

Review Article

Reducing the Burden of Chronic Diseases: A Neglected Agenda in Iranian Health Care System, Requiring A Plan for Action

Sadaf Ghajarieh Sepanlou MD¹, Farin Kamangar MD^{2,1}, Hossein Poustchi MD¹, Reza Malekzadeh MD.¹

Abstract:

Chronic non-communicable diseases cause substantial morbidity and mortality in both developed and developing countries. Current studies indicate an increasing burden of chronic diseases in the near future, especially in developing countries. Chronic diseases have received much less attention than infectious diseases in Iran's health care system, which is a major cause for concern. Data on the dimensions of the epidemic and its health impact and financial burden in Iran are not adequate. A comprehensive action plan should start with a comprehensive research plan and should end in a multi-faceted intervention plan, involving the entire health network in Iran. Studies in some developed countries have demonstrated that a comprehensive intervention will lead to a reduction in the burden of chronic diseases in a relatively short time. The effect of such interventions and the methods to implement them should be tested in Iran's health system too.

Keywords: behavioral risk factor surveillance system, chronic disease, risk factors,

Introduction

Chronic non-communicable diseases, such as heart disease, stroke, cancer, diabetes, chronic respiratory diseases, chronic liver disease, and chronic renal disease cause substantial mortality worldwide. According to a WHO report, chronic diseases were responsible for 35 of the 58 million (60%) of

all global mortality in 2005¹ double the number of deaths from all infectious diseases (including HIV/AIDS, tuberculosis and malaria), maternal and perinatal conditions, and nutritional deficiencies combined. Up to 45% of chronic disease deaths and 86% of the burden of chronic diseases occur in people under 70 years of age.²

The aforementioned chronic diseases and several other chronic conditions such as visual impairment and blindness, hearing impairment and deafness, oral diseases, and genetic disorders also cause significant morbidity and reduce quality of life.

Chronic non-communicable diseases started to replace infectious diseases as the main causes of death mainly in the 20th century, a phenomenon that has been dubbed "epidemiologic transition". Improved

Authors' affiliations: ¹Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran, ²Department of Public Health Analysis, School of Community Health and Policy, Morgan State University, Baltimore, MD, USA.

Corresponding author and reprints: Reza Malekzadeh MD, Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, North Kargar St., Tehran 14117, Iran. Telefax: +98-218-801-2992, E-mail: malek@ams.ac.ir

Accepted for publication: 13 June 2010

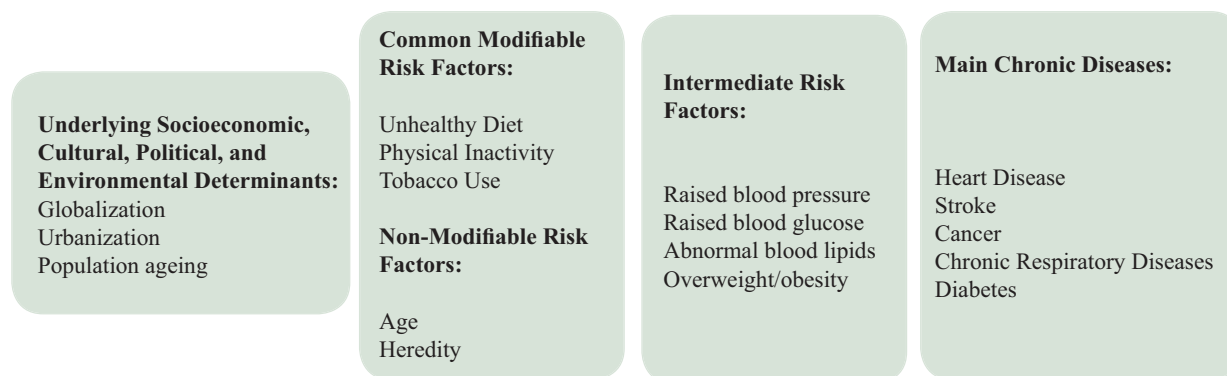


Figure 1. Causes of chronic diseases

hygiene, disinfection, availability of vaccines, and antibiotics were among many factors that contributed to the substantial reduction of infectious diseases and increased life, which in turn led to increased rates of chronic diseases. Epidemiologic transition first happened in Western countries. Indeed, by the middle of the 20th century chronic diseases were clearly the most important causes of the death in the United States and much of the developed world, while infectious diseases were still rampant in the low-income countries. Since then, however, developing countries have also experienced substantial reduction in the rates of infectious diseases, increased survival, and increased mortality and morbidity due to chronic diseases. For example, in Iran life expectancy increased from 54 years in 1970 to 71 years in 2008.³ With few exceptions, which are due to AIDS or long-term wars, similar trends are seen in most other developing countries.

Because of the significant increase burden of chronic diseases, intervention to reduce the burden of these diseases has become a priority for the World Health Organization (WHO). In 2005 WHO set a global goal to decrease mortality secondary to chronic diseases by 2% annually during the coming 10 years. The achievement of this goal means that 36 million deaths due to chronic diseases will be prevented by 2015. These averted deaths would also be associated with significant gains in countries' economic growth. It is estimated that achievement of this global goal would result in an accumulated economic growth of \$36 billion in China, \$15 billion in India and \$20 billion in the Russian Federation over the coming 10 years.³ This goal is ambitious but achievable. A small number of exposures, namely tobacco smoking, overweight and obesity,

high blood pressure, high cholesterol, excessive alcohol consumption, lack of exercise, and unhealthy diet contribute to a major fraction of all chronic diseases (Figure 1 and Table 1).² These major risk factors together account for approximately 80% of deaths from heart disease and stroke. Indeed, there is evidence that integrated and comprehensive preventive interventions have hindered and even reversed the rising trend of chronic diseases in a number of high income countries including Australia, Canada, United Kingdom and United States and even in the middle income country of Poland.³ However, without appropriate interventions, one could anticipate that the rates of morbidity and mortality from many chronic diseases would increase, especially in developing countries. If current trends continue, average levels of body mass index are projected to increase in almost all countries. By 2015, it is estimated that over 1.5 billion people will be overweight.²

Iran has a strong primary health-care system that has been very effective in reducing the burden of infectious diseases, infant and under 5 mortality, maternal mortality, and increasing the well-being of mother and child. For example, under 5 mortality rate decreased from 190/1000 in 1970 to 32/1000 in 2008.³ However, this system is not designed or well-prepared to manage and reduce the burden of chronic diseases.

In this paper, we review some of the major studies of the prevalence of the main risk factors of chronic diseases in Iran, report the prevalence of these exposures and incidence and mortality from chronic disease, and provide some suggestions on how to manage the increasing trend of chronic diseases in Iran.

Table 1. Deaths attributable to major risk factors in the global scale

Risk factors	n×10 ⁶ deaths/year
High blood pressure	7.1
Tobacco use	4.9
Raised total cholesterol level	4.4
Low fruit and vegetable consumption	2.7
Overweight or Obesity	2.6
Physical inactivity	1.9

Chronic diseases in Iran

Iran has one of the largest populations in the Middle East: 69.5 million in 2005. The causes of death cannot be reliably determined for a large proportion of the deceased in Iran, so presenting exact figures on causes of mortality is not possible. However, there is little doubt that like many other countries, ischemic heart disease, cancer, and stroke are major causes of death. For example, in a large cohort of 40 – 75-year-old individuals in Golestan Province of Iran, approximately 52% of all deaths were due to ischemic heart disease or stroke and 22% were due to cancers.⁴ The only major cause of death other than chronic diseases is road traffic accidents, which is mainly in younger individuals. The distribution of causes of death, based on a 2002 WHO report, is shown in table 2.⁵ Below, we provide some information about ischemic heart disease and cancer in Iran.

Heart disease

The aged-adjusted prevalence of coronary heart disease has been estimated to be 21.8% in Tehran (22.3% in women and 18.8% in men).⁶ In a study by Esteghamati et al., patients with myocardial infarction (MI) were compared with those who suffered from unstable angina. Five out of 9 patients with fatal MI were diabetics. Hypertension and current smoking was significantly higher in patients with MI compared to patients with unstable angina. Ninety-seven percent of all patients had at least one of the cardiovascular risk factors including hypertension, smoking, diabetes, high cholesterol, and low HDL-cholesterol levels. Authors concluded that in this study, 19 out of 20 patients with acute coronary event had at least one of conventional cardiac risk factors.⁷

Cancer

Based on National Cancer Registry reports from 2003 to 2006, population-based cancer registry reports from 5 provinces in 2006 and National Death Registry reports from 1999 to 2004, the age-standardized incidence rate of cancers was 110 and 98 per 100,000 among males and females, respectively. The male to female standard ratio was 1.12. The most common cancers among men and women were stomach cancer and breast cancer, respectively. The estimated total mortality rate for cancer was 65 and 41 per 100,000 for males and females, respectively, in 2004.⁸

Table 2. Contribution of major diseases to overall mortality based on the Mortality Country Fact Sheet in 2002

Cause of death	Deaths		Years of lost life (%)
	n×1000	%	
All causes	384	100	100
Ischemic Heart Disease	81	21	12
Road traffic accidents	40	11	16
Cerebrovascular disease	31	8	4
Perinatal conditions	18	5	10
Hypertensive heart disease	11	3	1
Stomach cancer	9	3	2
Chronic obstructive pulmonary disease	8	2	1
Diarrheal diseases	8	2	5
Inflammatory heart diseases	7	2	1
Lower respiratory infections	6	2	2

Table 3. Prevalence of certain chronic diseases and their risk factors in Iran (%)

	Diabetes mellitus	Impaired fasting Glucose	Prehypertension	Hypertension	Overweight	Obesity	Central obesity	Morbid obesity	Hypertriglyceridemia	Hypercholesterolemia
First National Survey (2005) ^{11,12,15}	7.7	16.8	46	25	35.8%	19.6%	9.7–43.4	3.4	36.4	42.9
Third National Survey (2007) ^{13,14}	8.7	—	—	26.6	36.3%	22.3	53.6	—	—	—
Golestan Cohort Study (2005) ²¹	6.2	—	—	35.7	34.2	28	—	—	—	—
Nation-wide surveillance of overweight and obesity ²⁰	—	—	—	—	42.8–57	11.1–25.2	—	—	—	—
Population-based study (2007) ¹⁹	—	—	—	—	34.8	18.8	28.3	—	—	—
Tehran Lipid and Glucose Study (2007)	8.1–10	6.3–8.7								
Systematic review on hypertension (2008) ¹⁸	—	—	—	23–50	—	—	—	—	—	—
Diabetes meta-analysis (2009) ¹⁷	9.8–10.7	—	—	—	—	—	—	—	—	—

Studies suggest that cancer can be traced back to a number of risk factors and thus it may be possible to prevent a large number of cancers through control of those risk factors. These risk factors include socio-economic status, diet, tobacco smoking, and other environmental factors.^{9–13}

Risk factors of major chronic diseases in Iran

In order to determine the magnitude of the problem associated with chronic diseases in the population of Iran, the national surveys of chronic diseases risk factors have been conducted annually since 2005 in collaboration with and using recommendations from the World Health Organization (WHO).¹⁴ The first, the second, and the third surveys were performed in 2005, 2006 and 2007, respectively.^{15–19} Other population-based studies and reviews have also been performed in recent years to estimate the burden of chronic diseases and their risk factors in Iran.^{6,7,20–30} A summary of these studies is presented as follows in Table 3.

Here, we briefly discuss some of these risk factors.

Diabetes

As demonstrated in Table 3, the prevalence of

diabetes has been estimated in several studies. Esteghamati et al. have demonstrated that MI is significantly higher in diabetic patients, and diabetic patients are more hypertensive compared to non diabetic patients.⁷ Diabetes is more frequent among women than men.^{7,20} Almost half of diabetic patients are not diagnosed and an additional 16.8% or 4.4 millions of Iranian adults have impaired fasting glucose.¹⁶ The high prevalence of diabetes in working-age adults is an ominous sign for our developing nation. As the relatively young Iranian population ages and urbanization accelerates, the prevalence of diabetes will likely increase.¹⁶ Haghdoost et al. have concluded that the rate of type 2 diabetes has increased during recent years in Iran and there is a strong association between age and diabetes.²⁰

In the cohort study by Harati et al., after a median follow-up of 6 years, the age and sex standardized cumulative incidence of 6.4% (95%CI: 5.6 – 7.2) and incidence rate of 10.6 (9.2 – 12.1) per 1000 person years were documented. Besides classical diabetes risk factors, female sex, and low education level significantly increase risk of diabetes in

age adjusted models. In full model, the independent predictors have been age, family history of diabetes, body mass index, abdominal obesity, high triglyceride, isolated impaired fasting glucose (IFG), and isolated impaired glucose tolerance (IGT).²⁸

Based on Tehran Lipid and Glucose Study, the prevalence of diagnosed and undiagnosed diabetes, isolated IFG, isolated IGT, and combined IFG/IGT are 8.1%, 5.1%, 8.7%, 5.4%, and 4.0% in men and 10%, 4.7%, 6.3%, 7.6%, and 4.5% in women, respectively. Participants with undiagnosed diabetes have higher age, body mass index (BMI), waist circumference, systolic and diastolic blood pressures, triglycerides and lower HDL-cholesterol compared to normoglycemic subjects. Undiagnosed diabetes is associated with family history of diabetes, increased BMI, abdominal obesity, hypertriglyceridemia, hypertension, and low HDL-cholesterol levels. In conclusion, screening individuals with high BMI, hypertension, abdominal obesity, and family history of diabetes may be quite efficient.²⁹

The age-standardized death rate attributable to heart disease and diabetes is estimated to be higher than 400 per 100,000. The gross domestic product (GDP) lost in Iran due to heart disease and diabetes in 2015 will be 167% of that in 2006.³¹ All the evidence states the necessity of the comprehensive preventive program to combat the epidemic of diabetes in Iran.

Hypertension

The prevalence of hypertension has been estimated in several studies and demonstrated in Table 3. The 2005 survey of non-communicable diseases showed a prevalence of 25% among the 25 – 64-year-old Iranians. Among hypertensive patients, 34% were aware of their elevated blood pressure and 25% took antihypertensive medications; of these treated subjects, only 24% had blood pressure values <140/90 mmHg. Hypertension and prehypertension were associated with age, male gender, obesity, central obesity, hypercholesterolemia, and diabetes.¹⁵ A sharp increase in the prevalence of hypertension by age, and also greater risk in females has been reported by Haghdoust et al.²¹

Overweight and obesity

The prevalence of overweight and obesity in Iran

is close to those seen in the United States³²; nearly half of the over 20-year-old population is either overweight or obese. Overweight as well as generalized and abdominal obesity are more prevalent in the 45 – 64-year age group.¹⁹ Age, low physical activity, low educational attainment, marriage, and residence in urban areas are strongly associated with obesity.^{22,23} Abdominal obesity is more common among women than men and greater with older age.²² Excess body weight appears to be common in Iran.²³

The overall prevalence of obesity has increased from 13.6% in 1999 to 19.6% in 2005 and 22.3% in 2007. For overweight subjects, the rates were 32.2%, 35.8%, and 36.3%, respectively. During this time period, the mean body mass index (BMI) increased from 25.03 in 1999, to 26.14 in 2005, and 26.47 in 2007. The increase in prevalence of obesity was observed in both genders and in both urban and rural residents.¹⁷ The increased consumption of calorie-dense food along with sedentary lifestyle contributes to the epidemic of obesity. The per capita consumption of carbonated beverages in Iran is 42 liters per year. Forty percent of Iranians consume more food than they need and the average Iranian consumes 40% more carbohydrate and 30% more fat than what he or she actually need.²⁵

Recent estimates show that the prevalence of obesity is seemingly increasing at alarming rates.^{27,30,33} In both sexes the fastest increasing trends in obesity and central fat accumulation are seen in the 30- to 40- and 20- to 30-year-old age groups.³⁰

The rapid growth of obesity during recent years in Iran indicates the necessity of primary prevention programs to counteract this undesired condition and its subsequent complications such as diabetes, coronary artery disease, hypertension, and osteoarthritis.^{17,22}

Facts to remember

There are several facts that help us in delineating strategies to combat chronic diseases (Table 4). Some of these facts have been misunderstood by people and policy makers concerning chronic diseases in middle and low income countries.

The costs of chronic diseases

Chronic diseases adversely affect national econo-

Table 4. Some facts about chronic diseases

Fact	Description
Chronic diseases are not concentrated in high income countries.	In reality 80% of deaths due to chronic diseases occur in low and middle income countries. ^{34,35}
Chronic diseases should be at least as seriously as infectious diseases.	Chronic diseases were responsible for nearly half of the burden of diseases in 2005, both worldwide and in low and middle income countries ³¹
Chronic diseases are not confined to rich people.	Chronic diseases impose significant financial burden on poor patients and can aggravate their poverty
Chronic diseases are not confined to old people.	Chronic diseases mainly affect the economically productive victims between 45 and 64 years of age in middle and low income countries
Chronic diseases mostly affect men.	Chronic diseases, including heart disease, are the most common cause of death in women too ²
The health system is responsible for preventing chronic diseases.	Governments have a pivotal responsibility for improving the health and well-being of populations, and for providing special protection for vulnerable groups: children and poor people
Chronic diseases are preventable.	Common, modifiable risk factors underlie the major chronic diseases: unhealthy diet, physical inactivity, and tobacco use.
Chronic disease interventions are cost effective.	Interventions for eliminating risk factors are quite inexpensive to implement.
The major burden of most chronic diseases can be traced back to a limited number of common risk factors.	Absence of chronic disease in the presence of risk factors and the presence of disease in the absence of risk factors happens, but it's rare
Chronic diseases result in lower quality of life in addition to sudden death.	Preventive interventions are associated with longer and healthier lives for vulnerable groups of societies.

mies. Medical expenses deplete savings and investments and reduce the quantity and productivity of labor. All these effects reduce the productivity of individuals and households, and worsen the national economy. Chronic diseases adversely affect earnings at the household level, and national income or gross domestic product at the national level.

The direct costs of chronic diseases are enormous and its estimates vary in different regions or years, which may reflect differences in the level of health-care access and delivery, the financing systems of the countries, and methodological variations.³⁶⁻⁴²

In the United States, the estimated total health-care costs resulting from heart disease increased from US\$ 298.2 billion in 2000, to US\$ 329.2 billion in 2001 and US\$ 351.8 billion in 2002.³⁶ The estimated 2 million stroke cases in the United States in 1996 cost the health-care system US\$ 8.3 billion, and caused 5.2 million work days to be lost. In the United Kingdom, heart disease cost the health-care system £1.7 billion (approximately US\$ 3 billion) in

1999, £2.4 billion (approximately US\$ 4.3 billion) in informal care and £2.9 billion (approximately US\$ 5.2 billion) in loss of productivity.⁴¹ Stroke cost the National Health Service £15,303 (approximately US\$ 27,306) over five years for every person who experienced a stroke, rising to £29,405 (approximately US\$ 52,470) if informal care was included. In Australia, stroke is estimated to be responsible for about 2% of the national total attributable direct health-care costs.^{43,44}

In Iran, 5.9% and 6.4% of the gross domestic product was spent on health in 2000 and 2007, respectively.⁴⁵ To the best of our knowledge, only one study by Esteghamati et al. has addressed the issue of cost of one of the major chronic diseases in Iran, namely the diabetes. According to this population-based study, total annual direct costs of diabetic and control participants are US\$152.3±14.5 and US\$52.0±5.8, respectively, which is indicative of 2.92 times higher costs in diabetic patients. The most expensive components of direct costs

are medications and devices, and hospitalization in diabetic patients (28.7% and 28.6%, respectively). Total indirect costs are US\$39.6±2.4 and US\$16.7±1.1 in diabetic and non-diabetic individuals. The aggregate annual direct costs of diabetes are estimated to be US\$112.424±10.732 million and US\$590.676±65.985 million in Tehran and Iran, respectively. Diabetes complications account for 53% of the aggregate excess direct costs of diabetes. Authors have concluded that diabetes is an expensive medical problem in Iran and planning of national programs for its control and prevention is necessary.⁴⁶

Action

The first step to combat the chronic diseases epidemic should encompass an extensive and comprehensive research process on the dimensions and actual burden of this group of diseases and their risk factors in Iran. In the first part of the current paper, we have mentioned the major studies on the prevalence and burden of chronic diseases in Iran. A continued effort to build on the currently available information is mandatory. Acquiring the proper insight and distributing the correct knowledge on the importance of chronic diseases and their risk factors among people and policy makers is thus the first step to attract attentions toward this neglected agenda in Iran.

The next step is to estimate the existing infrastructure that can handle interventions on the prevention of chronic diseases nation-wide. The truth is that the health system in Iran, from health houses in remote villages, to specialized hospitals in central cities of Iran, comprises a vast network that can easily and potentially handle and implement appropriately designed interventions for the prevention of chronic diseases in Iran. Currently this extensive network has been mostly focused on the longevity of children under 5 years of age and their mothers and simply neglects the destiny of those children who reach 15 years and above. There is no plan implemented for the prevention of increasingly prevailing risk factors for chronic diseases among the adolescent and adults and the mortality and morbidity of this group of diseases is simply neglected in the health system of Islamic Republic of Iran. In view of the fast speed of the epidemic of chronic diseases in Iran, the health system is completely unarmed. The

fact is that health assistants in villages (known as Behvarz) and family physicians in urban and sub-urban areas, along with their roles in monitoring the vaccination and growth of children, should be able to take on the responsibility of controlling risk factors among adolescents and adults. Risk factors such as obesity, unhealthy diet, inactivity, undiagnosed prehypertension, hypertension, and diabetes can be readily monitored and easily prevented through relatively simple and feasible population-based interventions that address the causes rather than the consequences of chronic diseases and can be central to attempts to prevent the emergence of future epidemics. Small reductions in the exposure of the population to risk factors such as tobacco use, unhealthy diet and physical inactivity will lead to population-level reductions in cholesterol, blood pressure, blood glucose, and body weight. More fundamentally, population-based interventions can also be effective in addressing the underlying determinants of chronic diseases.

The health system in Iran has the potential to launch specific interventions for individuals as well. These interventions focus on people who are at high risk and those with established chronic disease. These interventions reduce the risk of developing chronic disease, reduce complications, and improve quality of life. Population-wide and individual approaches are complementary. Comprehensive approaches should also be integrated.

It is not necessary to wait decades to realize the benefits of prevention and control activities. Risk factor reduction can lead to surprisingly rapid health gains, at both population and individual levels. This can be observed through national trends, sub-national epidemiological data, and clinical trials. Benefits can be realized quickly after two years, and full benefits will occur after five years.⁴⁷

The nation-wide population-based intervention can start from small community-based interventions as a starting point for national improvement. Successful community-based interventions require partnerships between community organizations, policy-makers, businesses, health providers, and community residents. Finland is a good example of how community-based programs, once shown to be successful can be lead to nation-wide improvements.⁴⁸

Initial reductions will occur partly as a result of the diffusion of health-related information among

the general population. Later, integrated and comprehensive approaches can be successfully implemented. Interventions may include school-based interventions,⁴⁹ workplace interventions,^{50,51} screening,^{52,53} clinical prevention, interventions for high-risk individuals, interventions to reduce the risks in established disease,⁵⁴ disease management, designing multidisciplinary health care teams, preparing evidence-based treatment guidelines,^{55–58} providing support for patient self-management,⁵⁹ rehabilitation,^{60–64} and palliative care.^{65–67} These approaches have been used to reduce chronic disease death rates in many countries, demonstrating the feasibility of achieving more widespread success. Many interventions are not only effective but are also suitable for resource-constrained settings. Historically, laws have played a crucial role in some of the greatest achievements in public health such as environmental control laws, seat-belt laws, warnings on cigarette packs and other tobacco control measures, and water fluoridation to reduce dental caries. Current laws relating to chronic disease have proved to be an effective and central component of comprehensive prevention and control strategies. Advertising bans for tobacco products and the reduction of salt in food (whether through voluntary agreement with industry or enforced) are both very cost-effective in all regions, as assessed by the WHO-CHOICE project.

Potential of fixed dose combination therapy: polypill

One strategy that has been proposed to reduce the burden of chronic disease is a fixed dose combination pill (now commonly known as a polypill).^{68,69} Because each component apparently works in addition to the others, net benefits are anticipated to be substantial. Fixed dose combinations are now a core component of care for people with HIV/AIDS, tuberculosis, and malaria. As well as improving clinical outcomes, they simplify distribution of multiple medications, which can be an important advantage in a resource-limited health-care setting.

Application of polypills requires further research on its effectiveness. Most recently polypills have been proposed to reduce the burden of cardiovascular diseases in primary or secondary prevention settings. Scant studies have been conducted on polypill in Iran,^{68,69} the most recent of which, done by Malekzadeh et al., demonstrated the effectiveness

of polypill in reducing blood pressure and LDL-cholesterol.⁷⁰

The major challenge remains one of implementation. Ideally, these strategies should integrate with systems for other long-term medication delivery. The components of a polypill are no longer covered by patent restrictions and could be produced at a cost of little more than US\$ 1 per patient per month. For people with cardiovascular disease in low and middle income countries, access to preventive care is usually dependent upon their ability to pay, and hence it is this large, underserved group that gains most from a polypill.^{71,72}

Conclusion

Chronic diseases are already the major cause of death in almost all countries, and the threat to people's lives, their health and the economic development of their countries is growing fast. Yet, the knowledge exists to deal with this threat and to save millions of lives. Effective and cost-effective interventions, and the knowledge to implement them, have been shown to be effective in many countries. If existing interventions are used together as part of a comprehensive, integrated approach, the global goal for preventing chronic diseases can be achieved.

References

1. Yach D, Hawkes C, Gould CL, Hofman KJ. The global burden of chronic diseases: overcoming impediments to prevention and control. *JAMA*. 2004; **291**: 2616 – 2622.
2. WHO. *Preventing Chronic Diseases: A Vital Investment: WHO Global Report*. Geneva: World Health Organization; 2005. Available from: URL: http://www.who.int/chp/chronic_disease_report/en/
3. UNICEF: Statistics, Iran, Islamic Republic of. 2009. Available from: URL: http://www.unicef.org/infobycountry/iran_statistics.html#72
4. Khademi H, Etemadi A, Kamangar F, Nouraie M, Shakeri R, Abaie B, Pourshams A, et al. Verbal Autopsy: Reliability and Validity Estimates for Causes of Death in the Golestan Cohort Study in Iran. *PLoS one*. 2010; **5**:e11183.
5. WHO. *World Health Statistics 2006*. Geneva: World Health Organization. Available from: URL: <http://www.who.int/whosis/whostat2006.pdf>
6. Hadaegh F, Harati H, Ghanbarian A, Azizi F. Prevalence of coronary heart disease among Tehran

- adults: Tehran Lipid and Glucose Study. *East Mediterr Health J.* 2009; **15**: 157 – 166.
7. Esteghamati A, Abbasi M, Nakhjavani M, Yousefizadeh A, Basa AP, Afshar H. Prevalence of diabetes and other cardiovascular risk factors in an Iranian population with acute coronary syndrome. *Cardiovasc Diabetol.* 2006; **5**: 15.
8. Mousavi SM, Gouya MM, Ramazani R, Davanlou M, Hajsadeghi N, Seddighi Z. Cancer incidence and mortality in Iran. *Ann Oncol.* 2009; **20**: 556 – 563.
9. Islami F, Kamangar F, Nasrollahzadeh D, Aghcheli K, Sotoudeh M, Abedi-Ardekani B, et al. Socio-economic status and oesophageal cancer: results from a population-based case-control study in a high-risk area. *Int J Epidemiol.* 2009; **38**: 978 – 988.
10. Islami F, Malekshah AF, Kimiagar M, Pourshams A, Wakefield J, Gogiani G, et al. Patterns of food and nutrient consumption in northern Iran, a high-risk area for esophageal cancer. *Nutr Cancer.* 2009; **61**: 475 – 483.
11. 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.
12. Pourfarzi F, Whelan A, Kaldor J, Malekzadeh R. The role of diet and other environmental factors in the causation of gastric cancer in Iran--a population based study. *Int J Cancer.* 2009. **125**: 1953 – 1960.
13. Pourshams A, Saadatian-Elahi M, Nouraie M, Malekshah AF, Rakhshani N, Salahi R, et al. Golestan cohort study of oesophageal cancer: feasibility and first results. *Br J Cancer.* 2005. **92**: 176 – 181.
14. WHO. STEPwise approach to surveillance (STEPS). 2008. Available from: URL: http://www.who.int/ncd_surveillance/media/en/269.pdf
15. Esteghamati A, Abbasi M, Alikhani S, Gouya MM, Delavari A, Shishehbor MH, et al. Prevalence, awareness, treatment, and risk factors associated with hypertension in the Iranian population: the national survey of risk factors for noncommunicable diseases of Iran. *Am J Hypertens.* 2008; **21**: 620 – 626.
16. Esteghamati A, Gouya MM, Abbasi M, Delavari A, Alikhani S, Alaedini F, et al. Prevalence of diabetes and impaired fasting glucose in the adult population of Iran: National Survey of Risk Factors for Non-Communicable Diseases of Iran. *Diabetes Care.* 2008; **31**: 96 – 98.
17. Esteghamati A, Khalilzadeh O, Mohammad K, Meysamie A, Rashidi A, Kamgar M, et al. Secular trends of obesity in Iran between 1999 and 2007: national surveys of risk factors of non-communicable diseases. *Metab Syndr Relat Disord.* 2010; **8**: 209 – 213.
18. Esteghamati A, Meysamie A, Khalilzadeh O, Rashidi A, Haghazali M, Asgari F, et al. Third national Surveillance of Risk Factors of Non-Communicable Diseases (SuRFNCD-2007) in Iran: methods and results on prevalence of diabetes, hypertension, obesity, central obesity, and dyslipidemia. *BMC Public Health.* 2009; **9**: 167.
19. Kelishadi R, Alikhani S, Delavari A, Alaedini F, Safaie A, Hojatzadeh E. Obesity and associated lifestyle behaviours in Iran: findings from the First National Non-communicable Disease Risk Factor Surveillance Survey. *Public Health Nutr.* 2008; **11**: 246 – 251.
20. Haghdooost AA, Rezazadeh-Kermani M, Sadghirad B, Baradaran HR. Prevalence of type 2 diabetes in the Islamic Republic of Iran: systematic review and meta-analysis. *East Mediterr Health J.* 2009. **15**: 591 – 599.
21. Haghdooost AA, Sadeghirad B, Rezazadehkermani M. Epidemiology and heterogeneity of hypertension in Iran: a systematic review. *Arch Iran Med.* 2008. **11**: 444 – 452.
22. Hajian-Tilaki KO, Heidari B. Prevalence of obesity, central obesity and the associated factors in urban population aged 20 – 70 years, in the North of Iran: a population-based study and regression approach. *Obes Rev.* 2007; **8**: 3 – 10.
23. Janghorbani M, Amini M, Willett WC, Mehdi Gouya M, Delavari A, Alikhani S, et al. First nationwide survey of prevalence of overweight, underweight, and abdominal obesity in Iranian adults. *Obesity (Silver Spring).* 2007; **15**: 2797 – 2808.
24. Bahrani H, Sadatsafavi M, Pourshams A, Kamangar F, Nouraei M, Semnani S, et al. Obesity and hypertension in an Iranian cohort study; Iranian women experience higher rates of obesity and hypertension than American women. *BMC Public Health.* 2006; **6**: 158.
25. Malekzadeh R, Mohamadnejad M, Merat S, Pourshams A, Etemadi A. Obesity pandemic: an Iranian perspective. *Arch Iran Med.* 2005; **8**: 291 – 292.
26. Hosseinpanah F, Kasraei F, Nassiri AA, Azizi F. High prevalence of chronic kidney disease in Iran: a large population-based study. *BMC Public Health.* 2009; **9**: 44.
27. Hosseinpanah F, Barzin M, Eskandary PS, Mirmiran P, Azizi F. Trends of obesity and abdominal obesity in Tehranian adults: a cohort study. *BMC Public Health.* 2009; **9**: 426.
28. Harati H, Hadaegh F, Saadat N, Azizi F. Population-based incidence of Type 2 diabetes and its associated risk factors: results from a six-year cohort study in Iran. *BMC Public Health.* 2009; **9**: 186.

29. Hadaegh F, Bozorgmanesh MR, Ghasemi A, Harati H, Saadat N, Azizi F. High prevalence of undiagnosed diabetes and abnormal glucose tolerance in the Iranian urban population: Tehran Lipid and Glucose Study. *BMC Public Health*. 2008; **8**: 176.
30. Azizi F, Azadbakht L, Mirmiran P. Trends in overweight, obesity and central fat accumulation among Tehranian adults between 1998 – 1999 and 2001 – 2002: Tehran lipid and glucose study. *Ann Nutr Metab*. 2005; **49**: 3 – 8.
31. Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet*. 2007; **370**: 1929 – 1938.
32. Sarrafzadegan N, Kelishadi R, Siadat ZD, Esmailzadeh A, Solhpour A, Shirani S, et al. Obesity and cardiometabolic risk factors in a representative population of Iranian adolescents and adults in comparison to a Western population: the Isfahan Healthy Heart Programme. *Public Health Nutr*. 2010; **13**: 314 – 323.
33. Azadbakht L, Mirmiran P, Shiva N, Azizi F. General obesity and central adiposity in a representative sample of Tehranian adults: prevalence and determinants. *Int J Vitam Nutr Res*. 2005; **75**: 297 – 304.
34. Boutayeb A. The double burden of communicable and non-communicable diseases in developing countries. *Trans R Soc Trop Med Hyg*. 2006; **100**: 191 – 199.
35. Lopez AD, Mathers CD. Measuring the global burden of disease and epidemiological transitions: 2002 – 2030. *Ann Trop Med Parasitol*. 2006; **100**: 481 – 499.
36. American Heart Association. *Heart Disease and Stroke Statistics - 2001 Update*. Dallas, TX: American Heart Association; 2001.
37. Cohen JW, Krauss NA. Spending and service use among people with the fifteen most costly medical conditions, 1997. *Health Aff (Millwood)*. 2003; **22**: 129 – 138.
38. Currie CJ, Morgan CL, Peters JR. Patterns and costs of hospital care for coronary heart disease related and not related to diabetes. *Heart*. 1997; **78**: 544 – 549.
39. Druss BG, Marcus SC, Olfson M, Pincus HA. The most expensive medical conditions in America. *Health Aff (Millwood)*. 2002; **21**: 105 – 111.
40. Druss BG, Marcus SC, Olfson M, Tanielian T, Elinson L, Pincus HA. Comparing the national economic burden of five chronic conditions. *Health Aff (Millwood)*. 2001; **20**: 233 – 241.
41. Liu JL, Maniadakis N, Gray A, Rayner M. The economic burden of coronary heart disease in the UK. *Heart*. 2002; **88**: 597 – 603.
42. Russell MW, Huse DM, Drowns S, Hamel EC, Hartz SC. Direct medical costs of coronary artery disease in the United States. *Am J Cardiol*. 1998; **81**: 1110 – 1115.
43. Australian Institute of Health and Welfare/Centre for Health Program Evaluation. *Preliminary Estimates: Disease Costs and Impact Study (DCIS)*. Canberra: Australian Institute of Health and Welfare/Centre for Health Program Evaluation; 1995.
44. Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA. Cost of stroke in Australia from a societal perspective: results from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2001; **32**: 2409 – 2416.
45. WHO. *World Health Statistics 2010*. Geneva: World Health Organization. Available from: URL: http://www.who.int/whosis/whostat/EN_WHS10_Full.pdf
46. Esteghamati A, Khalilzadeh O, Anvari M, Meysamie A, Abbasi M, Forouzanfar M, et al. The economic costs of diabetes: a population-based study in Tehran, Iran. *Diabetologia*. 2009; **52**: 1520 – 1527.
47. Law MR, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischaemic heart disease? *BMJ*. 1994; **308**: 367 – 372.
48. Nissinen A, Berrios X, Puska P. Community-based noncommunicable disease interventions: lessons from developed countries for developing ones. *Bull World Health Organ*. 2001; **79**: 963 – 970.
49. UNESCO/UNICEF/WHO/World Bank. *Focusing Resources on Effective School Health: A FRESH Start to Enhancing the Quality and Equity of Education*. World Education Forum 2000, final report. Available from: <http://siteresources.worldbank.org/INTPHAAG/Resources/AAGSchoolHealth-FRESH.pdf>
50. Muto T, Yamauchi K. Evaluation of a multicomponent workplace health promotion program conducted in Japan for improving employees' cardiovascular disease risk factors. *Prev Med*. 2001; **33**: 571 – 577.
51. Moher M, Hey K, Lancaster T. Workplace interventions for smoking cessation. *Cochrane Database Syst Rev*. 2005; **(2)**: CD003440.
52. Wald NJ. Guidance on terminology. *J Med Screen*. 2001; **8**: 56.
53. Strong K, Wald N, Miller A, Alwan A; WHO Consultation Group. Current concepts in screening for noncommunicable disease: World Health Organization Consultation Group Report on methodology of noncommunicable disease screening. *J Med Screen*. 2005; **12**: 12 – 19.
54. WHO. *Prevention of Recurrent Heart Attacks and Strokes in Low and Middle Income Populations. Evidence-Based Recommendations for Policy*

- Makers and Health Professionals. Geneva: World Health Organization; 2003.
55. Field MJ, Lohr KN. *Guidelines for Clinical Practice – from Development to Use*. Washington DC: National Academy Press; 1992.
 56. International Diabetes Federation. *Guide for Guidelines: A Guide for Clinical Guideline Development*. Brussels: International Diabetes Federation; 2003.
 57. Grimshaw J, Eccles M, Tetroe J. Implementing clinical guidelines: current evidence and future implications. *J Contin Educ Health Prof*. 2004; **24** (suppl 1): S31 – S37.
 58. Garg AX, Adhikari NK, McDonald H, Rosas-Arellano MP, Devereaux PJ, Beyene J, et al. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. *JAMA*. 2005; **293**: 1223 – 1238.
 59. Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA*. 2002; **288**: 2469 – 2475.
 60. Outpatient Service Trialists. Therapy-based rehabilitation services for stroke patients at home. *Cochrane Database Syst Rev*. 2003; **(1)**: CD002925.
 61. Guzmán J, Esmail R, Karjalainen K, Malmivaara A, Irvin E, Bombardier C. Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database Syst Rev*. 2002; **(1)**: CD000963.
 62. Jolliffe JA, Rees K, Taylor RS, Thompson D, Oldridge N, Ebrahim S. Exercise-based rehabilitation for coronary heart disease. *Cochrane Database Syst Rev*. 2001; **(1)**: CD001800.
 63. McGrath PD. Review: exercise-based cardiac rehabilitation reduces all-cause and cardiac mortality in coronary heart disease. *ACP J Club*; 2004; **141**: 62.
 64. Oldridge NB, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. *JAMA*. 1988; **260**: 945 – 950.
 65. Hearn J, Higginson IJ. Do specialist palliative care teams improve outcomes for cancer patients? A systematic literature review. *Palliat Med*. 1998; **12**: 317 – 332.
 66. Salisbury C, Bosanquet N, Wilkinson EK, Franks PJ, Kite S, Lorentzon M, et al. The impact of different models of specialist palliative care on patients' quality of life: a systematic literature review. *Palliat Med*. 1999; **13**: 3 – 17.
 67. Wilkinson EK, Salisbury C, Bosanquet N, Franks PJ, Kite S, Lorentzon M, et al. Patient and carer preference for, and satisfaction with, specialist models of palliative care: a systematic literature review. *Palliat Med*. 1999; **13**: 197 – 216.
 68. Malekzadeh F, Pourshams A, Marshall T. The preventive polypill--much promise, insufficient evidence. *Arch Iran Med*. 2007; **10**: 430 – 431.
 69. Rastegarpanah M, Malekzadeh F, Thomas GN, Mohagheghi A, Cheng KK, Marshall T. A new horizon in primary prevention of cardiovascular disease, can we prevent heart attack by "heart polypill"? *Arch Iran Med*. 2008; **11**: 306 – 313.
 70. Malekzadeh F, Marshall T, Pourshams A, Gharravi M, Aslani A, Nateghi A. 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**:1220-1227
 71. Murray CJ, Lauer JA, Hutubessy RC, Niessen L, Tomijima N, Rodgers A, et al. Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. *Lancet*. 2003; **361**: 717 – 725.
 72. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ*. 2003; **326**: 1419.