

## Report

# The PERSIAN Cohort: Providing the Evidence Needed for Healthcare Reform

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## Abstract

In the past, communicable diseases caused the highest mortality in Iran. Improvements in socioeconomic status and living standards including access to safe drinking water, along with the inception of Health Houses in the 1980s, have changed disease patterns, decreasing the spread of and deaths from infectious and communicable diseases. The incidence and prevalence of non-communicable diseases (NCD), however, have now increased in Iran, accounting for nearly 80% of deaths and disabilities. Without interventions, NCD are predicted to impose a substantial human and economic burden in the next 2 decades. However, Iran's health system is not equipped with the necessary policies to combat this growth and must refocus and reform. Therefore, in the year 2013, the Ministry of Health and Medical Education funded a well-designed nationwide cohort study—Prospective Epidemiological Research Studies in Iran (PERSIAN)—in order to assess the burden of NCD and investigate the risk factors associated with them in the different ethnicities and geographical areas of Iran. The PERSIAN Cohort, which aims to include 200 000 participants, has 4 components: Adult (main), Birth, Youth and Elderly, which are being carried out in 22 different regions of Iran. Having an enormous dataset along with a biobank of blood, urine, hair and nail samples, the PERSIAN Cohort will serve as an important infrastructure for future implementation research and will provide the evidence needed for new healthcare policies in order to better control, manage and prevent NCD.

**Keywords:** PERSIAN, Cohort, NCD, Iran

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## Introduction

Non-communicable diseases (NCD) impose a substantial human and economic burden globally, but in the next 2 decades, it is projected that this burden will more seriously impact middle-income countries as their populations

and economies grow.<sup>1,2</sup> In 2008, nearly 80% of NCD deaths occurred in low- and middle-income countries. In Iran, deaths from NCD have increased from 49.02% to 79.2% in the years 1990 to 2015, and this figure is on the rise.<sup>2</sup> In response to this increase, change and reform in

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healthcare policies are urgently needed, not only for early diagnosis and treatment of NCD, but more importantly, for disease prevention in order to decrease morbidity, mortality and economic losses. Therefore, in the year 2013, the Iranian Ministry of Health and Medical Education established a nationwide cohort study, the Prospective Epidemiological Research Studies in IrAN (PERSIAN), in an attempt to gather the evidence needed for a healthcare reform. The purpose of this report is to explain the rationale behind the PERSIAN Cohort and introduce its four components.

### Disease Patterns in Iran

Going back a few decades, Iran's healthcare system faced entirely different disease patterns and a high number of deaths, especially in rural areas, were caused by communicable diseases, maternal and neonatal disorders and nutritional deficiencies.<sup>3</sup> In the early 1970s, the first efforts in implementation of primary healthcare (PHC) were introduced in Iran, but it was not until the early 1980s that the first Health Houses were conceived to bring PHC to every district and especially rural areas.<sup>3</sup> Community health workers or *Behvarz*, who were selected from their own communities, were the key element of the Health Houses. The *Behvarz* were trained in management of maternal and child health issues, communicable diseases as well as environmental concerns of each community. Even now, they continue to educate the community about various public health issues including sanitation, and aid individuals with simple tasks such as taking their prescribed medications.<sup>3</sup> With the successful implementation of the Health Houses, the incidence of communicable diseases, especially diarrheal diseases, and maternal and neonatal complications decreased

significantly (Figure 1). National vaccination programs for polio, hepatitis B and tuberculosis were also carried out by the health system, which also drastically affected reduction of communicable disease.

In addition to these health-related improvements, most economic indices show that over the past 40 years, overall living standards have improved significantly in Iran. Improvements in socioeconomic status including higher incomes, availability of electricity, access to safe drinking water and natural gas for heating and cooking, telephone communication and transport coverage of 98% in the urban areas and 95% of rural areas in today's Iran, have positively affected health conditions. As a result of all these health-related and economic improvements, deaths from communicable diseases has decreased from 23.57% in 1990 to 6.44% in 2015 and life expectancy at birth has increased by 32 years.<sup>2-5</sup>

Although communicable diseases are not a major health obstacle today, with the growing economy and modernization in Iran, NCD have now become a growing health concern. Cardiovascular diseases (CVDs), cancers, musculoskeletal disorders, neurologic disorders, gastrointestinal, respiratory and renal diseases constitute over 78% of all diseases.<sup>1,6</sup> With this change in disease patterns, the decision was made to include NCD prevention as a major component of PHC in rural areas, as well as the establishment of new PHC centers in urban areas as part of the Health Transformation Plan, aiming to provide universal healthcare for all Iranians.<sup>7</sup> Although a change in the right direction, these efforts have yet to control the growing rate of NCD.

### The Need for Cohort Studies

Unlike communicable diseases that are caused by an

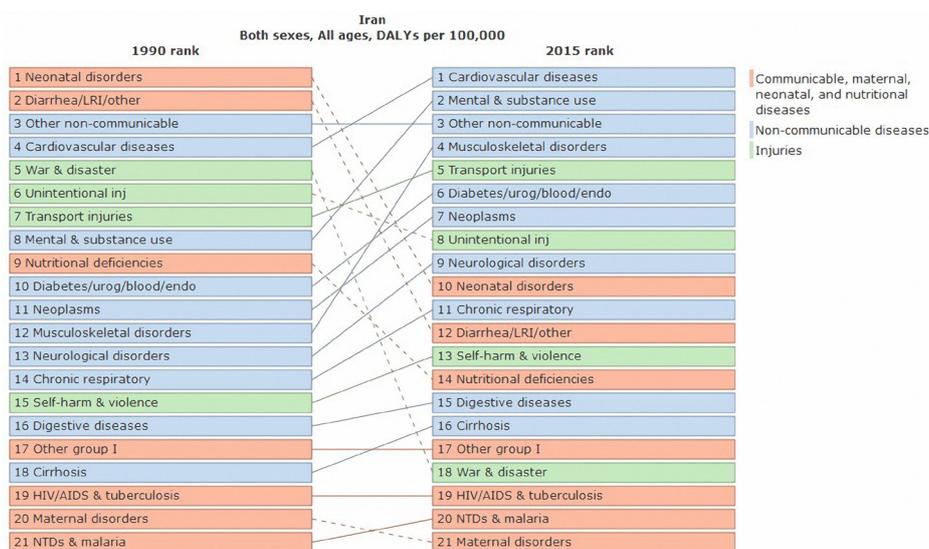


Figure 1. Changes in the Incidence of Communicable and Non-communicable Diseases in Iran From 1990 to 2015.<sup>5</sup>

outside pathogen, the etiology of most NCD is very complex and integrates different factors such as genetics, diet, physical activity, social and environmental exposures, etc.<sup>1</sup> Given the ethnically and geographically diverse population of Iran and the different cultures affecting each ethnicity's lifestyle, more evidence on the risk factors associated with NCD in different populations of Iran will help to find region-specific risk factors and will provide evidence for successful prevention of diseases in target populations. Since the etiology of diseases often takes decades to progress, careful recording of events over time is critical. Therefore, only a cohort study can collect the longitudinal information needed to investigate disease etiology, while serving as the infrastructure for future nested pragmatic intervention trials, ultimately leading to new evidence-based practice.<sup>8</sup>

The Golestan Cohort Study (GCS), the forerunner of cohorts in Iran and the largest single-center cohort study in the Eastern Mediterranean region, revealed the feasibility of cohort studies in Iran and the value of a cohort study specific to Iranians' lifestyles.<sup>9</sup> Habits such as drinking hot tea, opium consumption, poor oral health, etc in Golestan were found to be risk factors responsible for the very high incidence of esophageal cancer in that region.<sup>10-13</sup> These findings led to tailored education campaigns; for example, after identifying that drinking tea hotter than 60°C—a common habit in Golestan—is associated with esophageal cancer, not only were the GCS participants informed and educated, younger populations were also targeted with adequate education in order to modify this habit in the future generations. Another benefit of GCS and other cohort studies is that they set the foundation for many other nested case-control studies and clinical trials, which not only benefit the needs of the target community, but also tackle global health/medical problems. Today, over 20 sub-cohorts, case-control studies and clinical trials from GCS have contributed to the medical knowledge in the world.<sup>14-18</sup> Similarly, the PERSIAN Cohort has not only empowered 20 universities around the country by setting the infrastructure for high quality research, but will also set the foundation for many other future studies, this time in different ethnicities.

### PERSIAN Cohort Components

PERSIAN has 4 components with an overall sample size of 200 000 participants from different age groups, ethnicities and geographical areas. Although NCD are assessed in all components, the specific objectives of each component are unique to the needs of its population's age group. The PERSIAN Cohort includes the adult (main), birth, youth and elderly components, which will be explained briefly in the following sections. The ethics

committees at Tehran University of Medical Sciences, as well as all participating universities have approved the methodology of the cohort studies being carried out.

### PERSIAN Cohort—Main Adult and Eye Cohorts

The main and most extensive component of PERSIAN is to include 180 000 individuals aged 35–70 years from 19 distinct areas of Iran. The cohort sites are shown in Figure 2; these cohorts are run by the universities of medical sciences at (in alphabetical order): Ahvaz, Ardabil, Bandar Abbas, Fasa, Guilan, Kermanshah, Mashhad, Mazandaran, Qom, Rafsanjan, Sabzevar, Shahrekord, Shiraz (2 sites: Kharameh and Kavar), Tabriz, Urmia, Yasuj, Yazd, and Zahedan. These sites were chosen to include all the major ethnicities as well as the different geographical areas in Iran, in order to assess a wide range of cultural, genetic, lifestyle and environmental exposures that may positively or negatively affect disease development. Various questionnaires regarding medical, nutritional and lifestyle factors are completed and blood, urine, hair and nail samples are obtained from participants, who are to be followed-up for at least 20 years post enrollment to assess the occurrence of the study's outcomes of interest: deaths by cause and incidence of major NCD. The objectives and methodology of the PERSIAN Cohort have been extensively described before.<sup>8</sup> Although the primary objectives include determination of NCD incidence and burden, implementation of future studies on the cohort infrastructure to compare the relationship between risk and protective factors associated with NCD, as well as genetic studies in the different Iranian ethnicities are also of utmost importance, in order to individualize care. The PERSIAN Cohort enrollment phase began in September



**Figure 2.** PERSIAN Cohort Sites Throughout Iran. The Cohort sites have been chosen to include all the major ethnicities and geographical areas within Iran to capture different exposures.

2014.

In 6 of the PERSIAN Cohort sites, eye questionnaires and examinations are also performed evaluating refractive errors (Figure 2). Individuals are screened and referred for a complete ophthalmologic exam if they meet certain criteria or if suspicious findings are found, and imaging studies such as fundus photography and slit photos are performed.

#### PERSIAN Birth Cohort

The PERSIAN Birth Cohort aims to include 12000 neonates from the following four centers: Isfahan, Yazd, Semnan and Shiraz (Figure 2). The Universities of Medical Sciences at each of those locations oversee the cohort study. The main objective of the PERSIAN Birth Cohort is to study Developmental Origins of Health and Diseases (DOHaD) in an integrated multi-center cohort representing cultural and contextual variations in Iran. Expecting mothers in their first trimester of pregnancy are enrolled in the study and extensive questionnaires are completed for them and their husbands. Following birth, the newborns are followed for at least 18 years. Through the birth cohorts, the impact of socioenvironmental, psychological and genetic factors on pregnancy outcome, child mental and physical health, growth, development, and early-and late-onset chronic NCD are evaluated. Biological samples such as blood, urine, hair, nail, stool and cord blood are collected. The enrollment phase of the PERSIAN Birth Cohort started in October 2016.

#### PERSIAN Youth Cohort

The PERSIAN Youth Cohort is being conducted in 4 cities in Iran and will include 12000 males and females 15-34 years of age. The universities of medical sciences at Fasa, Kermanshah, Rafsanjan and Mazandaran oversee the project at their related cohort sites (Figure 2). The overarching objective of the PERSIAN Youth Cohort is to determine the annual incidence of common psychiatric disorders, psychosocial conditions and injuries in the youth population of Iran as well as the associated risk and protective factors. Besides the incidence of psychiatric disorders, initiation of alcohol and drug use, suicide, incidence of traffic and non-traffic injuries, hospitalizations for mental illness, course of mental disorder (chronicity, relapse, remission) and death are considered the Youth Cohort Study's main outcomes of interest. The PERSIAN Youth Cohort enrollment phase began in May 2015.

#### PERSIAN Elderly Cohort

The PERSIAN Elderly Cohort is to be conducted in the city of Neishabour as the Neishabour Longitudinal Study of Aging (NeLSA) (Figure 2). About 5000

individuals older than 50 years are to be included in this comprehensive assessment of the different aspects of aging. As part of this study, changes in health and well-being of participants are monitored and different economic, social, psychological, cognitive, health, biological and genetic data are collected to assess the needs of individuals through the aging transition, in an effort to improve the quality of life of the elderly. The main outcomes of interest in the PERSIAN Elderly Cohort include frailty/disability, morbidity/multi-morbidity and mortality from NCD, as well as hospitalizations and institutionalization. Enrollment began in Neishabour in December 2016.

#### Conclusion

The PERSIAN Cohort has started enrollment in all 4 components and will soon serve as an enormous dataset for research in medical, epidemiological and health-related fields. The evidence obtained from these studies can support a reform in Iran's healthcare system to confront the continuing increase in NCD. Through the already established Health Houses and *Behvarz* workers, as well as primary care physicians, policies based on the findings of the cohort can achieve greatness in control, management and prevention of NCD. National and international research ideas as well as collaborations are welcomed through the PERSIAN Cohort website at <http://persiancohort.com>.

#### Conflict of Interest Disclosures

The authors have no conflicts of interest.

#### References

1. Sepanlou SG, Kamangar F, Poustchi H, Malekzadeh R. Reducing the burden of chronic diseases: a neglected agenda in Iranian health care system, requiring a plan for action. *Arch Iran Med*. 2010;13(4):340-50. doi: 010134/aim.0015.
2. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2224-60. doi: 10.1016/s0140-6736(12)61766-8.
3. Iranian health houses open the door to primary care. *Bull World Health Organ*. 2008;86(8):585-6.
4. Health System Profile: Islamic Republic of Iran. Regional Health Systems Observatory. Geneva: World Health Organization; 2006.
5. Institute of Health Metrics and Evaluation. GBD Profile: Iran. Global Burden of Diseases, Injuries, and Risk Factors Study 2010. [http://www.healthdata.org/sites/default/files/files/country\\_profiles/GBD/ihme\\_gbd\\_country\\_report\\_iran.pdf](http://www.healthdata.org/sites/default/files/files/country_profiles/GBD/ihme_gbd_country_report_iran.pdf). Accessed September 28, 2016.
6. Sepanlou SG, Poustchi H, Kamangar F, Malekzadeh R. Effectiveness and feasibility of lifestyle and low-cost pharmacologic interventions in the prevention of chronic diseases: a review. *Arch Iran Med*. 2011;14(1):46-53.
7. Olyaeemanesh A, Majdzadeh R. Health technology assessment: A necessity in post-sanctions Iran while implementing the health transformation plan. *Med J Islam*

- Repub Iran. 2016;30:436.
8. Poustchi H, Eghtesad S, Kamangar F, Etemadi A, Keshtkar AA, Hekmatdoost A, et al. Prospective Epidemiological Research Studies in IrAN (The PERSIAN Cohort): Rationale, Objectives and Design. *Am J Epidemiol*. 2017. doi: 10.1093/aje/kwx314.
  9. Pourshams A, Khademi H, Malekshah AF, Islami F, Nouraei M, Sadjadi AR, et al. Cohort Profile: The Golestan Cohort Study--a prospective study of oesophageal cancer in northern Iran. *Int J Epidemiol*. 2010;39(1):52-9. doi: 10.1093/ije/dyp161.
  10. Islami F, Pourshams A, Nasrollahzadeh D, Kamangar F, Fahimi S, Shakeri R, et al. Tea drinking habits and oesophageal cancer in a high risk area in northern Iran: population based case-control study. *Bmj*. 2009;338:b929. doi: 10.1136/bmj.b929.
  11. Khademi H, Malekzadeh R, Pourshams A, Jafari E, Salahi R, Semnani S, et al. Opium use and mortality in Golestan Cohort Study: prospective cohort study of 50,000 adults in Iran. *BMJ*. 2012;344:e2502. doi: 10.1136/bmj.e2502.
  12. Gholipour M, Islami F, Roshandel G, Khoshnia M, Badakhshan A, Moradi A, et al. Esophageal cancer in Golestan province, Iran: a review of genetic susceptibility and environmental risk factors. *Middle East J Dig Dis*. 2016;8(4):249-66. doi: 10.15171/mejdd.2016.34.
  13. Ahmadi B, Alimohammadian M, Yaseri M, Majidi A, Boreiri M, Islami F, et al. Multimorbidity: epidemiology and risk factors in the Golestan Cohort Study, Iran: A Cross-Sectional Analysis. *Medicine (Baltimore)*. 2016;95(7):e2756. doi: 10.1097/md.0000000000002756.
  14. Merat S, Poustchi H, Hemming K, Jafari E, Radmard AR, Nateghi A, et al. PolyPill for prevention of cardiovascular disease in an urban Iranian population with special focus on nonalcoholic steatohepatitis: a pragmatic randomized controlled trial within a cohort (PolyIran - Liver) - Study protocol. *Arch Iran Med*. 2015;18(8):515-23.
  15. Ostovaneh MR, Poustchi H, Hemming K, Marjani H, Pourshams A, Nateghi A, et al. Polypill for the prevention of cardiovascular disease (PolyIran): study design and rationale for a pragmatic cluster randomized controlled trial. *Eur J Prev Cardiol*. 2015;22(12):1609-17. doi: 10.1177/2047487314550803.
  16. Malekzadeh F, Marshall T, Pourshams A, Gharravi M, Aslani A, Nateghi A, et al. A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy ('polypill') on cardiovascular risk factors. *Int J Clin Pract*. 2010;64(9):1220-7. doi: 10.1111/j.1742-1241.2010.02412.x.
  17. Roshandel G, Merat S, Sotoudeh M, Khoshnia M, Poustchi H, Lao-Sirieix P, et al. Pilot study of cytological testing for oesophageal squamous cell dysplasia in a high-risk area in Northern Iran. *Br J Cancer*. 2014;111(12):2235-41. doi: 10.1038/bjc.2014.506.

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