# The Prospective Urban Rural Epidemiology (PURE) study: PURE Turkey 

# The Prospective Urban Rural Epidemiology (PURE) çalıșması: PURE Türkiye 

Aytekin Oğuz, M.D., ${ }^{1}$ Özge Telci Çaklilı, M.D., ${ }^{2}$ Burcu Tümerdem Çalık, M.D. ${ }^{3}$ on behalf of the PURE Investigators*

${ }^{1}$ Department of Internal Medicine, İstanbul Medeniyet University Faculty of Medicine, İstanbul, Turkey<br>${ }^{2}$ Department of Internal Medicine, Kocaeli State Hospital, Kocaeli, Turkey<br>${ }^{3}$ Department of Health Management, Marmara University Health Sciences Faculty, İstanbul, Turkey


#### Abstract

Objective: The Prospective Urban Rural Epidemiology (PURE) study is a prospective cohort study that collects data on social, environmental, and individual risk factors and chronic diseases among residents of 25 countries in the range of 35 to 70 years of age, living in rural and urban areas. The PURE study is directed by the Population Health Research Institute of McMaster University in Canada. In Turkey, the study is conducted by the Metabolic Syndrome Society. Methods: In Turkey, the study is being conducted in 8 cities. The initial fieldwork began in 2008. Questionnaires were completed, and anthropometric measurements, blood and urine samples, handgrip strength evaluations, electrocardiogram readings, and spirometer and body composition measurements were obtained. Each year, participants were followed up via telephone. Every third year, questionnaires, field measurements, and biological data sampling were repeated. Results: PURE Turkey has 4056 participants (female: $60.7 \%$, male: $39.3 \%$; mean age: $50 \pm 9.1$ years). Among them, $43.9 \%$ had metabolic syndrome and $52.8 \%$ were obese. The prevalence of hypertension was $41.1 \%$ and proportion of controlled hypertension was 34\%. A total of 2098 (51.7\%) of the participants had a total cholesterol of $\geq 200 \mathrm{mg} / \mathrm{dL}$ or were using a lipid lowering agent. In patients with diabetes, $79.8 \%$ had low-density lipoprotein cholesterol levels $\geq 100$ $\mathrm{mg} / \mathrm{dL}$. Although a dramatic change was not observed in those parameters in the follow-up years, the prevalence of diabetes mellitus increased from 13.7\% in 2008 to $21 \%$ in 2015. The baseline and follow-up data of the PURE study were analyzed with the other countries participating in the study and reported for international publication. Conclusion: The PURE study is a large, ongoing, prospective epidemiological study that is investigating the "causes of the causes" of noncommunicable diseases in the world. In addition to revealing the health status of nations, the study also has the potential to affect health politics.


## ÖZET

Amaç: The Prospective Urban Rural Epidemiology (PURE) çalıșması sosyal, çevresel ve kișisel risk faktörleri ile kronik hastalıklar hakkında veri toplamayı amaçlayan, 35-70 yaş arası, şehirde ve kırsalda yaşayan 25 ülkeden katılımcıya sahip prospektif bir çalışmadır. Çalışma Kanada'da McMaster Üniversitesi Population Health and Research Institute tarafından yönetilmektedir. Türkiye'de ise çalıșmayı Metabolik Sendrom Derneği yürütmektedir.
Yöntemler: Çalışma için sekiz bölge seçildi. Saha çalışmaları 2008 yılında başlayan çalışmada antropometrik ölçümler, kan ve idrar örnekleri, el kavrama kuvveti, EKG, spirometre ve vücut kompozisyonu ölçümleri alındı. Katılım fazından sonra takip fazında her yıl katıımcılar telefon ile aranarak sağlık durumlarındaki yenilikleri analiz edecek soruları barındıran anketler yöneltildi. Üç yılda bir tekrar sahaya inilerek anketlere ek olarak başlangıçta yapılan antropometrik ölçümler, EKG, spirometre ve kan, idrar örnekleri tekrarlandı.
Bulgular: PURE Türkiye 4056 (\%60.7 kadın, \%39.3 erkek, ortalama yaş: $50 \pm 9.1$ ) katılımcı ile temsil edilmektedir. Katılımcıların \%43.9'unda metabolik sendrom vardır, \%52.8' ise obezdir. Hipertansiyon prevelansı \%41.1'dir ve kan basıncı kontrolü \%34 hastada sağlanmıştır. Toplam 2098 (\%51.7) katıımcının total kolesterolü $\geq 200 \mathrm{mg} / \mathrm{dL}$ 'dir veya bir lipit düşürücü ilaç kullanmaktadır. Diyabetli hastalar arasında \%79.8'inin LDL kolesterol seviyesi $\geq 100 \mathrm{mg} / \mathrm{dL}$ 'dir. Yıllar içerisinde bu hastalıklara sahip hasta sayısında ciddi artış görülmemekle birlikte diyabet prevelansı 2008'de \%13.7 iken 2015 yılında \%21'e çıkmıştır. PURE çalışmasının başlangıç ve takip verileri tüm ülkelerle birlikle analiz edilmekte, uluslararası yayınlar olarak paylaşılmaktadır. Sonuç: Sonuç olarak PURE çalışması ülkemizde ve dünyada halen devam eden, prospektif, geniş katılımlı bir epidemiyolojik çalışmadır ve temel amacı kronik hastalıkların "sebeplerinin sebeplerini" bulmaktır. Ülkelerin sağlık durumlarını göz önüne koymanın yanı sıra sağlık politikalarına yön verme potansiyeli mevcuttur.

[^0]TThe Prospective Urban Rural Epidemiology (PURE) study is a prospective cohort study that aims to collect data on social, environmental, and individual risk factors and chronic diseases in 25 countries in the world. ${ }^{[1]}$ The principal aim is to examine the impact of urbanization on the development of basic risk factors (physical activity and nutrition changes) and primary risk factors (obesity, hypertension, dysglycemia and dyslipidemia, smoking), and cardiovascular diseases (CVD). The participating countries have been divided into 4 main categories according to income: low, lower-middle, upper-middle, and high. Turkey has been classified as an upper-middle-income country.

The PURE study seeks to examine the relationship between societal influences and the prevalence of risk factors. Social determinants are measured using 4 variables: the built environment, food and nutrition policy, psychosocial/socioeconomic factors, and tobacco. The study collects data on socioeconomic status and environmental construction to ascertain their effects on health status.

Turkey is one of the countries with a growing prevalence of noncommunicable diseases and diabetes, and CVD is the leading cause of mortality and morbidity. ${ }^{[2]}$ PURE Turkey is an investigation of the prevalence of CVD in Turkey and the related risk factors, as well as many other societal influences that may demonstrate a possible association between chronic diseases and urban transition.

## METHODS

Professor Salim Yusuf is the lead investigator of the PURE study, and in Turkey, the study is being conducted by Metabolic Syndrome Society. Ethical approval was granted by Marmara University Ethics Committee (approval number: MAR-SBY-2005-0183). Approval of the Ministry of Health was also obtained.

## Sample size

The PURE study initially aimed to recruit 150,000 adults from communities in low-, middle-, and highincome regions of the world. The participants were 4 low-income countries (Bangladesh, India, Pakistan, and Zimbabwe), 7 upper-middle-income countries (Argentina, Brazil, Chile, Malaysia, Poland, South Africa, and Turkey), 3 lower-middle-income coun-
tries (China, Colombia, and Iran), and 3 high-income countries (Canada, Sweden, and United Arab Emirates). There are now more countries participating and the total number of individual participants

| Abbreviations: |  |
| :--- | :--- |
| ATP III | Adult Treatment Panel III |
| CVD | Cardiovascular diseases |
| HDL | High-density lipoprotein |
| IDF | International Diabetes <br>  <br> Federation |
| LDL | Low-density lipoprotein <br> MetS |
| Metabolic syndrome  <br> PURE Prospective Urban Rural <br>  Epidemiology |  | has grown to 225,000 . Urban and rural communities that include a group of people who were generally expected to have characteristics in common (sharing culture, socioeconomic status, and use of amenities, goods, and services) and who reside in a defined geographical area were identified in each country.

The sample size consists of participants within the age range of 35 to 70 years living in rural and urban areas. The objective was to have participation from different geographical areas, income groups, and representatives of different lifestyles. An area was defined as rural if the population was fewer than 10,000 and there was no established metropolitan municipality. Turkey is divided into 12 regions based on the European Union Nomenclature of Territorial Units for Statistics classification. After evaluating social and financial data of the Turkish Statistical Institute, the 12 regions were condensed for the study: West/East Marmara, Aegean, West/Central Anatolia, Mediterranean, East/West Black Sea, Northeast Anatolia, and Southeast Anatolia, which were represented by the cities of Kocaeli, Aydin, Nevsehir, Antalya, Samsun, Malatya, and Gaziantep, respectively. These 7 cities were selected using randomization. Istanbul, due to its large population, represents itself, and was selected directly.

## Households

For each city, a list was made of the income and population of the towns and villages based on data obtained from local authorities. According to the study protocol, blood samples are to be centrifuged within 2 hours; therefore, the list of towns was revised according to the distance from a centrifuge site. From this list, a town or village was chosen randomly and households were contacted. This random draw was continued until the targeted number of participants for the city was achieved.

The local authority in each neighborhood was visited and informed about the arrival of the study group.

Recruitment of households started with turning either left or right from the town center and continuing in that direction. Each household on the way was visited. If there was no one at home, a second visit was made later. A home was excluded from the research if there was no response on the third attempt, and a non-responder form was completed. A non-responder form was also completed for households in which the residents declined to participate.

## Inclusion-exclusion criteria

The inclusion criteria were age between 35 and 70 years, residence in the visited household, and expected continued residence there for at least the next 4 years. The exclusion criteria were the presence of a severe mental disorder, severe frailty or immobility, and inadequate communication skills.

## Data collection

Informed consent was obtained from all of the participants. The PURE questionnaires were translated into Turkish and used to collect the study data. Interviews took place in households, for the most part, and occasionally at a community center or a health facility using the face-to-face method. Interviewers were trained in groups to ask the questions correctly. The variables investigated are presented in Tables 1-3. For the nu-trition-related section, validation of the semi-quantitative food frequency questionnaire was conducted and a food atlas was created for participants (Fig. 1). ${ }^{[3]}$

Participants were also informed about blood tests, and electrocardiography (ECG) and spirometer measurements. Patient consent was obtained at every step. They were also informed that each procedure was to be performed free of charge. An appointment was made at a pre-specified health facility for medical procedures.

## Phases

There were 2 initial phases: recruitment and followup. The recruitment phase began in 2010 and 4056 participants were included in the study. Of these participants, 2632 lived in urban areas and 1424 lived in rural areas. The total number of households was 2578 . After recruitment, the annual follow-up phase began. Each year, participants were called via telephone, and new disease diagnoses and the death or morbidity of household members was determined using the followup questionnaires (Table 4). This included inquiries
about hospital admissions, diagnosis of atrial fibrillation, cancer, asthma, or pneumonia. Every third year, the follow-up was conducted in the field with questionnaires, as well as taking measurements (ECG, etc.) and biological data sampling. At the time of writing, 3 field follow-ups have been completed.

## Questionnaires

Three types of questionnaires were used: communitybased, household-based, and individual-based. Community data involved results from the Neighborhood Environment Walkability Scale and The Environmental Profile of a Community's Health (EPOCH) Instrument. Data from household questionnaires were also used to interpret community-level data.

For households, there were 2 main questionnaires: the Family Census Questionnaire and the Household Questionnaire. In addition, there was a non-responder Household Questionnaire form.

Individual data were gathered using the Adult Questionnaire, the International Physical Activity Questionnaire, and the semi-quantitative Food Frequency Questionnaire (validated in Turkish).

## Physical examination and other tests

The physical examination included two measurements of resting blood pressure (seated), anthropometric measurements (weight, height, waist, and hip), spirometer (forced expiratory volume in 1 second, forced expiratory vital capacity), and an ECG assessment. A $10-\mathrm{mL}$ fasting blood sample was collected from all consenting participants. Blood and urine samples were centrifuged and transferred to centralized, long-term storage in secure $-80^{\circ} \mathrm{C}$ freezers (bought for the study) at Ankara Duzen Laboratories. Buffy coat for DNA analysis was also obtained. In addition to the elements of the PURE study protocol, glucose, creatinine, alanine aminotransferase, glycated hemoglobin, thyroid-stimulating hormone, lipid profile, and complete blood count data were reported to the participants by mail.

The data were collected according to the study protocol by trained interviewers, and blood pressure measurements were performed by healthcare personnel trained according to the protocol. For each blood pressure measurement, the participants were at rest for $\geq 5$ minutes, without smoking, exercising, or eating in the previous 30 minutes, and without climbing stairs for 15 to 30 minutes prior to measurement. An Omron

Table 1. Environmental and household data variables


CVD: Cardiovascular disease; DM: Diabetes mellitus; HT: Hypertension; Tb: Tuberculosis.

Table 2. Medical data variables

| Medical history | Medical history 2 | Family history <br> of first degree <br> relatives | Tobacco use | Alcohol use | Sleep patterns | Nutrition |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| Limitation of <br> movement/ <br> Disability situation | Regular drug use | In father, mother, <br> brother and sister | Age of initiation | Age of initiation | Time of transition <br> to sleep | Nutritional habits <br> (milk and dairy |

## Malaria

HIV/AIDS
MI: Myocardial infarction.

Table 3. Physical measurements and blood tests

| Physical measurements | - Height <br> - Weight | - Blood pressure <br> - Heart rate | - Waist circumference <br> - Hip circumference | - Upper right arm circumference <br> - Right thigh circumference <br> - Head circumference | - Body muscle ratio <br> - Body fat ratio | - Non-dominant hand maximum grip strength <br> - Dominant hand maximum grip strength |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| ECG | - Pathological Q <br> - ST elevation <br> - ST depression | - T inversion <br> - R>S in V1 or V2 | - Left ventricular hypertrophy <br> - Left axis deviation <br> - Intraventricular conduction defect | QT interval <br> - Abnormal cardiac <br> - Other anomalies | hythm |  |
| Breath Test | FEV1 | FVC | PEFR |  |  |  |
| Biological specimens | - Blood and urine specimens from each participant to be stored in $-80^{\circ} \mathrm{C}$ freezer. | - Buffy coat |  |  |  |  |

ECG: Electrocardiogram; FEV1: Forced expiratory volume in 1 second; FVC: Forced expiratory vital capacity; PEFR: Peak expiratory flow rate.

Deluxe ComFit Cuff (Omron Healthcare, Inc., Lake Forest, IL, USA) was used to take 2 measurements from the right arm. The definition of hypertension was a systolic blood pressure of $\geq 140 \mathrm{~mm} \mathrm{Hg}$ and a diastolic blood pressure of $\geq 90 \mathrm{~mm} \mathrm{Hg}$. If the participant was already taking an antihypertensive agent, he/she was considered a hypertensive participant.

Patients who declared that they had diabetes and patients already using a glucose-lowering agent were accepted as patients with diabetes. Patients with a fasting glucose level of $\geq 126 \mathrm{mg} / \mathrm{dL}$ were also ac-

Table 4. Diseases and medical events investigated in the annual follow-up conversations

| Diseases and medical events investigated at annual |  |
| :--- | :--- |
| follow-up |  |
| Hospital admission | Hypertension |
| Deaths | Diabetes |
| Myocardial infarction | Cancer |
| Stroke | Tuberculosis |
| Angina | HIV/AIDS |
| Heart failure | Malaria |
| Atrial fibrillation | Chronic obstructive |
|  | pulmonary disease |
| Other heart diseases | Asthma |
|  | Pneumonia |
|  | Other lung diseases |

cepted as patients with diabetes.
A multifaceted approach was used with respect to disease diagnoses. In addition to the patient's statement about a diagnosis, the study investigators asked a set of exploratory questions. To finalize the disease diagnosis, medical documents of the patients were obtained from either the patients or from the medical facilities by the PURE Turkey headquarters.

## Overview of PURE analysis and publications

The baseline and follow-up data of all of the countries participating in the PURE study were analyzed and reported in international publications. Data regarding our country are stored in our own data pool and analyzed. Some of the data from the baseline and third-year follow-up have been shared as abstracts at various conferences (see text for supplementary data). Here, instead of reporting all of the results, we have shared some of the striking findings of the overall PURE study and the PURE Turkey results.

## RESULTS

The PURE Turkey analysis was conducted with 4056 participants. The mean age of the participants was $50 \pm 9.1$ years. There were 2462 female participants and 1594 male participants ( $60.7 \%$ vs. $39.3 \%$ ). Elementary school was the highest level of education achieved for $57.7 \% ~(n=2340)$ of the total cohort. Two


Figure 1. Images from the food atlas.
percent had a history of stroke and $5.6 \%$ had a coronary heart disease history. In all, $55.4 \%$ had never smoked, whereas $27.9 \%$ were current smokers, and $16.7 \%$ were former smokers. Furthermore, $88.2 \%$ had never consumed alcohol, $5.2 \%$ had in the past, and $6.6 \%$ were current consumers of alcohol.

The prevalence of hypertension was $41.1 \%$. In $66 \%$ of the patients with hypertension, blood pres-
sure control was not achieved. Hypertension awareness was observed in $63.3 \%$. Participants living in urban areas represented $39.6 \%$ of the participants, and $46.6 \%$ of the rural residents had a hypertension diagnosis. Among female participants, $52 \%$ had hypertension, and $48 \%$ of the males were hypertensive.

The diabetes prevalence was $13.7 \%$. In rural areas, the prevalence was $12.6 \%$, while it was $15.8 \%$ in ur-
ban areas. Glycemic control had been achieved in $25 \%$, whereas it had not been in $75.1 \%$ of the patients. The frequency of prediabetes was $9.4 \%$ : in rural areas it was $9.2 \%$ and in urban areas it was $9.6 \%$. Diabetes awareness was determined to be $87.4 \%$. A diabetes diagnosis was most frequently seen in the 60-64 age group ( $29.4 \%$ ). Follow-up data showed that in 2015, the prevalence of diabetes mellitus had increased to $21 \%$.

There were 2098 ( $51.7 \%$ ) participants with a total cholesterol $\geq 200 \mathrm{mg} / \mathrm{dL}$ or using a lipid-lowering agent. The mean high-density lipoprotein (HDL) cholesterol level was $46.2 \pm 13.2 \mathrm{mg} / \mathrm{dL}$ in rural areas and $47.6 \pm 14 \mathrm{mg} / \mathrm{dL}$ in urban locations. The rate of low HDL cholesterol level ( $<40 \mathrm{mg} / \mathrm{dL}$ in males and $<50 \mathrm{mg} / \mathrm{dL}$ in females) was $53.5 \%$. In patients with diabetes, $79.8 \%$ had a low-density lipoprotein (LDL) cholesterol level $\geq 100 \mathrm{mg} / \mathrm{dL}$.

According to the Adult Treatment Panel III (ATPIII) criteria, $36.7 \%$ of the participants had metabolic syndrome (MetS), whereas according to the International Diabetes Federation (IDF) criteria 43.9\% had MetS. Among female patients, 39.3\% had MetS according to the ATP III criteria and it was $44.8 \%$ according to the IDF criteria, whereas in males, the rate was $30.2 \%$ and $40.7 \%$, respectively. When urban and rural regions were compared with regard to MetS, $34.6 \%$ of the participants living in rural areas and $34.8 \%$ of those living in urban locations had MetS according to the ATP III criteria. Using the IDF criteria, the rate was $42.6 \%$ and $42.9 \%$, respectively. According to body mass index, $52.8 \%$ of the participants were obese. The mean waist circumference of males was $95 \pm 12 \mathrm{~cm}$, and it was $90 \pm 12 \mathrm{~cm}$ for female participants in the study.

The initial data of the PURE Turkey study have demonstrated that obesity is an epidemic in Turkey. With more than half of the cohort classified as obese, it is no surprise that the frequency of MetS was $42.7 \%$.

## DISCUSSION

PURE aimed to illuminate differences between urban and rural environments. It is often acknowledged that urban transition has increased the incidence of noncommunicable disease, and individuals who live in cities and other industrialized areas have more risk factors. Analysis of worldwide PURE data has shown that although cardiovascular risk factors are less prominent in countries with a lower income, the rates
of CVD and mortality are higher than in high-income countries. ${ }^{[4]}$ The event rates are higher in rural areas of low- and middle-income countries, whereas they are lower in the rural areas of high-income countries. This underlines the fact that there are country-specific dynamics affecting CVD risk factors.

Hypertension is a health burden to many countries, including Turkey. A report of world PURE data analysis indicated that the hypertension prevalence is $40.8 \%$, and that only $32.5 \%$ of patients had reached blood pressure targets. ${ }^{[5]}$ The figures are similar in Turkey. For both Turkey and the world, better follow-up of hypertension is clearly needed. One of the main reasons for the low rate of blood pressure control in the world is the affordability of medications. Analysis of world PURE data has shown that the proportion of communities with 4 drug classes available for hypertension was $13 \%$ in low-income countries, whereas it was $94 \%$ in high-income countries. ${ }^{[6]}$ Another analysis revealed that drugs for secondary prevention are also unavailable and unaffordable in most countries, even upper-middle-income countries. ${ }^{[7]}$ In low income countries the proportion of patients with cardiovascular disease on three medications was alarmingly low ( $0-2.5 \%$ ). For Turkey it was $12 \%{ }^{[8]}$ Turkey is one of the upper middle income countries of the study. The proportion of participants with cardiovascular disease who were taking three or more secondary prevention medications differed in this income group from $7 \%$ (Malaysia) to $26.7 \%$ (Poland). Due to the fact that in Turkey medications are free of charge for most of the population reasons for this low rate should be well investigated. A better training for physicians regarding cardiovascular diseases may improve the rate as well as increasing awareness of the population for benefits of the drugs can have beneficial effects.

An interesting finding of the PURE study was the relationship between urinary potassium excretion and blood pressure. Mente et al. ${ }^{[9]}$ reported a decrease in blood pressure with increased potassium intake. This effect of potassium was also notable in mortality analysis of PURE participants: there was a decreased cardiovascular event rate with increased potassium consumption. This report has also particularly pointed out a different view with regard to sodium consumption. Analysis revealed that sodium excretion of less than 3 g per day was associated with higher mortality rates compared with the reference of 4-5.99 g. ${ }^{[10]}$

Analysis of PURE countries has shown a $3.2 \%$ rate of CVD and a $1.6 \%$ rate of stroke in upper-middle-income countries. The prevalence of stroke in Turkey is slightly higher and almost twice as high for CVD. ${ }^{[11]}$ This report demonstrates the need for interventions to increase secondary prevention rates worldwide. Almost 1 out of 3 people in Turkey smoke. Although smoking is a major modifiable risk factor for CVD, analysis of worldwide PURE data revealed that even in patients with established CHD, $18.5 \%$ continued to smoke. Only 4\% of this cohort has embraced a healthier lifestyle. ${ }^{[12]}$

Alcohol consumption is also a modifiable risk factor for death. The Turkish population has a lower rate of alcohol use compared to the other participating countries. While the association between alcohol consumption and mortality differs according to region, a high intake has been associated with high mortality rates. ${ }^{[13]}$

Diet is a key component of cardiovascular health. In Turkey, half of the cohort had high cholesterol with low HDL cholesterol levels. Lifestyle and dietary changes are often recommended to patients with these results. Analysis of the international PURE cohort has revealed that a greater intake of total fat, saturated fatty acids, and carbohydrates was associated with higher blood pressure, while a greater protein intake was associated with lower blood pressure. ${ }^{[14]}$ Replacement of saturated fatty acids with carbohydrates was associated with adverse effects on lipids; however, replacement of saturated fatty acids with unsaturated fats improved LDL cholesterol and blood pressure, but seemed to worsen other HDL cholesterol and triglycerides. A point worth mentioning is that in the PURE cohort, the ratio of apolipoprotein B to apolipoprotein A was the best indicator of the effect of saturated fatty acids on CVD. Mortality and diet analysis of the world PURE data was consistent with these findings. ${ }^{[15]}$ A high carbohydrate intake was associated with a greater risk of total mortality (hazard ratio: 1.28). Fat was not associated with CVD, myocardial infarction, or CVD mortality, and saturated fat had an inverse association with stroke. These results challenge what is already known about diet and cardiovascular health. However for fruit, vegetable and legume consumption, a decreased rate of mortality (non-cardiovascular) was reported, which is consistent with literature. ${ }^{[16]}$ Also in agreement with general knowledge was the
finding that physical activity was related to a lower risk of mortality and major CVD events. ${ }^{[17]}$

The PURE study has explored different associations regarding CVD, as well as validating what is already known. Reduced grip strength has been linked to mortality and CVD. The PURE study has demonstrated this association in the largest reported population and announced that grip strength is a predictor of mortality. ${ }^{[18]}$

Although PURE has recruited households instead of volunteering individuals, PURE Turkey has more female participants than males. This is a limitation of our cohort.

## CONCLUSION

The PURE study is a large, ongoing, prospective, international epidemiological study providing data on the health status of the world. It compares regions, nations, and urban and rural environments, along with evaluating demographic, anthropometric, genetic, and environmental factors. PURE Turkey has one of the largest cohorts in the study according to population. Analysis of this cohort has provided and will provide more insight on CVD and other chronic diseases in Turkish population.

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    Correspondence: Dr. Aytekin Oğuz. İstanbul Medeniyet Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, İstanbul, Turkey.
    Tel: +90 216-5069195 e-mail: aytekinoguz@hotmail.com

