men, physical inactivity is more frequent among women and as a result, BMI is higher among women and overweight and obesity are more prevalent. Central obesity and hypertension are specifically very common among women. Women are also more prone to hypertension, diabetes, and to overall clustering of components of metabolic syndrome,

Table 4 Metabolic syndrome and its components based on two main definitions in participants of Pars Cohort Study, Pars province, Iran, 2014

	Adult treatment panel (ATP) definition			International diabetes federation (IDF) definition		
	Total (%)	Men (%)	Women (%)	Total (%)	Men (%)	Women (%)
Central obesity						
No	5440 (59.0)	3752 (88.2)	1688 (34.0)	4314 (46.8)	2352 (55.3)	1962 (39.5)
Yes	3778 (41.0)	504 (11.8)	3274 (66.0)	4904 (53.2)	1904 (44.7)	3000 (60.5)
High fasting blood sugar						
No	5322 (57.5)	2530 (59.3)	2792 (56.1)	5617 (60.7)	2679 (62.8)	2938 (59.0)
Yes	3927 (42.5)	1738 (40.7)	2189 (43.9)	3632 (39.3)	1589 (37.2)	2043 (41.0)
High triglycerides						
No	5621 (60.8)	2650 (62.1)	2971 (59.7)	5656 (61.2)	2668 (62.5)	2988 (60.0)
Yes	3628 (39.2)	1618 (37.9)	2010 (40.3)	3593 (38.8)	1600 (37.5)	1993 (40.0)
Low high density lipoprotein						
No	7876 (85.2)	3899 (91.4)	3977 (79.8)	7876 (85.2)	3899 (91.4)	3977 (79.8)
Yes	1373 (14.8)	369 (8.6)	1004 (20.2)	1373 (14.8)	369 (8.6)	1004 (20.2)
High blood pressure						
No	6273 (67.8)	3091 (72.4)	3182 (63.8)	6444 (69.6)	3163 (74.0)	3281 (65.8)
Yes	2984 (32.2)	1181 (27.6)	1803 (36.2)	2813 (30.4)	1109 (26.0)	1704 (34.2)
Metabolic syndrome						
No	6792 (73.6)	3681 (86.4)	3111 (62.6)	6832 (74.3)	3405 (80.2)	3427 (69.2)
Yes	2435 (26.4)	579 (13.6)	1856 (37.4)	2369 (25.7)	843 (19.8)	1526 (30.8)

Differences in prevalence of metabolic syndrome and all of its components were significant between men and women (*p* values <0.05)

Table 5 Mortality by cause in Pars Cohort Study, Pars province, Iran, 2012–2014

Mortality by cause	Men *N* (%)	Women *N* (%)	Total *N* (%)
Myocardial infarction	16 (45.7 %)	7 (50.0 %)	23 (46.9 %)
Cerebrovascular accident	2 (5.7 %)	1 (7.1 %)	3 (6.1 %)
Colorectal cancer	2 (5.7 %)	1 7.1 %)	3 (6.1 %)
Stomach cancer	3 (8.6 %)	0 (0 %)	3 (6.1 %)
Traffic accidents	3 (8.6 %)	0 (0 %)	3 (6.1 %)
Chronic kidney disease	1 (2.9 %)	1 (7.1 %)	2 (4.1 %)
Prostate cancer	2 (5.7 %)	0 (0 %)	2 (4.1 %)
Leukemia	2 (5.7 %)	0 (0 %)	2 (4.1 %)
Sepsis	1 (2.9 %)	0 (0 %)	1 (2.0 %)
Brain tumor	0 (0 %)	1 (7.1 %)	1 (2.0 %)
Pregnancy	0 (0 %)	1 (7.1 %)	1 (2.0 %)
Suicide	1 (2.9 %)	0 (0 %)	1 (2.0 %)
Asthma	0 (0 %)	1 (7.1 %)	1 (2.0 %)
Esophageal cancer	1 (2.9 %)	0 (0 %)	1 (2.0 %)
Breast cancer	0 (0 %)	1 (7.1 %)	1 (2.0 %)
Lower respiratory infection	1 (2.9 %)	0 (0 %)	1 (2.0 %)
Total	35 (100 %)	14 (100 %)	49 (100 %)

which subsequently makes them prone to heart disease. However, the occurrence of stroke and cancers doesn't seem to be different between men and women. An interesting finding, however, is the lower prevalence of underweight among women, which may be explained by the effective reproductive health care.

There is a difference between the two main definitions of the metabolic syndrome. Based on the definition of Adult Panel Treatment (ATP) for metabolic syndrome, 13.6 % of men and 37.4 % of women are affected, while the respective figures for the definition of International Diabetes Federation (IDF) are 19.8 and 30.8 %. Therefore, the difference between men and women based on IDF definition is less. The difference between the two definitions is mainly due to differential definition of central obesity. Existing evidence on an effective threshold for defining central obesity in men and women in Iran is quite controversial and there is no general agreement on the best threshold. Validation studies are required to define the best cut-off for waist circumference at national level. Previous reports have defined a unique threshold of 90 cm to define central obesity in both men and women in Iran. Further studies are required to investigate the validity of these reports.

Ultimately we observed 49 deaths in PCS from 2012 to 2014. The main point is the high frequency of cardiovascular diseases that comprise more than half of all deaths. This finding is in line with several previous reports at national and sub-national levels and the cause of deaths reported by the Ministry of Health in Iran. This extreme observation in a rural low-socio-economic area in Iran implies a probably much worse situation among urban duelers who are more exposed to recognized risk factors of CVDs. Service packages should be developed and implemented in the setting of the primary health network in Iran so that the epidemic of NCDs and specifically CVDs can be effectively tackled and controlled. The setting of the PCS can be an excellent platform for investigating the cost-effectiveness of integrated policies in rural areas of Iran with limited resources and low-socio-economic status.

The strengths of PCS include: establishment of a large population-based cohort study using the tools and instruments already validated in GCS, measurement of the main risk factors and exposures for NCDs which are the most common causes of death and disability in this population, capacity building in terms of training researchers locally and in DDRI, creating a research infrastructure, conducting follow-up with negligible loss and detailed cause of death information, implementing international standards for long-term bio-banking of biological samples, and establishment of PCS as a platform for nested case–control studies and clinical trials, including the trial of Polypill within the setting of this cohort study.

PCS has certain weaknesses as well. This study involves a predominantly adult cohort limited to study people older than 40. The second weakness is related to our inability to collect stool for future study on the role of gut microbiota in chronic diseases, which has recently become a hot topic in research.

Despite the weaknesses, establishment of PCS proves the feasibility of prospective studies in low resource settings in developing countries. Although successful experiences of prospective cohort studies may be oases in a desert, their existence proves that they are feasible. Negative attitude toward establishment of these costly studies may be the main reason for their scarcity, especially among low income developing countries. Our successful experience may serve as an example for our neighboring countries and other countries in the region of Middle East and North Africa with similar socio-economic and cultural status. Results of such comprehensive studies can have significant policy implications in the field of public health. Fortunately, new initiatives in the Ministry of Health in Iran have recently been launched in which an integrated approach towards NCDs and their risk factors has been envisioned. To be effective, these initiatives should involve all stakeholders in health and should enhance inter-sectoral collaboration.

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Compliance with ethical standards

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Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional research committees of both Shiraz University of Medical Sciences and Tehran University of Medical Sciences and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in this study.

Conflict of interest None of the authors declare any conflict of interest.

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