


Cohort Profile

Cohort Profile: The Urmia Lake Cohort Study (ULCS)

Javad Aghazadeh-Attari,¹ Hossein Poustchi,² Davoud Vahabzadeh,^{1,3} Ramin Shakeri,⁴ Rasool Entezar Mahdi,¹ Habibollah Pirnejad,⁵ Sareh Eghtesad,² Zahra Mohammadi,² Maryam Sharafkhah,² Amaneh Shayanrad,² Neda Valizadeh,^{6,7} Mohammadreza Pashaei,⁷ Nilza Dourandish,⁷ Maryam Majidinia,⁸ Marjan Kouhnavard,¹ Jamal Ahmadzadeh ,¹ Ali Sadaghyanifar⁹ and Iraj Mohebbi^{1*}

¹Social Determinants of Health Research Center, Clinical Research Institute, Urmia University of Medical Sciences, Urmia, Iran, ²Liver and Pancreatobiliary Diseases Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran, ³Department of Nutrition and Biochemistry, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran, ⁴Digestive Oncology Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran, ⁵Patient Safety Research Center, Clinical Research Institute, Urmia University of Medical Sciences, Urmia, Iran, ⁶Maternal and Childhood Obesity Research Center, Urmia University of Medical Sciences, Urmia, Iran, ⁷Department of Internal Medicine, Urmia University of Medical Sciences, Urmia, Iran, ⁸Solid Tumor Research Center, Cellular and Molecular Medicine Institute, Urmia University of Medical Sciences, Urmia, Iran and ⁹Urmia Health District Center, Urmia University of Medical Sciences, Urmia, Iran

*Corresponding author. Social Determinants of Health Research Center, Urmia University of Medical Sciences, Resalat St., Urmia, Iran. E-mail: irajmohebbi@umsu.ac.ir

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Key features

- This cohort was established to determine the incidence and burden of non-communicable diseases (NCDs) in a sub-rural area of Urmia and to provide a platform for future studies in identifying risk factors associated with prevalent NCDs.
- The Urmia Lake Cohort Study (ULCS) is the first large-scale prospective cohort in the West Azerbaijan province of Iran.
- The cohort aimed to include all individuals aged 35–70 years residing within the areas of Qushchi and surrounding villages, with a 15-year follow-up period.
- The categories of data collected were sociodemographic, medical, nutritional, laboratory and anthropometric.
- This cohort was supported by the Deputy of Research and Technology, Ministry of Health and Medical Education of Iran, and data can be accessed through formal request via the cohort website [www.persiancohort.com].

Why was the cohort set up?

The prevalence of non-communicable diseases (NCDs) is increasing in Iran. Based on previous studies, the four main NCDs—cardiovascular diseases, chronic respiratory disorders, cancers and diabetes—are responsible for 81.0% of premature deaths in Iran.^{1,2} The prevalence of NCDs in the West Azerbaijan province of Iran has not yet been reported through reliable sources. Cohort studies provide reliable evidence for determining the prevalence of NCDs, their aetiology as well as contributing risk factors.^{3–5} Therefore, the Prospective Epidemiological Research Studies in IrAN (PERSIAN), a nationwide cohort study, was launched in 2014 in an attempt to identify risk factors associated with the most prevalent chronic diseases in different provinces of Iran, and to encourage researchers in different fields such as medicine, epidemiology, health and nutrition to be more involved in large-scale, longitudinal studies. The PERSIAN Cohort not only tries to improve the health status of Iranians but also to help advance global knowledge in medicine and health.^{6–8}

The Urmia Lake Cohort Study (ULCS), as one of the PERSIAN cohort centres, started enrolment in February 2017 in Qushchi, West Azerbaijan. This region is unique because of its close proximity to the Urmia Lake, one of the largest salt lakes in the world—which has been drying over the past decades.^{9,10} Because of the lake's rapidly declining water level, it has been regarded as a potential source of pollution in the future. Dry wetlands are the source of dust storms in different areas of the world. Salt storms increase the risk of irreversible ecosystem modifications, diminish fertility in the nearby agricultural lands and produce biotoxicity and chronic health issues.^{11,12}

Numerous scientific studies have documented multiple adverse health outcomes following dust storms in dry wetlands, including upper respiratory discomforts such as runny and stuffy nose, sinusitis, sore throat, wet cough, head cold, hay fever and burning red eyes.^{11,13,14} Lower respiratory tract problems, including wheezing, dry cough, phlegm, shortness of breath and chest pains, have also been reported.^{13,15,16} Moreover, increased particulate matter concentrations have been linked with decreased lung function. Asthma in children, as well as aggravation of past diseases in adults and children, are also well associated with particulate matter concentrations.^{14,15,17}

The primary objective of ULCS is to determine the incidence and burden of NCDs in this sub-rural area of Urmia and also to provide a platform for future studies in order to assess the relationship between risk and protective factors associated with identified NCDs, as well as genetic studies in the different populations around the Urmia Lake.

Who is in the cohort?

In this study, 5159 participants were enrolled from 8 February 2017 to 21 September 2018. The follow-up phase began immediately after enrolment, so 3 years of follow-up have passed successfully. The West Azerbaijan province comprises different native ethnicities and religious groups, including Azeris, Kurds and Armenians, with unique cultural practices and lifestyles. This province is located in a mountainous region. The central target region for ULCS is a rural region known as Qushchi, and its surrounding villages, with geographical coordinates of 37°59'16" N and 45°3'52" E in DMS (Degrees Minutes Seconds) or 37.9 and 45.0 (in decimal degrees). Qushchi is located 75 km south of Salmas and 45 km north of Urmia, the capital of West Azerbaijan province. ULCS encompasses a 5-km ribbon around the lake's border (Figure 1), and has a total area of 1686 km². The population of Qushchi and its surrounding villages is about 43 000 individuals, of whom all men and women meeting the eligibility criteria (explained below) were invited to participate in the study. Most Qushchi residents engage in farming, animal husbandry and truck driving.

Eligibility criteria for ULCS enrolment included age 35–70 years and residing in the designated area around Qushchi for at least 9 months prior to enrolment. Migrants with intermittent residency, who had Iranian nationality based on valid documentation, were also included. Individuals not willing to participate in the study or those unable to communicate effectively because of disabilities were excluded from the study. Of the total population (43 000), 6100 individuals met the eligibility criteria and were all invited by cohort personnel to participate in the ULCS. Of these individuals, 5159 men and women responded to the invitations and participated in the study.

How often have they been followed up?

Follow-up is both active and passive. In active follow-up, participants are contacted by telephone each year after enrolment. They are asked questions about any hospitalization and the incidence or diagnosis of new diseases; this information is recorded in a database. In the case of a chronic illness, an outcome review form is completed. For certain outcomes of interest, including cancers, a blood sample is also taken from that participant at the ULCS cohort centre and stored in the biobank. In addition, the participant's pathology block is requested. A validated verbal autopsy form is completed in the case of death.

Passive follow-up is also performed through registries such as the Iran National Cancer Registry, Diabetes Registry, Iranian Myocardial Infarction Registry and other



Figure 1 Location of the cohort in Urmia County, West Azerbaijan. Qushchi and its surrounding villages border the Urmia Saline Lake (indicated on map as the red region)

disease registries pertinent to the study's outcomes of interest. Follow-up is planned to continue for 15 years after enrolment. Follow-up will be performed annually.

To limit loss to follow-up, information from volunteers' close friends and family members is collected during enrolment and, if there is no response when calling the participant or his/her acquaintances after six attempts within 2 weeks, a visit to the individual's home is performed to try to find the participant.

What has been measured?

Individuals who met the eligibility criteria of the study were invited by the door-to-door method, where trained personnel visited the participants' homes, introduced the study and explained the benefits of participation, providing information pamphlets. Those who agreed to participate were later contacted by phone to schedule an appointment date to visit the Urmia Lake Cohort centre. All data and biological sample collections were made on the interview date and at the cohort centre. In case someone missed their appointment, they were re-scheduled for another day for up to three times; if they did not attend, they were regarded as being no longer interested in participating. On visiting the cohort centre, individuals first provided written

informed consent to participation in the study and were then registered and provided with a unique 11-digit identifier, which was used to label all documents/specimens. A cohort ID card was also provided for easier follow-up.

Laboratory measurements

Biological samples were taken from all participants immediately after registration. The volunteers were asked not to eat or drink anything other than water for 12 h prior to visiting the cohort center; 25 ml of blood were obtained from each individual in one 7-ml clot tube and three 6-ml EDTA tubes. After centrifugation at 3000 rpm for 10–15 min, the contents of the clot tubes were divided into serum and clot, and the EDTA tubes were aliquoted into plasma, buffy coat and red blood cells. These samples were further aliquoted and stored at -70°C . In addition, the following biochemical tests were performed on the same date using a small amount of the blood sample: complete blood count (CBC), fasting blood sugar (FBS) level, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), triglycerides, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), γ -glutamyl transpeptidase (γ -GLT), blood urea nitrogen (BUN) and creatinine.

A urine sample for urinalysis was also obtained from each individual and stored in the biobank at -20°C . In addition, hair and nail samples were collected. All test results were archived in a specific laboratory database linked to the main PERSIAN Cohort database. Laboratory test results were provided to each participant as an informative feedback sheet and to acknowledge their participation in the study. If abnormalities were seen in the test results, participants were encouraged to visit their family physician.

Anthropometric measurements

Height and weight, as well as wrist, waist and hip circumferences, were measured and recorded while the participant was still fasting. Weight was measured in light clothing using the Seca 755 standing scale. Height was measured without shoes using the Seca 206 stadiometer. Waist, hip and wrist circumference measurements were made according to Iranian National Institute of Health Research protocols, with an accuracy of 0.1 cm. After completing the laboratory and anthropometric sections, participants were provided with breakfast before completing the questionnaire section.

General, medical and nutritional assessment

Data were gathered by a trained and qualified interviewer, through three major questionnaires, on participants' general, medical and nutritional status. In the general questionnaire, completed by three skilled interviewers, information on demographics, years of education, household status, socioeconomic status, income, fuel and living status, sleep patterns, work experience, lifestyle, physical activity, animal contact history and pesticides and herbicides use were collected. In the nutrition assessment, a food frequency questionnaire was used by four trained interviewers to determine food consumption during the year previous to the interview as well as usual dietary habits. In the medical section, participants were questioned by two nurses about chronic disease history, medication use, women's reproductive history, family history of chronic diseases, oral health status, smoking and drug and alcohol use. Blood pressure and pulse rate measurements were also recorded and a physical examination for the presence of any skeletal abnormalities was performed.¹⁸ All questionnaires and collected data were checked for accuracy, precision and quality by field quality-control supervisors.

What has been found?

The average response rate for enrolment was 84.57%. [Table 1](#) shows the baseline characteristics of the cohort

population. The average age of participants was 49.62 ± 9.64 years, and 43.7% were men. Most participants belonged to the Turk/Azeri (80.0%) and Kurd (19.5%) ethnicities. Over two-thirds of the cohort were illiterate or with primary school literacy only; twice as many women as men were illiterate or had primary school literacy only. The dominant occupations for male participants were farming and driving heavy trucks. Most women were housewives. About 14.0% of men smoked daily. Based on body mass index, 60.4% of men and 81.7% of women were overweight or obese. Over 64.0% of total participants reported light and moderate physical activity levels ([Table 1](#)).

The prevalence of identified NCDs in this cohort, based on the World Health Organization definitions, was 72.2% for both sexes. The most common NCDs were hypertension (17.8.9%), kidney stones (12.3%), depression (8.3%), diabetes (6.3%), chronic headache (7.5%), ischaemic heart disease (5.8%) and thyroid diseases (6.0%). Except for kidney stones, all other diseases were more common in women than men. Depression, chronic headache and thyroid disease were significantly more prevalent in women than men ($P < 0.001$) ([Table 2](#)).

Laboratory findings of participants at the time of enrolment are shown in [Table 3](#). There were significant differences in the mean \pm standard deviation for all variables between the two sexes ($P < 0.05$). Based on laboratory measures, 582 individuals among the total studied population had fasting blood sugar (FBS) levels greater than or equal to 110 mg/dl (228 males and 354 females). Of these individuals, 240 presented with prediabetes FBS levels (110–126 mg/dl) and 342 with FBS levels concordant with diabetes (< 126 mg/dl). However, as shown in [Table 2](#), only 325 participants reported a history of diabetes or taking antidiabetic medications. Therefore, through the ULCS laboratory results, an additional 230 individuals with abnormal FBS levels were detected who may possibly have diabetes. These individuals were advised to attend their family physician or health care providers for further follow-up. For cases of other abnormal test values, similar work was also done.

What are the main strengths and weaknesses?

The main strength of ULCS, similar to other PERSIAN Cohort studies throughout Iran, is the population-based design and its large sample size. Including individuals from different native ethnic groups in West Azerbaijan provides researchers with an enormous dataset on various exposures such as diet, lifestyle, environmental factors and socioeconomic factors. Due to language differences, all questionnaires

Table 1 Baseline characteristics of participants in the Urmia Lake Cohort Study, 8 February 2017 to 21 September 2018

Variables	Males	Females	Total
Age, mean \pm SD, (years)	49.1 \pm 9.7	50.0 \pm 9.6	49.6 \pm 9.6
Sex, <i>n</i> (%)	2250 (43.6)	2909 (56.4)	5159 (100)
Ethnicity, <i>n</i> (%)			
Turk	1800 (80.0)	2332 (80.1)	4132 (80.0)
Kurd	448 (19.9)	561 (19.3)	1009 (19.5)
Fars	<30	<30	<30
Other ethnic groups	<30	<30	<30
Education, <i>n</i> (%)			
Primary school or illiteracy	1268 (56.3)	2356 (81.0)	3624 (70.2)
Middle school	314 (13.9)	271 (9.3)	585 (11.3)
High school	562 (25.0)	251 (8.6)	813 (15.7)
University or higher	105 (4.6)	<30	129 (2.5)
Marital status, <i>n</i> (%)			
Never married	24 (1.1)	88 (3.0)	112 (2.2)
Married	2206 (98.0)	2459 (84.5)	4665 (90.4)
Widowed	<30	340 (11.7)	351 (6.8)
Divorced	<30	<30	<30
Others	<30	<30	<30
Anthropometric measurements and BMI			
Waist circumference, mean \pm SD, (cm)	94.7 \pm 10.5	96.4 \pm 11.6	95.7 \pm 11.2
WHR, mean \pm SD, (cm)	0.8 \pm 0.3	0.95 \pm 0.1	0.91 \pm 0.2
BMI, mean \pm SD, (kg/m ²)	28.2 \pm 52.7	30.1 \pm 11.3	29.2 \pm 35.7
Normal (<24.99)	806 (35.8)	495 (17.0)	1301 (26.1)
Overweight (25-29.9)	941 (41.8)	1061 (36.5)	1957 (39.2)
Obese (\geq 30)	418 (18.6)	1317 (45.3)	1735 (34.7)
Occupation, <i>n</i> (%)			
Farmer	875 (38.9)	16 (0.5)	891 (17.3)
Driver	340 (15.1)	<30	341 (6.6)
Office employee	105 (4.6)	16 (0.5)	121 (2.3)
Housekeeper	7 (0.3)	2668 (91.7)	2675 (51.8)
Retired	114 (5.1)	<30	116 (2.2)
Self-employed	549 (24.4)	46 (1.6)	595 (11.5)
Unemployed	231 (10.3)	160 (5.5)	391 (7.6)
Physical activity level (MET)			
First tertile	595 (26.4)	1062 (36.5)	1657 (33.1)
Second tertile	474 (21.0)	1190 (40.9)	1664 (33.4)
Third tertile	1090 (48.4)	567 (19.5)	1657 (33.3)
Personal habits, <i>n</i> (%)			
Smoker, ^a yes (%)	315 (14.0)	22 (0.8)	337 (6.5)
Drug use, ^b yes (%)	232 (10.3)	<30	237 (4.6)
Alcohol drinker, ^c yes (%)	245 (10.9)	<30	251 (4.9)

WHR, waist-to-hip ratio; BMI, body mass index; MET, metabolic equivalent of task.

^aSmoker—participant who has smoked at least 100 cigarettes in his or her lifetime.

^bDrug use—using illicit drugs once per week for at least 6 months.

^cAlcohol use—drinking approximately 200 ml of beer or 45 ml of liquor, once per week for at least 6 months.

were completed by local personnel. ULCS is not a representative sample of West Azerbaijan province, but some generalizations can be made through statistical adjustments. Perhaps the main challenge of this cohort is limiting loss to follow-up, especially since our response rate for enrolment was lower than originally expected. To overcome this limitation,

continuous encouragement by raising awareness about the benefits of participating in the study and tracking their health status is provided to participants, and selected medical services at facilities and clinics affiliated with Urmia University of Medical Sciences are offered to participants free of charge, upon showing their active cohort ID cards.

Table 2 The prevalence of non-communicable diseases in the Urmia Lake Cohort Study population, 8 February 2017 to 21 September 2018

Variables	Male, <i>n</i> (%)	Female, <i>n</i> (%)	<i>P</i> -value	Total, <i>n</i> (%)
Hypertension ^a	242 (10.7)	679 (23.3)	<0.001	921 (17.8)
Diabetes ^b	101 (4.5)	224 (7.7)	<0.001	325 (6.3)
Ischaemic heart diseases ^c	114 (5.1)	187 (6.0)	0.030	301 (5.8)
Myocardial Infarction ^c	25 (1.1)	18 (0.6)	0.050	43 (0.8)
Stroke ^c	15 (0.7)	25 (0.8)	0.700	40 (0.8)
Renal failure ^c	23 (1.0)	42 (1.0)	0.160	65 (1.2)
Fatty liver	50 (2.2)	150 (5.1)	0.160	200 (3.9)
COPD ^c	60 (2.7)	99 (3.4)	0.110	159 (3.1)
Cancers ^c	11 (0.5)	30 (1.0)	0.020	41 (0.8)
Thyroid disorders ^c	25 (1.1)	273 (9.4)	<0.001	308 (6.0)
Kidney tone ^c	368 (16.3)	267 (9.2)	<0.001	635 (12.3)
Chronic headache ^c	82 (3.6)	306 (10.5)	<0.001	388 (7.5)
Depression ^c	91 (4.0)	339 (11.6)	<0.001	430 (8.3)

COPD, chronic obstructive pulmonary disease.

^aBased on blood pressure >130/90 and used medications.

^bBased on fasting blood sugar level >126 mg/dl and used medications.

^cBased on valid medical documentation, diagnosis during hospitalization and valid acquired data from different registries.

Table 3 The baseline levels of laboratory test values for participants in the Urmia Lake Cohort Study, 8 February 2017 to 21 September 2018

Variables	Male (mean ± SD)	Female (mean ± SD)	<i>P</i> -value	Total (mean ± SD)
White blood cells (1000/mm ³)	6.5 ± 1.5	6.4 ± 1.6	0.080	6.5 ± 1.5
Red blood cells (mL/mm ³)	5.1 ± 0.4	4.6 ± 0.3	<0.001	4.8 ± 0.4
Haemoglobin (mL/dl)	15.5 ± 1.1	13.5 ± 1.1	<0.001	14.4 ± 1.5
Haematocrit (%)	45.5 ± 3.4	40.0 ± 3.2	<0.001	42.3 ± 4.3
Platelets (1000/mm ³)	217.8 ± 45.1	248.1 ± 53.1	<0.001	235.6 ± 52.2
Fasting blood sugar (mg/dl)	94.5 ± 24.6	96.6 ± 33.1	0.010	95.7 ± 29.5
Blood urea nitrogen (mg/dl)	11.8 ± 5.7	8.7 ± 4.9	<0.001	10.1 ± 5.5
Creatinine (mg/dl)	0.9 ± 0.2	0.7 ± 0.2	<0.001	0.8 ± 0.2
Triglyceride (mg/dl)	157.3 ± 133.4	130.0 ± 85.7	<0.001	142.4 ± 114.6
Total cholesterol (mg/dl)	178.7 ± 40.6	190.5 ± 41.3	<0.001	185.2 ± 41.7
Alkaline phosphatase (IU/ml)	206.8 ± 70.7	193.0 ± 66.7	<0.001	199.0 ± 68.7
Alanine transferase (IU/ml)	31.5 ± 17.3	26.4 ± 12.6	<0.001	28.5 ± 15.0
Aspartate transferase (IU/ml)	29.7 ± 13.1	26.9 ± 11.3	<0.001	28.0 ± 12.1
High-density lipoprotein cholesterol (mg/dl)	44.6 ± 10.2	51.0 ± 11.4	<0.001	48.2 ± 11.4
Gamma glutamyl transferase (IU/ml)	26.4 ± 29.9	19.6 ± 14.9	<0.001	22.7 ± 23.0
Low-density lipoprotein (mg/dl)	102.8 ± 33.2	113.6 ± 35.9	<0.001	108.8 ± 35.4

Can I get hold of the data? Where can I find out more?

Data are available for researchers and analysts who fulfil eligibility criteria for analysis, publication or any future needs. The Urmia Lake Cohort is incorporated in the Iran Cohort Consortium with other PERSIAN Cohort centres in other provinces. Data can be accessed through formal request from this website: [<http://persiancohort.com/access/>].

Ethics approval

The design of ULCS, as a PERSIAN Cohort centre, was approved by the ethics committees of the Ministry of Health and Medical Education, the Digestive Diseases Research Institute (Tehran University of Medical Sciences) and also by the local ethics committee of the executing university, Urmia University of Medical Sciences (ethical code identifier IR. umsu.rec.1395.586). Prior to enrollment, written informed consent was obtained from each participant based on valid personal identification documents. Throughout the entire study period, the executive team adhered to the Principles of

Helsinki; participants were allowed to quit the study whenever desired.

Author contributions

J.A., I.M. and H.P. designed the study. D.V., J.A., R.M., R.E., H.P., S.E., Z.M., M.S., A.S.H., N.V., M.P., N.D., M.M., M.K. and A.S. directed the study's implementation. J.A., I.M. and H.P. designed the analytical strategy and helped to interpret the findings. D.V. and J.A. conducted the literature review and helped to prepare the Introduction and Methods sections of the text. J.A., I.M., D.V. and J.A. drafted the Discussion.

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Conflict of interest

None declared.

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