Type 2 Diabetes in Iranian women; determinants, prevention and control

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Iran

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Type 2 Diabetes in Iranian women; determinants, prevention and control

A thesis submitted in partial fulfilment of the requirement for the degree of

Master of Public Health

by

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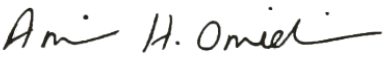
Iran

Declaration:
Where other people's work has been used (either from a printed source, internet or any other source) this has been carefully acknowledged and referenced in accordance with departmental requirements.
The thesis Type 2 Diabetes in Iranian women; determinants, prevention and control is my own work.

Signature: 

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Abstract

Currently, there is a health transition in Iran towards Non-Communicable Diseases. The prevalence of diabetes as one of the NCDs has increased in recent decades in Iran. It was reported about five percent in 2000 while it is predicted to be 12.5% among adults in 2030.

The burden of diabetes in Iranian women is almost two times than that of men. Also, relative risk of deaths in diabetic women is higher than men. This study aims to describe the determinants of diabetes in Iranian women, and through the analysis of secondary data, to quantify the association between women's socio-demographic characteristics and diabetes. The findings will be contrasted against the existing health policies and interventions in Iran.

To review the literature, the following databases and research engines were searched by keywords and the defined search strategy: PubMed, Iran Medex (in Persian), SID (in Perisan), Google and Google scholar. Binomial logistic regression was conducted to analysis the secondary data was collected for the Islamic Republic of Iran's Multiple Indicator Demographic and Health Survey 2010 (IrMIDHS).

In this research, 17 studies were included through literature review. Findings from these studies showed current evidences indicated that older age, family history of diabetes, some genetic factors, dyslipidemia, hypertension, obesity, stressful events and living in urban areas are positively correlated with the risk of diabetes. While healthy diet, physical activity, access to primary health care services and higher education were associated with reduced risk of diabetes.

Analysis of secondary data, indicated that having diabetes in women 15-49 years old is positively associated with older age, lower education, watching less TV, living in urban areas, having asthma, cardiovascular and musculoskeletal diseases.

The national programme for prevention and control of diabetes in Iran is more focused on high risk population and provide health care services for pre-diabetic or diabetic patients. Recommendations were suggested including; Conduct studies at national level to define all determinants of diabetes among Iranian women, Develop a framework for determinants of diabetes in Iran, Implement population-wide interventions.

Keywords;
Diabetes, Iran, Prevention, Intervention

Word counts; 11324

Abbreviations

BMI: Body Mass Index
DBP: Diastolic Blood Pressure
Diabetes: type 2 diabetes
DM: Diabetes Mellitus
FDR : First-Degree Relatives
GDP; Gross Domestic Product
HDL: High-density lipoprotein
IFG; Impaired Fasting Glucose
IGT; Impaired Glucose Tolerance
IrMIDHS; Iran's Multiple Indicator Demographic and Health Survey
LDL: Low-density lipoprotein
MDGs; Millennium Development Goals
MENA; Middle East and North Africa region
MOHME; Ministry of Health and Medical Education
NCDs; Non Communicable Diseases
PCOD: Poly Cystic Ovary Disease
SBP: Systolic Blood Pressure
TG: Triglyceride
VIF; Variance Inflation Factor
WC: Waist circumference
WHR: Waist to Hip Ratio

Introduction

Since the initial years of studying medicine in Tehran University of medical sciences (TUMS), my personal passionate enthusiasm about public health issues led me to participate in relative courses and achieve the Master of Public Health (MPH) simultaneously in Iran. During studying, I started working in Knowledge Utilization Research Center (KURC) and collaborated in research studies in field of health policies. After graduation, following my acquired knowledge, I worked in the field of improving quality of health services in Iran and continued my collaboration with KURC. Gaining experience in public health researches along with participating in International Course in Health Development in Royal Tropical Institute, made me more familiar with the state and importance of Non-Communicable Diseases (NCDs) and related risk factors.

Currently, there is a health transition in Iran towards NCDs. The prevalence of diabetes as one of the NCDs has increased in recent years. It was reported about 9.73% in adults aged 15-64 years and its mortality was estimated at 2% of total deaths.

The burden of diabetes in Iranian women is almost two times than that of men. Also, relative risk of deaths in diabetic women is higher than men. Life expectancy of women is higher compared to men, so they suffer from diabetes for longer, it could result in socioeconomic consequences in households and also influence health system economically. Implementing cost-effective interventions to reduce the burden of diseases was always one of the main concerns of policy makers. To make appropriate policies, sufficient information and evidences are needed. The availability of data from a national survey including information about risk factors and outcomes (diabetes) in female Iranians is a great opportunity to understand better the situation.

Therefore In my research, I tried to describe the determinants of diabetes in Iranian women, and through the analysis of secondary data to quantify the association between women's socio-demographic characteristics and diabetes to contrast the findings against the existing health policies and interventions in Iran. I hope this thesis to be influential in develop appropriate interventions and health policies for reduction of incidence of diabetes in Iran.

1. Background information on Iran

1.1General background

Iran is an upper middle income country, located in Middle East region.[1] Based on the last census in 2011, the population of Iran is more than seventy million, the annual population growth is 1.29% and total fertility rate is 1.9 per woman.[2,3] Male female ratio is 1.01 and most of people live in urban areas. The mean age of population is 30 years. In terms of household characteristics, more than 95% of households live in a brick/cement house with a tap water, electricity and a bathroom.[2] These households have access to improved water sources and use an improved toilet waste disposal system.[4]

Life expectancy for males and females is 72.1 and 74.6 years respectively. Under five mortality rate is 18 deaths per 1000 live births and probability of dying between 15 and 64 years for males and females is 156 and 84 per 1000 population respectively.[5] Non-Communicable Diseases (NCDs), at 73%, is the leading cause of deaths in Iran. Among NCDs, cardiovascular diseases, cancers, respiratory diseases and diabetes are the main causes of deaths. Figure 1 shows mortality of all causes in Iran.[6] In addition to mortality due to NCDs, they lead to morbidities. Disability Adjusted Life Years (DALYs) due to NCDs in Iran is amounts to 13,665 thousand years annually while total DALYs due to all causes is 19,401 thousand years.[7]

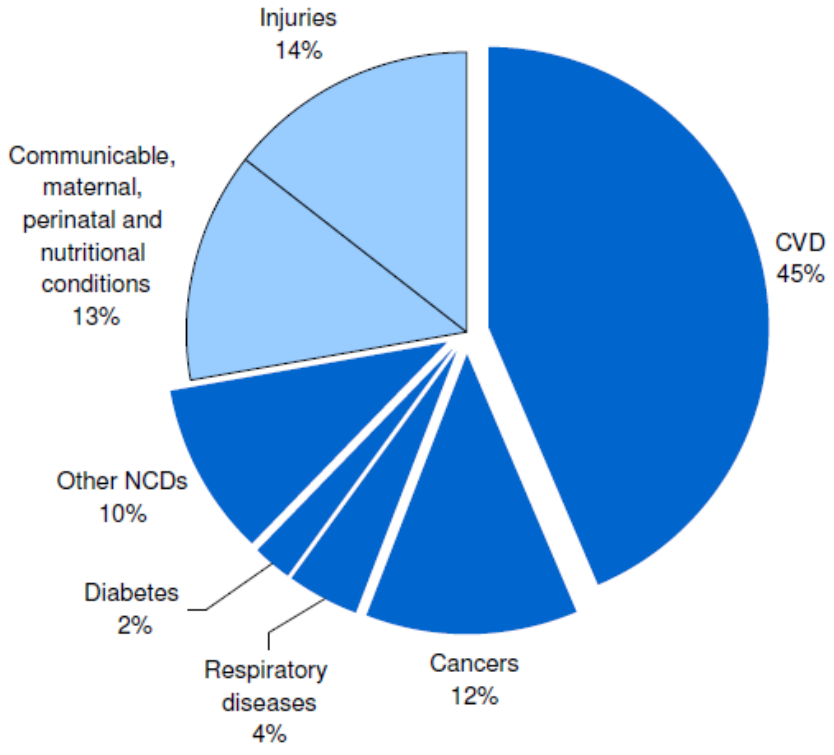
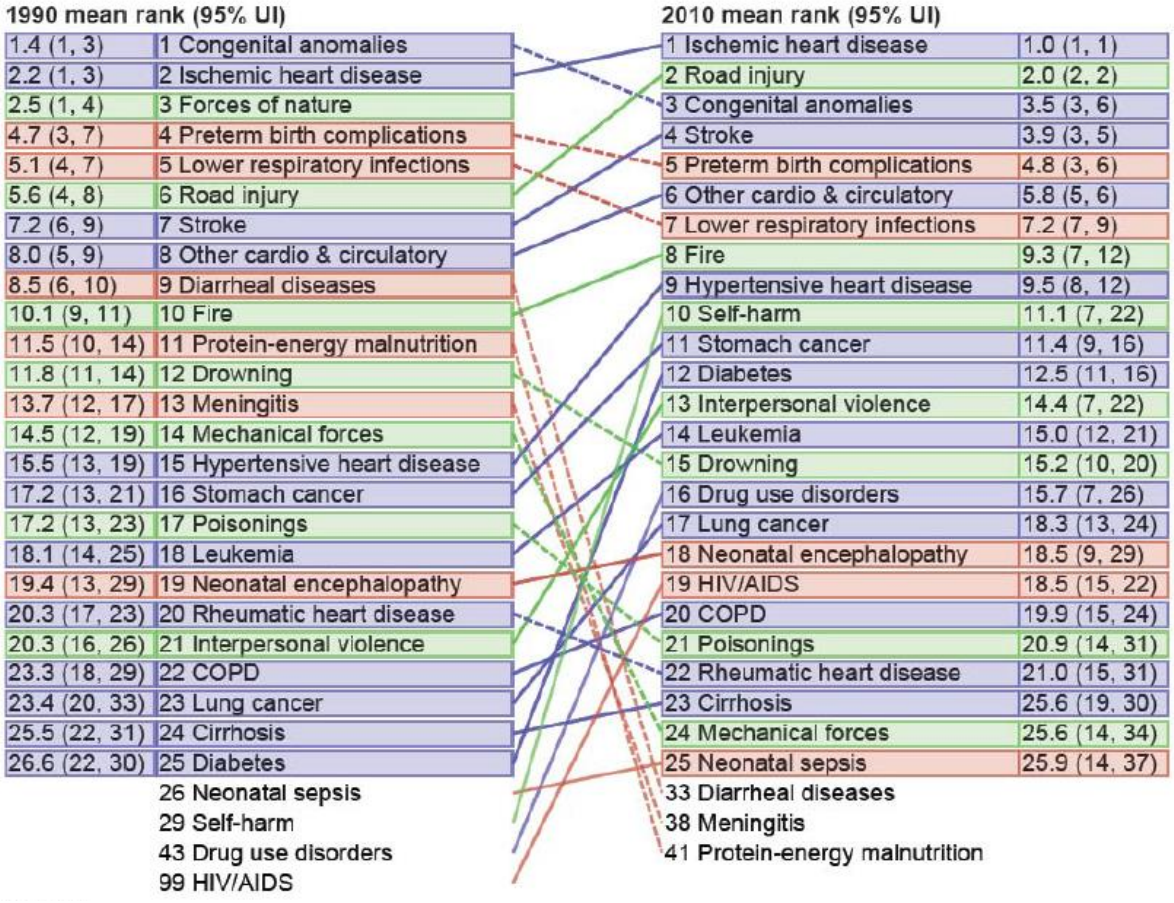


Figure 1. Mortality (all causes) in all ages in Iran (% of total deaths)[6]

Currently, there is a health transition in Iran towards NCDs; it is predicted that the burden of these diseases will increase and they will play a more important role in the health status of Iran in future years.[8,9] For example, diabetes became one of the top causes of deaths in Iran having increased by 40% in the recent two decades and the number of years of life lost increased drastically compared to 1990.[9] Figure 2 shows changes in the top causes of years of life lost from 1990 to 2010 in Iran.



Communicable, maternal, neonatal and nutritional, **Non-communicable**, **Injury**

Figure 2. Years of Life Lost (YLL) rank in Iran in all ages and both sexes, 1990-2010.

1.2 Health system in Iran

Total health expenditure in Iran as percentage of Gross Domestic Product (GDP) is 6.7%.[5] General revenue financing, out of pocket payments and health insurances are the methods of health system financing in Iran.[11] Social health insurance cover 83% of population but t due to limited benefit packages, high co-insurance and lack of agreement between social health insurances and private hospitals or physicians, they are not efficient.[4, 12] Therefore, out of pocket expenditure is more than 50% in Iran.[11]

The health system in Iran supervised by Ministry of Health and Medical Education (MOHME). The public health care system as the main part of the total health care system, consists of three levels: district, provincial and national levels. At national level, MOHME is responsible for policy making, planning, financing and implementing the programs. At province level, medical universities are supervised by MOHME across the country. In each province at least one medical university is working as a health care organization responsible for public health, health care provision in public facilities, and medical education. At urban and rural level, a district health network has been established including district health centers, rural and urban health centers, health houses and health posts.[13,14]
Rural health house is a first contact point of the health network in rural areas and provides primary health care by one or more *Behvarz* (community health worker), chosen preferably from the local inhabitants. These health houses are supported by a rural health center where a physician is in charge. Urban health centers provide ambulatory care. In health posts, vaccination and maternal and child health care services are provided in urban areas. This primary health care network is supported by district hospitals. Figure 3 indicates the structure of public health care system in Iran.[13,14]

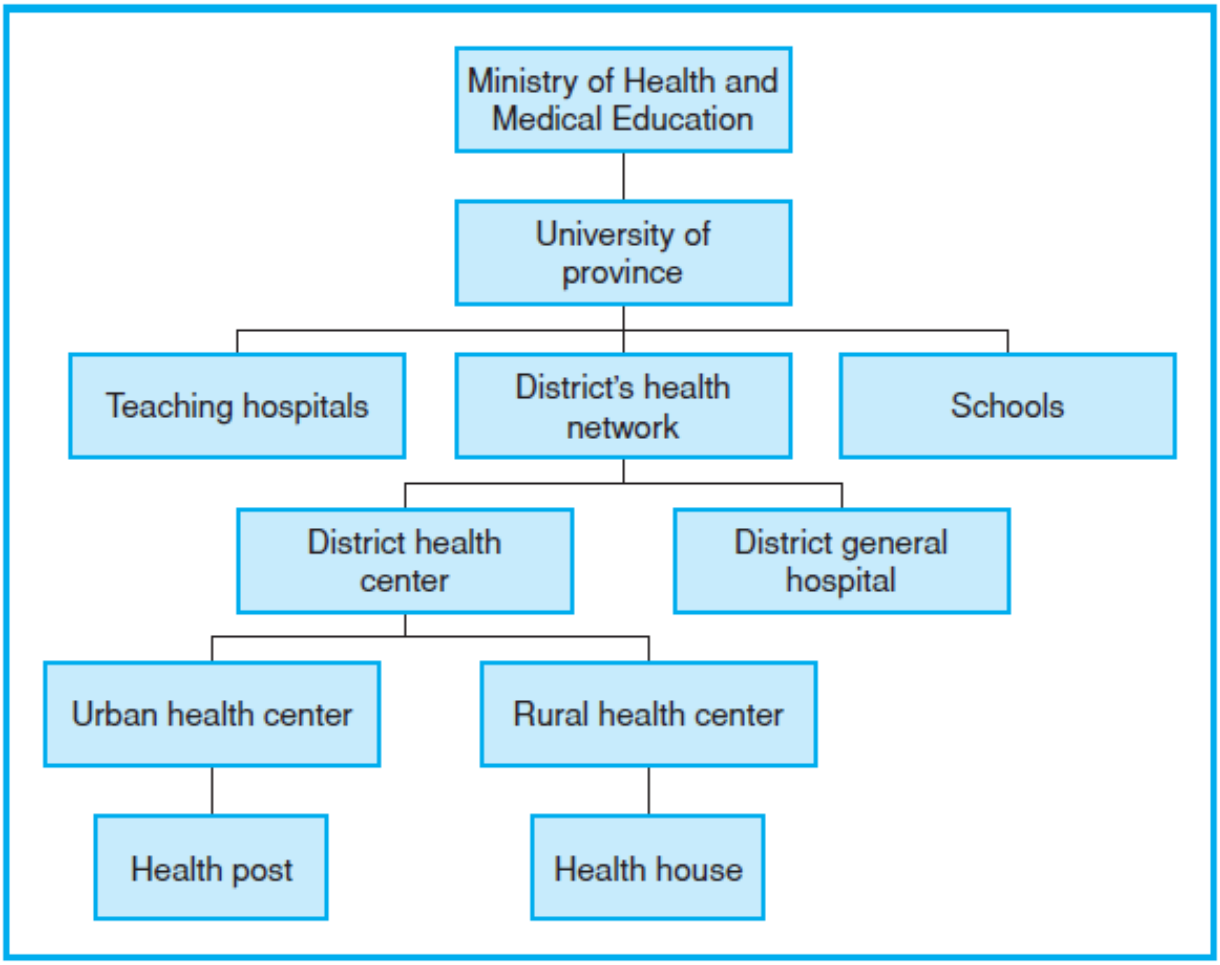


Figure 3. Public health care system in Iran [14]

1.3 Health policies and interventions with regard to diabetes in Iran

Diabetes has received a lot of critical attention from Iranian authorities in last decades. When the Eastern Mediterranean Regional Office of the World Health Organization called countries for action about the prevention and control of diabetes mellitus, Iran was one of the first countries who have responded. From 1990 efforts for prevention and control of diabetes have been initiated by the group of prevention of metabolic diseases and nutrition. The programme have been implemented as a pilot study in rural and urban areas of Kashan, Borojen and Tarom in 1991, but a nonstandard screening tests, the high cost for each screening test and lack of well-equipped health centers led to discontinuation of the study in 1993. Since 1996, with the formation of the National Diabetes Advisory Committee, a national strategy was designed with the purpose of prevention and control of diabetes. In 1997 and 1998, six extensive diabetes workshops have been held by MOHME, with the coordination of the National Diabetes Advisory Committee for physicians, nurses and nutritionists. The pilot project of prevention and control of diabetes has been implemented in universities of medical sciences of 17 provinces of Iran in 1999. The evaluation of the programme was conducted in 6 medical sciences universities in order to find the drawbacks and improve the quality of the project. The results of the evaluation led to development and approval of the implementation of diabetes, hypertention, hyperlipidemia and obesity clinics in 2000. At last, In 2004 "The national diabetes prevention and control programme" has been successfully integrated with the existing health system of the country and implemented in all rural and small cities. To run the programme in the urban areas, it was decided to merge it with family physician programme in 2012 but it has not been implemented completely in urban areas.[15,16]

2.Problem Statement & Justification

The rising trend of type II diabetes prevalence in recent decades, has made it an important health issue worldwide. The total number of people with diabetes increased from 153 to 347 million globally from 1980 to 2008 while 90% of them have type 2 diabetes.[10,17] This can be partly due to the population increase, higher life expectancy, but also to a significant increase in mean fasting plasma glucose over these years. Worldwide, the age standardized adult diabetes prevalence was estimated at 9.8% and 9.2% for males and females respectively in 2008 while the highest prevalence of diabetes in the world of 12,5% has been reported in the Middle East and North Africa region (MENA).[10, 18]

Iran is one of the countries located in the MENA region that has a higher prevalence of diabetes compared to the global average. It was reported 9.43% and 10.07% in 15-64 years old males and females respectively in 2007.[20] Similar to the global trend, the diabetes prevalence is also increasing in Iran. It was reported about five percent in 2000 while it is predicted to be 12.5% among adults in 2030.[18, 19] Incidence rate of diabetes in Iran is estimated to be 10.6 per 1000 person years.[20]

Diabetes as a chronic disease causes lifelong complications such as neuropathy, retinopathy, diabetic foot ulcer, hypertension which increase the risk of cardiovascular diseases, renal failure and visual loss.[21] Furthermore, diabetes is one of the most preventable causes of premature mortality in the world. In 2004, 3.4 million people died due to high fasting blood sugar consequences. Eighty percent (80%) of deaths due to diabetes occurs in low and middle income countries.[22,23] In Iran, diabetes is responsible for two percent of all deaths.[6] These consequences not only affect the patients' quality of life but also has economic cost and burden for their family and society.[24] DALYs of type 2 diabetes was reported as 4.75 per 1000 of the population in Iran and the total national cost for type II diabetes was estimated at 3.78 billion US Dollars in 2009. It consumes about nine percent of total health expenditure of Iran.[25]

The burden of diabetes in women is almost two times than that of men in Iran. DALYs of diabetes in females was reported as 6.08 per 1000 of the population. Also, relative risk of deaths in diabetic women is higher than men.[25] Mean fasting blood glucose has been increased in females in Iran over the past three decades while it was almost stable in males.[6] Life expectancy of women is higher compared to men, so they suffer from diabetes for longer, it could result in socioeconomic consequences in

households such as catastrophic health care expenditure and also influence health system economically.[25]

Although national diabetes prevention and control programs have been implemented in recent decades in Iran, but taking into account the current incidence, prevalence and burden of diabetes in Iranian females, it is still one the most important health issues that should be addressed appropriately. [15, 16] To make effective policies and implement appropriate interventions, it is necessary to have enough data and evidences with regard to diabetes and its determinants in Iran.

There is evidence that Different factors influencing diabetes and health outcome in diabetic patients such as biological risk factors, health behaviors, psychosocial factors, social and physical environment, primary health services and underlying factors such as socioeconomic status, social capital, education, public policy.[26] However, there are few studies describing the association between risk factors and diabetes in Iranian population. The availability of data (not analyzed yet) from a national survey (Iran's Multiple Indicator Demographic and Health Survey) including information about risk factors and outcomes (Diabetes) in female Iranians is a great opportunity to understand better the situation. Ideally I would have preferred to study determinants of diabetes in males and females but for the time being this is what I have in hand.

This study aims to describe the determinants of diabetes in Iranian women, and through the analysis of secondary data, to quantify the association between women’s socio-demographic characteristics and diabetes. The findings will be contrasted against the existing health policies and interventions in Iran.

3. Objectives

3.1 General objective

The main objective of this research is to describe the determinants of diabetes in Iranian women, and through the analysis of secondary data to quantify the association between women's socio-demographic characteristics and diabetes to contrast the findings against the existing health policies and interventions in Iran.

3.2 Specific objectives

This study aims to;

1. Describe and analyze the determinants of diabetes in women in Iran based on current evidences.
2. Analyze and quantify the association between Iranian women's socio-demographic characteristics and diabetes.
3. Contrast and discuss the findings of the previous two objectives against the current interventions and health policies in Iran for reduction of diabetes incidence and morbidity in women.
4. Formulate appropriate recommendations in relation to the findings of the study.

4.Methods

4.1 The framework

In this study comprising of a literature review and secondary data analysis, a framework published by Australian Health Ministers' Advisory Council for causal pathways influencing chronic diseases and health outcomes was used to achieve the objectives.[26]

This framework has been chosen based on available evidence regarding risk factors and determinants of preventable chronic diseases including diabetes type II. A part of the framework was selected, consists of underlying determinants (e.g. socioeconomic status, community characteristics, housing and so on), non-modifiable factors (e.g. age, sex, genetic, family history and ethnicity), behavioral factors (e.g. diet, physical activity, smoking, alcohol use), psychosocial factors (e.g. social support, emotional well-being and so on), early life factors (e.g. maternal health, low birth weight) and biological risk factors (such as obesity, hypertension, impaired glucose tolerance and dyslipidemia).

Furthermore, this framework includes health system related factors including use of preventive health services and primary health care. It indicates the role of the health system in preventing diabetes in healthy population. These determinants and factors have been conceptualized in this framework covering a many stages of life from infants up to the elderly. There are also some other models to describe and analyze determinants of a health such as Dahlgren and Whitehead or Lalonde models.[27, 28] They are more general though than the framework selected for this study, and therefore not as comprehensive as this framework. The part of the framework used in this study is presented in Figure 4 in a red box.

4.2 Literature Review

To achieve objectives one and three, the following databases and research engines were searched by keywords and the defined search strategy: PubMed, Iran Medex (in Persian), SID (in Perisan), Google and Google scholar. The Iranian Ministry of Health and Medical Education's website was also searched to find related interventions, policies and reports.

The keywords were determined based on the selected framework. Keywords included; Age, Sex, Family history, Genetic, Health behavior, Physical activity, Practice, Diet, Food, Nutrition, Alcohol, smoking, Life style, Biologic, Pregnancy, Gestational, Obesity, Psychosocial, Impaired glucose tolerance, Socioeconomic, Economic, Community, Job, Work, Social, Gender, Marital, married, Culture, Education, Information access, Social capital, Policy, Intervention, strategy, environment, rural, urban, primary health, preventive health, seeking behavior, insurance, determinant, Diabetes, Iran. See search strategy was used to search Pubmed in Annex 1.

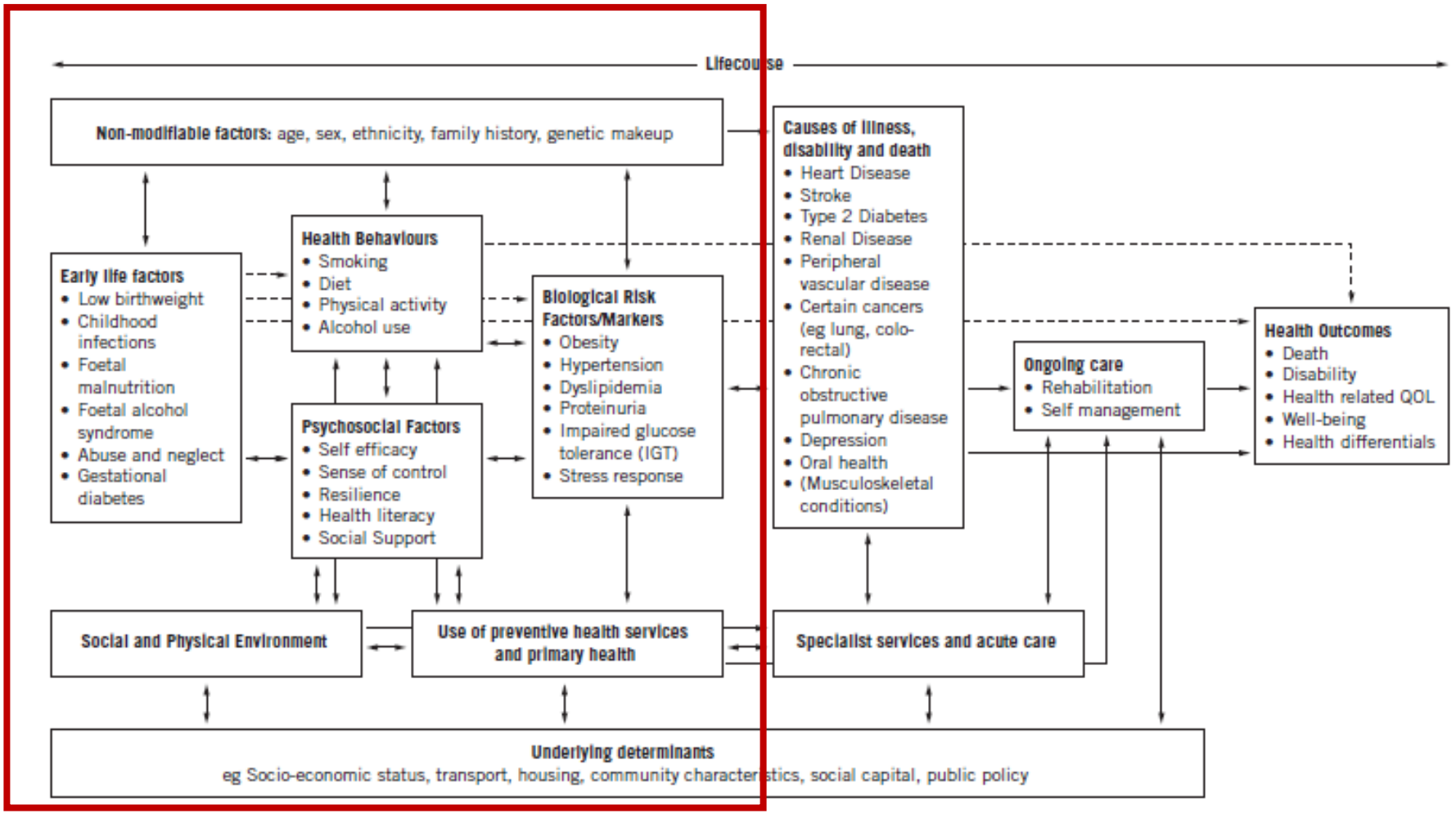


Figure 4. Framework : Schema of causal pathways influencing chronic disease and health outcomes[28]

4.3 Inclusion criteria

First, all titles were screened and irrelevant studies and reports were removed. Then abstracts of studies were reviewed and finally full-texts of remaining abstracts obtained and were assessed. Studies with following criteria were included;

- Studies in Persian or English language
- Quantitative studies
- Studies assessed one of the determinants of diabetes in an Iranian population based on original data.
- Studies assessed the effectiveness of interventions related to determinants of diabetes in an Iranian population.

Finally related data were extracted based on the frameworks determinants and risk factors. These data included year of publication, title, location, study period, participants, sample size, analytical method, assessed determinants and outcome.

4.4 Secondary Data

To achieve objective two, raw data was obtained through Iranian National health Research Institute and which was collected for the Islamic Republic of Iran's Multiple Indicator Demographic and Health Survey 2010 (IrMIDHS). A "cross-sectional multi-stage stratified cluster-random survey was conducted through face-to-face household interviews".[29] Sampling was performed in all 31 provinces of Iran including both urban and rural areas. The study included a total of 31350 households. Three types of questionnaires were used in the survey: household, women aged 15-54 and children under five. The survey provided data related to population and health issues in Iran at national and provincial levels. Quality assurance for this survey was performed in all stages including sampling, training, survey implementation, data entry and analysis.

Data related to the objectives of this current study following the selected framework, were extracted from the two datasets namely the household and women. The data included age, education, access to information (watching TV, reading newspaper, use of internet), marital status, number of deliveries, insurance, job, household characteristics (monthly income, surface area of living house), residence (urban/rural) and NCDs (diabetes, asthma, musculoskeletal, skin and cardiovascular diseases). The data related to NCDs and other variables was self-reported by women. The data from both datasets were merged together, using Statistical Package for Social Science (SPSS) software version 21.0 (IBM Inc., Armonk, USA). One dataset was made and reordered to prepare for analysis.

4.5 Analysis

To determine and quantify the association of socio-economic characteristics of women and the outcome of diabetes, analysis of data was done using binomial logistic regression. Having diabetes (a dichotomous variable) was defined as the dependent variable and socio-economic characteristics as independent variables.[30]

Before conducting the analysis, all the following assumptions were tested:

1. Independence of cases: in the merged dataset all cases were independent. No duplicate cases were found
2. A linear relationship between the continuous independent variables and the logit transformation of the dependent variable: Ln age and Ln surface area of living house were calculated and this assumption was tested using Box-Tidwell procedure.
3. No multicollinearity; to test this assumption, bivariate correlations between all independent variables were calculated using the Pearson correlation test for continuous variables and the Spearman correlation coefficient for categorical variables. Significant correlations with a correlation coefficient higher than 0.7 between two variables was considered highly correlated. Also, muticollinearity was checked using tolerance and Variance Inflation Factor (VIF). Tolerance less than 0.2 or VIF more than 5 shows multicollinearity between independent variables. Among highly correlated variables, only one of the variables were included in the final binary logistic regression model.
4. No significant outliers; to detect outliers, descriptive analysis including frequency of all variables was done.
5. Categories of the dependent variable are mutually exclusive and exhaustive; none of the categories violate this assumption.

The binary logistic regression was conducted with one independent variable at a time and the dependent variable. Based on the result of this stage, some of independent variables were excluded from the binary logistic regression model if they didn't have any significant correlation. Finally, binary logistic regression analysis was run using remaining independent variables. Level of significance of 5% maintained for all analysis.

5. Results

5.1 Literature review

Electronic searches identified 1463 studies. After title screening 157 abstracts were reviewed. Then 63 full-texts were retrieved and read. Finally 17 full-texts included in this study based on the inclusion criteria; 9 Persian and 8 English articles.

These included studies were conducted in different geographical areas of Iran. All of them were original studies with cohort (four papers)[20, 31-33], cross-sectional (seven papers)[30,34-39] case-control (five papers)[40-44] and controlled trial (one paper)[45] designs. More than one determinant has been assessed in eight of them while other studies (nine) has assessed only one of the determinants of diabetes. Details of included studies are described in Table 1 on characteristic of included studies.

5.2 Secondary Data Analysis

In total, the data of 34333 women were included in the analysis. The mean age of participants was 31.45 years old (15-54, Standard Deviation; 10.75) while 905 of them were diabetic (2.6%). Descriptive analysis of independent variables, showed many missing cases in some variables and were excluded from subsequent analyses performed. Table 1 shows the details of socio-demographics of participants and their household characteristics.

Table 1. Characteristics of women, 15-54 years, and their households, included in the study (N=34333)

Variables	Mean (range)				Total (%)	Missing (%)
Age	31.45 (15-54)				34333 (100)	
Deliveries	1.81 (0-18)				34321 (99.9%)	12 (.03)
Surface area of living house	185.1 (3-998)				34333 (100)	
News Reading	Never	Every day	Every week	Less than every week		
Frequency (%)	9354 (27.2)	2986 (8.7)	7728 (22.5)	9399 (27.4)	29467 (85.8)	4866 (14.2)
TV Watching						
	769(2.2)	31383(91.4)	1788(5.2)	393(1.1)	34333 (100)	
Use of Internet						
	859 (2.5)	1462 (4.3)	2336 (6.8)	2109 (6.1)	6766 (19.7)	27567 (80.3)
Marital status	Married	Widow	Single			

	23661 (68.9)	1311 (3.8)	9361 (27.3)			34333 (100)	
CVDs	No	Yes					
	32918 (95.9)	1415 (4.1)				34333 (100)	
Asthma	No	Yes					
	33761 (98.3)	572 (1.7)				34333 (100)	
Skin diseases	No	Yes					
	33492 (97.6)	841 (2.4)				34333 (100)	
MSDs	No	Yes					
	29493 (85.9)	4840 (14.1)				34333 (100)	
Insurance	No	Yes					
	5567 (16.2)	28672 (83.5)				34239 (99.7)	94 (0.3)
Job	Jobless	Employed	Student	House keeper			
	4013 (11.7)	3668 (10.7)	4697 (13.7)	21812 (63.5)		34190 (99.6)	143 (0.4)
Rural/Urban	Urban	Rural					
	23878 (69.5)	10455 (30.5)				34333 (100)	
Monthly income	Less than 250	250 to 500	500 to 1000	1000 to 2000	More than 2000	No response	Total	
	9412 (27.4)	14981 (43.6)	5959 (17.4)	886 (2.6)	134 (0.4)	2949 (8.6)	34321 (99.9)	12 (0.03)
Education	Illiterates	Primary school	Elementary	High school	Diploma	University degree		
	3763 (11.0)	8432 (24.6)	4981 (14.5)	4921 (14.3)	6669 (19.4)	5565 (16.2)	34333 (100)	

5.3 Binary Logistic Regression Analysis results

Regard to high number missing cases in "use of internet" and "news reading", these variables were excluded from analysis. Binary logistic regression analysis of each independent variable and the dependent variable showed that there was no significant relation between skin diseases, surface area of living house, monthly income and diabetes in women. It was however, significant for some independent variables.These variables were checked for multicollinearity. Based on the cutoff point of Pearson correlation explained before, only age and delivery were highly correlated (Pearson correlation = 0.74, p value ≤ 0.000), but the Tolerance and VIF was 0.58 and 1.71 respectively. Therefore, although they were highly correlated but no multicollinearity was found. Other variables were not high correlated and Tolerance was more than 0.2 and VIF was less than 5 between all of them implying no multicollinearity.

A final logistic regression model only included independent variables that were associated with the dependent variable when tested univariately, i.e. one independent variable at a time. Therefore, skin disease, surface area of living

house and monthly income were excluded from the analysis. At the last stage, before running the final regression analysis, based on the Box-Tidwell procedure, the interaction term "Ln age by age" was included in the logistic regression model as it was notstatistically significant (P value = 0.051 , 95% of CI; 0.871-1.000). It showed that there is a linear relationship between age variable and the logit transformation of diabetes variable.

Finally, binary logistic regression analysis was conducted including the remaining independent variables; age, education, TV watching, marital status, number of deliveries, cardiovascular disease, asthma, musculoskeletal diseases, insurance, job, access limitation and rural/urban. The analysis showed that 34173 cases were included in the model while 901 of them were diabetic. The model was statistically significant. ($X2$=1603.75, $p < 0.000$) and achieved a good fit based on the Hosmer and Lemeshow test (p=0.76). It explained 21% of the variance in diabetes regard to Nagelkerke R^2 and correctly classified 97.4% of cases. The following independent variables were significant: age, education, watching TV, cardiovascular diseases, Asthma, musculoskeletal disease, marital status and residence.

Younger and single women who have higher education, watch TV more, don't have cardiovascular disease, asthma and musculoskeletal diseases and live in rural areas are less likely to have diabetes than women with opposite characteristics. See details in Table 2.

5.4 Determinants of Diabetes

The results from the secondary analysis and the review of the literature following the factors outlined in the selected framework, are presented in this section for women in Iran. Although the objectives of this study focus on women, please note that all the included studies evaluated the determinants in both sexes. None of the studies from the literature review focused solely on women, demonstrating the gap that this study potentially fills. Further, no study was found for some influencing factors in the framework related to "early life factors", "psychosocial factors" and some of underlying determinants.

5.4.1 Non-modifiable factors

Age

Correlation of age and diabetes were evaluated in six of the included studies. These studies were conducted at national level and in five large provinces including Tehran, Isfahan, Golestan, Kerman and greater Khorasan. All of them showed that there is a significant positive correlation between age and diabetes in Iranian population. The findings from regression analysis also showed that older Iranian women are 1.106 (95%CI: 1.094, 1.118) times more likely to have diabetes than younger women. (See Table 2). It is comparable with the findings of included studies. In Golestan province[31], adjusted prevalence of diabetes increased 21% for every 10 years increase in age. In Tehran[20], Khorasan[35] and

Kerman[30] the odds of having diabetes in older people was 1.2 (95% CI: 1.1, 1.3), 1.031 (95% CI: 1.029, 1.052) and 1.047 (95%CI: 1.036, 1.58), 1. 05 (1. 03 - 1. 08) more than younger people, respectively. While in first degree relatives of diabetic patients in Isfahan it was 1. 05 (1. 03 - 1. 08).[34] The cross sectional study was conducted at national level showed that the prevalence of diabetes in people aged 65-70 years was 29.18% (25.44–32.91) while it was 3.27% (1.92–4.61) in people aged 25.34 years.[37]

Family history

Family history of diabetes were studied in four of the included papers. Findings of a cross-sectional study showed that the prevalence of diabetes is 4.3% higher in first degree relatives of diabetic patients than in the general population.[34] A case-control study indicated that family history of diabetes is 40% higher in diabetic patients than the control group ($p \leq 0.05$).[44] The third study concluded that people with family history of diabetes of the mother are more likely to have diabetes than people who have history of diabetes of father (OR: 15.06, 95%CI: 6.95, 33.3).[39] A cohort study showed that people with family history of diabetes are 2.4 2.4 *(*95% CI: *2.6, 7.5*) times more likely to have diabetes than people without family history.[20]

Genetic

Three studies were included in this study regarding the genetic role in Diabetes in Iranians. These studies showed that diabetes is associated with some polymorphisms and genotypes including GG genotype of G-2548A polymorphism, CXCL5 -156 G/C polymorphism and SNP-43 of Calpain 10 gen.[41-43] See details and related information in Annex 1.

5.4.2Health behavior factors

Smoking

One cohort study in Golestan province showed that the prevalence of diabetes is significantly lower - 30% - in current smokers than never smokers. Also it was 32% lower in ever-hookah, Nass or pipe smokers than never smokers.[31] Another cohort study in Theran didn't show any significant association.[20] While a controlled trial study with life style interventions including decreasing smoking showed 65% (95% CI: 30%, 83%, $p \leq 0.003$) relative risk reduction of diabetes.[45]

Diet

Only one study was included related to diet and diabetes. In the controlled trial mentioned above, diet improvement was one of the life style interventions

combined with decreased smoking and increased physical activity. These interventions resulted in relative risk reduction of diabetes significantly.[45]

Physical activity

Two cross sectional studies[30, 39], one cohort study[31] and one controlled trial study[45], assessed the association of diabetes and physical activities. All of them indicated that physical activity has a significant association with reduced risk of diabetes. For example the cohort study showed that the prevalence of diabetes is 42% less in people who do regular or intense physical activity at work than people who don't and the cross-sectional study in Tehran found that aerobic physical activity more than 150 minutes per week is associated with decreased risk of diabetes (OR= 0.56; 95%CI: 0.35-0.91).[36] See details in Annex 1.

5.4.3Biological risk factors

Impaired Glucose Tolerance (IGT)

A six years cohort study showed that the probability of diabetes incidence in people with IGT is 7.1 times (95% CI: 5.1, 9.8) more than people with normal glucose tolerance. While people with Impaired Fasting Glucose (IFG) and combined IFG and IGT, 8.3 (95% CI: 4.2, 16.5) and 42.2 (CI 95%: 25.8, 75.7) times more likely to become diabetic than people with normal glucose tolerance, respectively.[20]

Hypertension

Association of hypertension was evaluated in five of the included studies which were conducted in different geographical areas of Iran (two cross-sectional, two cohort and one case-control). All the findings showed that there is a significant association between hypertension and increased risk of diabetes. See details in Annex 1. The cohort study in Golestan province[31] and the case-control study[44] in Shiraz city showed that prevalence of diabetes is 82% and 22.9% more in participants with hypertension than those who have normal blood pressure. Results of a cohort study in Tehran also indicated that people with hypertension are 1.9 (95% CI: 1.4, 2.6) times more likely to have diabetes than healthy people.[20] Cross sectional studies in Kerman[30] and Isfahan[34] showed that there is a significant positive association between systolic blood pressure and increased risk of diabetes, OR: 1.054 (95% CI: 1.03, 1.077) and 1.35 (95% CI: 1.17, 1.56) respectively.

Dyslipidemia

Three cross-sectional studies, one cohort and one case control from different provinces of Iran evaluated the correlation of dyslipidemia and

diabetes. High-density lipoprotein (HDL), Low-density lipoprotein (LDL), Cholesterol and Triglyceride (TG) are the biological factors that were assessed in these studies. Findings showed that low HDL, high LDL and High TG have association with increased risk of diabetes. The cohort study showed this association for low HDL and High TG with OR: 1.4 (95% CI: 1.0, 1.19) and OR: 2 (95% CI: 1.5, 2.6) respectively.[20] Also less HDL (3 mg/dL less in case group) and higher TG (48 mg/dL more in case group) were reported in the case control study.[44] Cholesterol in this study is significantly lower in diabetic group(21 mg/dL less in case group, P< 0.05), while other studies showed it has association with increased risk of diabetes. See details in Annex 1.

Obesity

In 10 of 18 included studies,[20, 30-37, 44] obesity and related factors including body mass index, weight, waist circumference (WC), waist hip ratio (WHR) and hip circumference were assessed with diabetes. All studies, showed a significant correlation between obesity and overweight and increased risk of diabetes. For instance results from recent study at national level have demonstrated that obese and morbidly obese people are more likely to have diabetes compared to people with normal BMI (OR: 1.06 (95% CI: 1.01–1.11) and OR: 1.12 (95% CI: 0.06–1.17) respectively)). See details in annex 1.[37]

Some Biological factors were not mentioned in the framework but has been evaluated in a case control study; polycystic ovary syndrome, hirsutism and irregular menstruation. The study showed that prevalence of these factors was significantly higher in Diabetic patients. (Respectively, 3.1%, 6.1% and 6.1% higher in case group, P< 0.05).[37]

Stress response

One cross-sectional study was included related to psychosocial factors. The association of number of important stressful events and prevalence of diabetes in first degree relatives of diabetic patients was assessed. It showed the prevalence of diabetes or pre-diabetes were 14.7% higher significantly in participants who experienced stressful events in the recent two years than participants who didn't have any stressful event. Interestingly, the higher number of stressful exposure events (eight or more) was also associated with higher risk of type 2 diabetes mellitus. (OR = 3.8, 95%CI: 1.44, 10.05, *p* value=0.008)[38]

5.4.5Preventive health services and primary health care

A case-control study assessed the effectiveness of diabetes management by rural primary health-care workers at national level. The result of the

study, showed that addition of primary health care workers was associated with reduction of mean fasting plasma Glucose in district level.[40] Each addition primary health care worker is associated with 0.09 mmol/L (CI95%: 0.01, 0.18) decrease in mean fasting plasma glucose.

5.4.6Underlying determinants

Some of determinants such as education were evaluated in included studies and the analysis but has not been mentioned in the framework but they could be an underlying determinant. They are discussed in the following parts.

Education

A cross sectional study in Khorasan didn't showed any significant association between education and diabetes[35] but the cohort study in Goletsan showed that prevalence of diabetes is 15% lower in people with higher education than illiterate people (*p* value < 0.0001).[31] Also the cohort study conducted in Tehran indicated that people with diploma or higher degree are 0.5 times less likely to have diabetes than people who are illiterate or at primary school level, OR: 0.5 (95% CI 0.4, 0.8).[20] This is also confirmed by the secondary data analysis. Women with education at primary school, elementary school and high school are 1.90 (95%CI: 1.33, 2.73), 1.74 (95%CI: 1.19, 2.55) and 1.55 (1.024, 2.35) times more likely to have diabetes than women with university education. However, the data did not illustrate a significant association for illiterate women (OR: 1.46, 95% CI: 0.988, 2.1) or women who obtained a diploma (OR: 0.92, 95% CI: 0.627, 1.37).

Access to information

The association of watching TV and having diabetes were assessed in the analysis. Women watch TV less than every week and every day are 0.442 (95% CI: 0.211, 0.924) and 0.629 (95% CI: .437, 0.906) times less likely to have diabetes than women never watch TV.

Marital status

The analysis showed that single women are less likely to have diabetes than married women. (OR: 0.552, 95% CI: 0.359, .851). It was also assessed in the cross-sectional study in Khorasan province, but the association of marital status and diabetes was not significant (*P* value= 0.09).[35]

Job

Results of analysis showed that housekeeper women are less likely to have diabetes than jobless women. (OR: 0.757, 95% CI: 0.574, 0.999). While no significant association was found in student or employed women

compared to jobless women. The Khorasan cross-sectional study showed there is no significant association between different categories of job and diabetes in regression analysis but the prevalence of diabetes was significantly higher in retired group than other categories (*p* value < 0.001).[35]

Residence area

Association of living in rural or urban areas and diabetes, has been evaluated in three of included studies (one cohort and two cross-sectional) and in the analysis. The Golestan cohort[31] and the national cross-sectional study[37] showed that the prevalence of diabetes is 10% and 5% respectively is higher in urban than rural areas. The cross sectional study in Khorasan showed that people who live in urban areas 2.73 (95% CI: 1.89, 3.92) times more likely to have diabetes than people live in rural areas.[35] It is confirmed also by findings of the analysis. It was showed that women living in rural areas are 0.698 times (95% CI: 0.587, .829) less likely to have diabetes than women live in urban areas.

Comorbidities

Results of the analysis showed that there is a significant correlation between having asthma, cardiovascular or musculoskeletal diseases and diabetes. Women who have cardiovascular diseases, Asthma or musculoskeletal disease are 2.805 (95% CI: 2.337, 3.367), 1.44 (95% CI: 1.043, 1.997) or 1.32(95% CI: 1.13, 1.53) times more likely to have diabetes than women who don't have cardiovascular diseases.

Other variables including number of deliveries, access limitation and having medical insurance were not significant in the logistic regression model. See details in table 2.

Table 2. Odds ratio of having Diabetes according to participant's characteristics						
	Ref. category	**β**	***P* value**	**Odds Ratio**	**95% C.I.** Upper limit	**95% C.I.** Lower limit
Age		.100	.000	1.106	1.094	1.118
Education	University degree		.000			
Diploma		-.074	.711	.928	.627	1.376
High school		.440	.038	1.552	1.024	2.353
Elementary school		.557	.004	1.745	1.193	2.552
Primary school		.645	.000	1.906	1.330	2.732
Illiterate		.385	.057	1.469	.988	2.184
TV Watching	Never		.031			
Less than every week		-.817	.030	.442	.211	.924
Every week		-.276	.219	.759	.488	1.178
Every day		-.463	.013	.629	.437	.906
Cardiovascular	No disease	1.031	.000	2.805	2.337	3.367
Asthma	No disease	.367	.027	1.443	1.043	1.997
Musculoskeletal	No disease	.278	.000	1.320	1.133	1.538
Marital Status	Married		.025			
Widow		-.015	.911	.985	.752	1.290
Single		-.594	.007	.552	.359	.851
Deliveries		.022	.254	1.022	.984	1.062
Insurance	No insurance	.190	.080	1.209	.978	1.496
Job	Jobless		.191			
Employed		-.338	.060	.713	.502	1.014
Student		-.342	.374	.711	.335	1.508
Housekeeper		-.278	.049	.757	.574	.999

Residence area	Urban	-.360	.000	.698	.587	.829
Access limitation	No limitation	-.057	.491	.945	.803	1.111

5.4 Diabetes related interventions and health policies in Iran

Currently, there is a national comprehensive program for prevention and control of diabetes in Iran. The programme at national level has been designed based on characteristics of current health care system and has been adopted accordingly in 2004. First it was implemented in rural areas and small cities, then in 2012 it was implemented in all rural and urban areas by merging with family physician program in Iran. The program is funded by MOHME and it provides diabetes related health services through public health system but it is tried to encourage private health sectors to involve in the programme. At national level, it is managed and supervised by the management center of non-communicable diseases in ministry of health and medical education and at provincial level, medical universities are responsible for the program.[15,16]

The main objective of this program is prevention and control of type 2 diabetes and its complications. The specific objectives include;

Primary prevention: reducing the incidence and prevalence of type 2 diabetes in pre-diabetic individuals

- life style modification in pre-diabetic and high risk populations
- Screening and early detection of at-risk population according to national guidelines
- Follow up and care of at-risk population according to national guidelines
- Improvement of knowledge and awareness of the health care providers, authorities and community about diabetes, predisposing factors and its complications.

Secondary prevention: prevention and reduction in incidence of short-term and long-term complications

- Early detection of diabetes by screening at-risk population and pregnant women
- Care and treatment of detected patients in order to controlling disease and stopping its progression
- Enhancement of the awareness and comprehension of other cardiovascular disease risk factors and prevention and control of these factors. For instance: smoking, high blood pressure, hyperlipidemia, obesity and low physical activity in diabetic patients, their family and health workers.

Tertiary prevention: reduction incidence of disabilities and early death caused by diabetes complications to reduce years of life lost in diabetic patients.

- Screening diabetic patients for early detection of ophthalmic, neurologic, nephrologic and cardiovascular complications
- Early care and treatment of complications
- Long term follow up of patients

To achieve these objectives, following care services are been providing in three levels.

- ***First preventing level***: Primary health care and screening are provided by family physicians in rural and urban health centers.
- ***Level of specialists services***: diabetes centers (located in privates/governmental hospitals and/or clinics.
- ***Level of subspecialist services***: third level of care providers in subspecialist privates/governmental hospitals, sub-specialist clinics, diabetes or metabolism and endocrine research centers. Table 3 shows all details related to the program.

Table 3. Three levels of national diabetes program in Iran[15,16]

Level I	**Level II**	**Level III**
Family physician, Behvarz and Kardan (primary health care providers)	Internist, educational nurse, nutritionist, consultant physicians	Internist (endocrinologist), educational nurse, nutritionist, consultant physicians
• Screening for diabetes • Evaluate at-risk population, educating patients, their family and health workers • Early diagnosis and treatment of diabetic patients • Refer diabetic patients to second level for receiving specialists care • Care for late complications of diabetes according to protocol • Completing patients electronic files • Data gathering and reporting to higher levels	• Provide care for referred cases from first level • Diagnosis, treatment and providing other health care services in professional and specialist level • Screening common chronic complication in diabetic patients including nephropathy, neuropathy, retinopathy and cardiovascular diseases • Care and treatment for acute and chronic diabetes complications by internist,	• Admission of referred patients from second level for providing special care including: ○ Care and treatment for cardiovascular complications, diabetic nephropathy, diabetic foot and diabetic neuropathy ○ Prenatal and delivery care for diabetic patients • Giving feedbacks and therapeutic patterns to diabetes centers, providing Scientific guide for program at

• Follow up patients • Cooperation in conducting research studies.	ophthalmologist and other specialists • Refer patients to higher level for receiving subspecialist care (endocrinologist, nephrologist…). • patient admission if it is needed • Recording the results of consults, modifying the therapeutic patterns and give feedbacks to first level • Data gathering and reporting to province health network or other higher levels	university level and assurance about quality of care provided in second level • Cooperation in educational package for patients and at risk population • Recording data and reporting to health deputy of university • Suggesting research studies in order to improving the quality of the program • Cooperation in conducting research projects
rural houses, rural and urban health centers	privates/governmental hospitals and/or clinics and privates/governmental poly clinics	Subspecialist privates/governmental hospitals, sub specialist poly clinics and clinics, diabetes, metabolism and endocrine research centers

5.5 Diabetes interventions in the world

To achieve objective four and formulate recommendations based on findings from literature review, secondary data analysis and diabetes programme in Iran, it is needed to review effective interventions and programs related to diabetes.

Based on the survey was conducted in 2006 by International Federation of Diabetes, 54 of 89 countries which participated, had a national program of diabetes. In 96% of these countries the first target was diabetic patients while 76% had targeted whole population. Most of this program (91%) were focused more on clinical care and secondary prevention. It was concluded that to reduce the incidence of diabetes, in addition to early detection of high risk population and reduction of risk factors, it is needed to focus more on primary prevention with an environmental and whole population approach.[46]

A whole population approach for diabetes interventions in USA also was discussed in a study published in 2000. Public health interventions were defined at three level. Downstream interventions cover diabetic patients and focus on tertiary prevention. Midstream interventions includes secondary prevention to reduce risk factors in high risk population and primary prevention to reduce risk of diabetes in community. Upstream interventions includes national level regulation and policies and addresses the whole population. Figure 6 illustrates these categorization of interventions for control and prevention of diabetes.

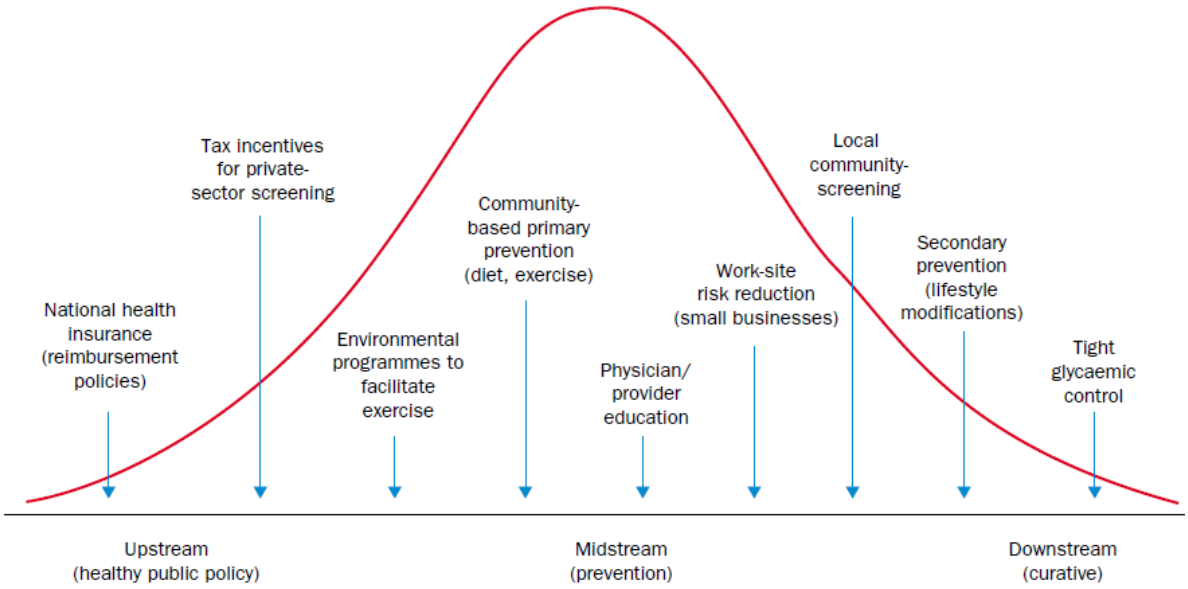


Figure 5. Possible interventions for diabetes[47]

Interventions for diabetes in the Global status report on NCDs was published by WHO has been divided in two categories; population-wide and individual interventions.[48]

5.5.1 Population-wide interventions

Population-wide approach aims to reduce risk factors in the entire population. Compared to previous categorization, they can include all upstream and some midstream interventions. The report of WHO, evaluated and summarized current population-wide interventions in terms of cost-effectiveness, cost, avoidable burden and feasibility based on the available evidences.[48,49]

Concepts were used to evaluate them were "good buy" and "best buy". A best buy means that the intervention is high cost-effective, cheap and feasible to implement while a good buy includes interventions cost more and make less benefits but they have value for money.[48]

In terms of unhealthy diet the "best buy" interventions to reduce the risk include salt intake reduction strategy, replacing trans-fat with polyunsaturated fat in food industries and communication strategies for raising awareness to promote health foods. Some other interventions such

as taxation increase of unhealthy foods and reducing prices of healthy foods are also cost effective and studies in China, Zambia and USA showed that it can be effective and change the behavior of population in buying foods. To promote physical activities, the best buy is mass media interventions to promote physical activity. There are also other interventions such as improving the built environment to support active transport strategies and developing national physical activity guidelines can be effective in promoting physical activities. The interventions are effective in reduction of risk factors of non-communicable diseases are described in Table 4.

Table 4. Population-wide interventions for risk factors of NCDs [48]

Risk factor (DALYs, in millions; % global burden)[a]	**Interventions / actions** (* core set of 'best buys', Others are 'good buys')	**Avoidable burden** *(DALYs averted, millions)*	**Cost-effectiveness** [b] *(US$ per DALY prevented) [Very = < GDP per person; Quite = < 3xGDP per person Less = >3xGDP per person]*	**Implementation cost** *(US$ per capita) [Very low = < US$0.50 Quite low = < US$ 1 Higher = > US$ 1]*	**Feasibility** *(health system constraints)*
Tobacco use (> 50m DALYs; 3.7% global burden)	Protect people from tobacco smoke * Warn about the dangers of tobacco * Enforce bans on tobacco advertising * Raise taxes on tobacco *	Combined effect: 25-30 m DALYs averted (> 50% tobacco burden)	Very cost-effective	Very low cost	Highly feasible; strong framework (FCTC)
	Offer counselling to smokers		Quite cost-effective	Quite low cost	Feasible (primary care)
Harmful use of alcohol (> 50m DALYs; 4.5% global burden)	Restrict access to retailed alcohol * Enforce bans on alcohol advertising * Raise taxes on alcohol *	Combined effect: 5-10 m DALYs averted (10-20% alcohol burden)	Very cost-effective	Very low cost	Highly feasible
	Enforce drink-driving laws (breath-testing) Offer brief advice for hazardous drinking		Quite cost-effective	Quite low cost	Intersectoral action Feasible (primary care)
Unhealthy diet (15-30m DALYs; 1-2% global burden)[c]	Reduce salt intake * Replace trans-fat with polyunsaturated fat * Promote public awareness about diet * +	Effect of salt reduction: 5 m DALYs averted Other interventions: Not yet assessed globally	Very cost-effective	Very low cost	Highly feasible
	Restrict marketing of food and beverages to children Replace saturated fat with unsaturated fat Manage food taxes and subsidies		Very cost-effective (more studies needed)	Very low cost	Highly feasible
	Offer counselling in primary care Provide health education in worksites Promote healthy eating in schools		Quite cost-effective	Higher cost	Feasible (primary care)
			Less cost-effective	Quite low cost	Highly feasible
Physical inactivity (> 30m DALYs; 2.1% global burden)	Promote physical activity (mass media) * +	Not yet assessed globally	Very cost-effective	Very low cost	Highly feasible
	Promote physical activity (communities) Support active transport strategies Offer counselling in primary care Promote physical activity in worksites Promote physical activity in schools		Not assessed globally	Not assessed globally	Intersectoral action
			Quite cost-effective	Higher cost	Feasible (primary care)
			Less cost-effective		Highly feasible

5.5.2 Individual interventions

Interventions for individuals is targeting high risk population or diabetic patients.[49] It can be included some of midstream and all downstream interventions.

They include interventions such as life style modifications in high risk population, blood pressure control of diabetic patients, and care for diabetic foot, neuropathy and nephropathy. Table 5 illustrates the evidence-based effective individual interventions for diabetes and their benefits. Table 5,6 described more details regard to these interventions for diabetes and cardiovascular diseases.[48]

Furthermore, self-care programmes can be effective in management of diabetes. "Self-care is defined by WHO as including activities that individuals, families, and communities undertake with the intention of enhancing health, preventing disease, limiting illness and restoring health". These kinds of program improve health status of people, increase their knowledge and self-efficacy.[48]

Table 5. Effective individual interventions for diabetes

Interventions with evidence of efficacy	Benefit
Lifestyle interventions for preventing type 2 diabetes in people at high risk	Reduction of 35–58% in incidence
Metformin for preventing type 2 diabetes for people at high risk	Reduction of 25–31% in incidence
Glycaemic control in people with HbA1c greater than 9%	Reduction of 30% in microvascular disease per 1 percent drop in HbA1c
Blood pressure control in people whose pressure is higher than 130/80mmHg	Reduction of 35% in macrovascular and microvascular disease per 10 mmHg drop in blood pressure
Annual eye examinations	Reduction of 60 to 70% in serious vision loss
Foot care in people with high risk of ulcers	Reduction of 50 to 60% in serious foot disease
Angiotensin converting enzyme inhibitor use in all people with diabetes	Reduction of 42% in nephropathy; 22% drop in cardiovascular disease

Table 6. Cost effectiveness of individual interventions

Disease (% global burden; DALYs)	**Interventions / actions** (**core set of 'best buys')**	**Avoidable burden** *(DALYs averted, millions)*	**Cost–effectiveness** *(US$ per DALY prevented) [Very = < GDP per person; Quite = < 3 GDP per person Less = >3 GDP per person]*	**Implementation cost** *(US$ per capita) [Very low = < US$ 0.50; Quite low = < US$ 1 Higher = > US$ 1]*	**Feasibility** *(health system constraints*)
Cardio vascular disease (CVD) and diabetes (170 m DALYs; 11.3% global burden)	**Counselling and multidrug therapy (including glycaemic control for diabetes mellitus) for people (≥30 years), with 10-year risk of fatal or nonfatal cardiovascular events ≥ 30%**	60 m DALYs averted *(35% CVD burden)*	Very cost-effective	Quite low cost	Feasible (primary care)
	Aspirin therapy for acute myocardial infarction	4 m DALYs averted *(2% CVD burden)*	Very cost-effective	Quite low cost	
	Counselling and multidrug therapy (including. glyceamic control for diabetes mellitus) for people (≥ 30 years), with a 10-year risk of fatal and nonfatal cardiovascular events ≥ 20%	70 m DALYs averted *(40% CVD burden)*	Quite cost-effective	Higher cost	

6.Discussion

In this research, 17 studies were included through literature review form English and Persian databases. Findings from these studies showed statistical significant associations between age, family history of diabetes, genetic factors, smoking, diet, physical activity, dyslipidemia, hypertension, obesity, stressful events, primary health cares, residence, education and risk of diabetes. Analysis of secondary data confirmed some of these factors and indicated that diabetes in women 15-49 years old is associated significantly with age, education, watching TV, residence area, having comorbidities and marital status.

Non modifiable factors

In terms of non-modifiable factors, our findings from the included studies and secondary data analysis, showed that diabetes is more prevalent in older women with family history of diabetes. Studies in other countries with different income level such as China, Taiwan and Guinea also have showed the same, diabetes is positively associated with older age and family history of diabetes.[50-52]

Three of the included studies, showed that there is a positive correlation between some genes and diabetes. They had small ample size and were limited to three provinces of Iran, while large studies conducted in the world showed genetic factors do play a role in the development of diabetes. Some of these studies tried to better understand the genetic architecture of type 2 diabetes, it will help to detect high risk population based on the genetic factors.[53-56] These kinds of studies are limited in Iran.

In terms of ethnicity, only one of the included studies showed that prevalence of diabetes was higher in non-Turkmen population than Turkmen people in Golestan,[31] one of the provinces of Iran. While there are seven major different Iranian ethnicities but there are limited data about the correlation of ethnicity and diabetes in Iranians.

Health behaviors

Our finding related to association of diabetes and smoking from the included studies showed that there is a negative association or no significant association between smoking currently or smoking in the past respectively and diabetes. Results of a survey in eastern India also has showed that smoking is not associated with prevalence of diabetes.[57] While a cross-sectional study in Qatar found that smokers are 3.5 times more likely to have diabetes than non-smokers.[58] Also a study in USA, showed that the risk of incident diabetes is higher in smokers and abstainers compared to never-smokers, even to quit smoking could result in weight gain and increase the risk of diabetes in a short time.[59] It is the same in Greek population, the odds of having diabetes is associated with smoking

while the odds of having diabetes is higher in abstainers.[60] Furthermore, the included clinical trial in this study showed that life style intervention including decreasing smoking could decrease the risk of diabetes.[45] Therefore, negative association of smoking and risk of diabetes is inconsistent with other studies' findings while it is resulted from a large study with more than fifty thousand participants. It could be because of a reverse causation. Sick people may care more about their health and follow the medical advice better, so they don't smoke or stop smoking.

The only included study regard to diet, indicated that diet improvement in an Iranian population decreased the diabetes incidence.[45] Although, based on this study due to co-interventions it is not possible to judge about the effect of diet improvement on risk of diabetes but other studies in different countries also showed that diet could be one of the determinants of diabetes.[61-63] There is not a consensus for the best anti diabetic diet, however, results of a meta-analysis with 136,846 participants has showed that Mediterranean diet is correlated with 23% reduction of the incidence in diabetes.[61] Mediterranean diet usually has high consumption of fruits, vegetables, legumes, whole grain cereals and olive oil, moderate use of dairy products and fish and low consumption of meat and sugar.[61] While in Iran, fruit and vegetable consumption is low. Prevalence of consuming fruits and vegetables less than five times per day is about 86.1% for females.[19]

Many studies, reported that more physical activity is correlated with reduced risk of diabetes.[51,57,58,64,65] Findings of the included studies, showed the same in Iranian population. Physical activity could reduce the risk of diabetes while the mean of total physical activity among Iranian women is about 78.8 minutes per day. It is 2.39 times less than average physical activity of Iranian men. It includes all physical activities for transport, at work and house.[19] It could make them at risk of obesity and then other NCDs including diabetes.

Biological risk factors

Based on World Health Organization, diagnostic criteria for IGT is fasting blood glucose <7.0mmol/l and 7.8 ≤ plasma glucose after 2 hours <11.1mmol/l (after 75 gram oral glucose ingestion). It is not a clinical disease but it is the risk factor of developing diabetes and adverse outcomes. Therefore it refers to pre-diabetes and it means that increase the risk of developing diabetes. Findings of the included study in this research also showed the increased risk of diabetes in people with IGT.[66,67]

Included studies indicated that there is an association between high blood pressure and increased risk of diabetes in Iranian population. This finding is consistent with a systematic review of studies published from 1980 to 2010 in China.[51] Although, causality could not be proven by these kinds of studies but this association is important and shows that the risk of developing diabetes in women with hypertension is more than women with normal hypertension. While the prevalence of hypertension (SBP ≥140 and/or DBP ≥ 90 mmHg) is 17.12% in Iranian women.[19]

Findings of the included studies in this research showed that high TG, high LDL and low HDL is associated with increased risk of diabetes. These findings are in accordance with other published studies.[51, 68,69] With regard to cholesterol, one of the included studies indicated a reverse association between cholesterol and diabetes compared to the other included studies. It could be due to higher consumption of lipid lowering drugs in diabetic group than control group (44% and 12%, respectively). Based on the last survey on NCDs risk factors surveillance in Iran, mean total cholesterol in Iranian females is 189.9 mg/dl and the prevalence of women with total cholesterol more than 200mg/dl is 36.38%. Percentage of women with HDL ≤ 50mg/dl and TG ≥ 200 mg/dl is 70% and 16.72%. It means that, there is a high proportion of women who are at risk of diabetes due to dyslipidemia.[19]

Obesity and related factors were the only determinants evaluated in 10 of the included studies. The findings are similar to other reports published in the world. In all relative studies a significant correlation between obesity and overweight and increased risk of diabetes was reported.[70-72] In some studies the effect of this risk factor is assessed with the association of other risk factors like hypertension. The results of evaluating the impact of hypertension and BMI on diabetes development in a study conducted in Kuwait suggested that the association of BMI and diabetes onset could be augmented by pre- existing condition of hypertension.[72]

Primary health care services

In primary health care settings, interventions in different countries has been implemented to prevent and control diabetes. Published reports from Australia, The Netherlands, Nigeria and Egypt has showed the important role of primary health care services in prevention and diabetes control programs.[73-77] The only included study in this research with regard to primary health care services in Iran related to diabetes also showed that the effectiveness of primary health care workers in reduction of mean fasting blood glucose.

Other determinants

In terms of socioeconomic status (SES), no study was included to evaluate it. But level of education as one of the indicators of SES were evaluated in this research. Through the included studies and data analysis, it was shown that there is a negative significant association between higher education and risk of diabetes. It is in accordance with other studies that assessed the association of level of education and risk of diabetes. Low level of education could result in low awareness of diabetes, high prevalence of unhealthy behaviors, less job opportunity and consequently low income, low access to health care services and more stressful life.[78,79] Although diabetes and its complications also could affect people to not be able to continue education and use job opportunity to have more income.

Income level as another indicator of SES has been reported to be associated with risk of diabetes in other studies. It was analyzed in this research but was not included in the final multivariate logistic regression model since no association was illustrated based on univariate analysis between level of income and risk of diabetes in women. The available income level data was total income per household per month while for this kind of analysis it is better to have income level of household per each member of households. It is the same for surface area of living house, the data was not available per person. It could be the justification that it was not significant.

Watching TV was not mentioned in the framework but it has been studied in relation to diabetes in previous reports in other countries. No study related to watching TV and risk of diabetes was found in Iran but the analysis of secondary data in this research, showed that watching TV every day or less than every week was negatively associated with having diabetes in women compared to never watch TV. These findings are inconsistent with other studies in USA and Europe.[80,81] They showed that prolong watching TV increased the risk of diabetes independently and through decreasing of physical activity and increasing the BMI. A study has been conducted in India reported no significant correlation between watching TV and incidence of diabetes.[82] An explanation for the findings from our current study is that in the secondary data we used, watching TV is an indicator of wealth rather than physical activity. There was no question about the number of hours watching TV.

In terms of comorbidities based on the available data, analysis showed that there is a correlation between having diabetes and having cardiovascular diseases, asthma and musculoskeletal diseases. Coexistence of diabetes has been shown in other studies and their findings indicated that having diabetes increased the risk of CVDs. Diabetes and CVD have some common risk factors such as obesity and hyperlipidemia, so they may be exist simultaneously. Furthermore, diabetes have vascular complications and could be a risk factor for CVDs.[83,84]

Association of Asthma and Diabetes was confirmed by previous studies.[85-88] Obesity is one of the factors that increases mediators of asthma and as there is a correlation between obesity and diabetes, association of asthma and diabetes could be justified. Furthermore, it was reported that Asthma could be a risk factor for developing diabetes although the pathogenesis of this association is not known completely.[88]

Several studies showed the positive correlation of diabetes and musculoskeletal disorders. Although the pathogenesis of this association is not obvious but some of them reported the role and effects of diabetes in developing musculoskeletal diseases. Therefore our findings is in accordance with previous studies.[89-93]

Included studies reported that women who live in urban areas are more likely to have diabetes. It was confirmed by the analysis too. The results of this research is in agreement with findings of studies in India, China, Guinea and Oman [50,51,57,94] while studies in countries such as USA and Australia

[95,96] has showed reverse association, living in rural area is correlated with increased risk of diabetes. Higher prevalence of diabetes in urban areas in Iran could be due to changes in life style makes people to expose more with risk factors such as lower physical activity and high calorie intake.[97] It could increase the prevalence of hypertension, dyslipidemia, overweight and obesity in urban areas. While, some of the reasons of high prevalence of diabetes in rural than urban areas in USA are less access to primary health care services, exercise facilities and fruits or vegetables.

Some of determinants were listed in the framework while their correlation with diabetes have not been assessed in the included studies or analysis: early life factors, psychosocial factors, physical and social environment, some of underlying determinant including transport, housing, social capital, public policy, community characteristics.

These determinants were evaluated in previous reports/studies in different countries and have been indicated to be associated with diabetes. Inverse association between birth weight and risk of diabetes is reported in several studies, in which the lowest levels of birth weight is directly related to highest risks of diabetes. Furthermore, fetal under-nutrition is suggested to be effective in developing adulthood diabetes. Studies showed that reducing growth due to fetal malnutrition is associated with a greater risk of diabetes incidence.

The association between child abuse and neglect, as another early risk factor for diabetes was not assessed in many studies. However in a cohort study conducted in US, the strong link between these factors and diabetes were conclusively demonstrated. The study suggests that abuse could lead to overweight and high BMI among adults who suffered from abuse in childhood with various physiologic and psychological mechanisms. Therefore efforts to find these mechanisms and design weight control interventions would help to reduce the risk of diabetes.

Several available evidence confirm that Gestational Diabetes Mellitus (GDM) increased risk of development of diabetes in mothers, while no document has been found to show the links between GDM and risk of diabetes in their children's adulthood.

Moreover, studies have revealed obvious significant links between psychosocial factors and future risk of diabetes; however more extensive data is needed to conclude the relation of each psychosocial factor like self-efficacy and sense of control with development of diabetes.

We found that single women are less likely to have diabetes than married women. Since our data showed married women are usually older than single women, one theory could be that the significant higher risk of diabetes in married women is influenced by the effect of their higher ages, not only their marital status. This association was also assessed in one of our included studies; however the association of marital status and diabetes was not significant.

Our results showed higher risk of developing diabetes in jobless women compared with housekeeper women, no significant difference was found between student or employed women and jobless women. The first significant result could be justified with the higher physical activity of the housekeeper women in contrast to lower physical activity of jobless women. However this thought could not explain the insignificancy between employed and jobless women.

National diabetes programme in Iran

The national programme for prevention and control of diabetes in Iran is more focused on high risk population and provide health care services for pre-diabetic or diabetic patients. While in primary prevention, there are only two interventions regard to whole community. One of them is raising awareness of population about diabetes and its risk factors and the other one is active screening of population aged more than 30 years in rural areas and passive screening of urban residents for risk factors of diabetes every three years. [15,16]

Regard to selected framework, the objectives of the program are focused more on the right part of the framework. They addresses non-modifiable and biological risk factors, primary health services, specialist services and acute care, diabetes, ongoing care and health outcomes. objectives While findings from the included studies and the secondary data analysis showed that many other modifiable determinants are associated with increased risk of developing diabetes, but theses determinants such as smoking, diet, physical activity and comorbidities have not been addressed appropriately in this national program. For example life style modification was considered in the specific objectives but as an intervention targeted pre-diabetic or high risk population. In fact, all the interventions in the current program are individual-based.

Furthermore, implementation of interventions to achieve the objectives of the programme needs enough human resources in the public health system particularly in primary health care network. Because, most of activities should be done by rural houses and rural or urban health centers, while they have already other activities related to primary health care services. However, the program in rural area was successfully implemented. Because it was needed less financial and human resources compared to implement in urban and the health network in rural area has been very well stablished. But to run the program in the urban areas, it was decided to merge with the physician family program. While physician family program is a new developed program in urban areas and it has not been implemented completely in urban areas yet and still there are some limitations to implement this program in all urban areas.[16] Therefore, the program for prevention and control of diabetes was not implemented very well in urban areas while more than 70% of Iranian population live in Iran.[4]

Limitations

The current study had some limitations with regard to secondary data. It was available only for women and the data on diabetes and other comorbidities was self-reported. It was estimated that half of the diabetic patients are not aware of their diseases. Therefore it could underestimate the association of determinants and risk of diabetes.

There was not any data available about the onset date of diabetes or date of diagnosis. Therefore, it was not possible to know whether determinants begins earlier or after diabetes. It could underestimate the association too. For example, an illiterate woman who obtained a university degree after having had diabetes, was included as a woman with diabetes and university degree not as a diabetic illiterate women.

Advantages

It is the first study, analyzed secondary data related to diabetes in women at national level. Also, based on my knowledge, it was the first study, review literatures about diabetes and its determinants in Iran. In addition to providing relevant information, the findings showed a knowledge gap in determinants of diabetes in Iranian population. Furthermore, it revealed the needed interventions for prevention of diabetes.

7. Conclusions and recommendations

Findings of this research based on the current evidences indicated that older age, family history of diabetes, some genetic factors, dyslipidemia, hypertension, obesity, stressful events and living in urban areas are positively correlated with the risk of diabetes. While healthy diet, physical activity, access to primary health care services and higher education were associated with reduced risk of diabetes. The association of smoking and diabetes was not significant in one of the included studies and was negatively associated with the risk of diabetes.

Analysis of Iran's Multiple Indicator Demographic and Health Survey data to quantify the association between Iranian women's socio-demographic characteristics and diabetes indicated that having diabetes in women 15-49 years old is positively associated with older age, lower education, watching less TV, living in urban areas, having asthma, cardiovascular and musculoskeletal diseases. Based on what was discussed before, the correlation of having diabetes and marital status and job was not considerable although some categories compared to the reference category showed significant associations. Having insurance, limitation for access, number of deliveries, surface area of living house, monthly income level and having skin diseases were not associated with diabetes.

No studies were identified for some of the determinants in the framework related to diabetes in Iranian women. They included early life factors, psychosocial factors, alcohol use and some underlying determinants such as transport, housing, physical and social environment, social capital and public policy. Therefore the association of them and diabetes couldn't be answered by this research for Iranian population.

The national program for prevention and control of diabetes in Iran includes individual interventions which are implemented by the public health system. The main targets of these interventions in the first level is at-risk population to reduce the incidence of diabetes. Only one of the objectives in the primary prevention level (Raising awareness about diabetes, its risk factors and complication) addresses the whole community while second and third levels were designed for secondary and tertiary preventions.

The current program in Iran addresses high risk women who have biological risk factors for diabetes. Except raising awareness, this program doesn't have any intervention for prevention of these risk factors. Furthermore, no intervention for other modifiable determinants which were showed in the results, was implemented through this program. Furthermore, In fact, it

includes only individual interventions while there is no population-wide interventions.

According to findings of this research, the following recommendations for prevention of diabetes among Iranian women are suggested:

Research:

1. **Conduct studies at national level to define all determinants of diabetes among Iranian women.** Although, it costs and needs personnel to do at national level but there are national surveys such as Multiple Indicator Demographic Health Surveys and Integrated Monitoring Evaluation System (IMES) which are large-scale household survey conduct with regular intervals. With some modifications, these surveys could be used to collect data regard to determinants of diabetes. In addition to these surveys, several studies at provincial levels also provides related information. It could be possible to develop a guideline for conducting studies related to diabetes and support studies which follow this guideline and provide needed data.

Policy:

2. **Develop a framework for determinants of diabetes in Iran;** if enough data is provided with studies, it would not be very costly to design a framework for determinants of diabetes. This framework will help policy and decision makers to implement more appropriate interventions.

Intervention:

3. **Implement population-wide interventions;** this kind of interventions in combination with the current individual interventions in Iran could be more effective. They would be complementary and reduce risk factor in a larger population. These interventions are very important, because a small reduction of risk factors at the population level could decrease the burden of diseases considerablel.

    - **Communication interventions;** promote public awareness about diet and promote physical activity thorough mass media are the interventions that evidences showed that they are very cost effective, very low cost and feasible. It should be targeted Iranian women specially.

    - **Tax intervention;** Taxation on high fat and sugar foods, could decrease utilization of them. Simultaneously, subsides on healthy foods can encourage people to use it more. Also subsidies for goods and services related to physical activities, is another intervention could promote people to have more physical activity. These kinds of

intervention although needs global studies to show cost-effectiveness but already they were implemented in some countries and they were effective. they are very low cost and highly feasible. Income from taxes on some goods can be used for subsidies for other goods. Also, it could be allocated to primary health care services which is free in rural and urban houses for the people to provide better services.

- **Improving the environment;** Physical inactivity as a risk factor for diabetes is increasing in the urban areas in Iran. Providing exercise facilities in all cities and building walking or cycling ways in flat cities could increase the physical activity of people. These changes in the environment needs budget and human resources but it is feasible in Iran. Because, most of big cities have enough budget to do this kinds of project. Spending money on building larger streets and highways in recent years, resulted in lower cycling in cities such as Isfahan or Yazd which it was very common before.

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Annexes

Annex 1. Search strategy for Pubmed

1. Diabetes/
2. age OR sex OR family history OR genetic OR health behavior OR physical activity OR practice OR diet OR food OR nutrition OR alcohol OR smoking OR life style OR biologic OR pregnancy OR gestational OR obesity OR psychosocial OR impaired glucose tolerance OR socioeconomic OR economic OR job OR work OR social OR gender OR marital OR married OR culture OR education OR information access OR social capital OR policies OR policy OR strategy OR intervention OR environment OR rural OR urban OR primary health OR preventive health OR seeking behavior OR insurance OR determinant
3. 1 AND 2
4. Animals/
5. Humans/ and animals/
6. 4 NOT 5
7. 3 NOT 6
8. Iran [Title/Abstract]
9. 3 AND 9

Annex 2 .Characteristics of included studies							
Study ID	**Title**	**Location**	**Study design**	**Study period**	**Participants**	**sample size**	**Analytical Method**
Golzar 2011	Diabetes Mellitus and Its Correlates in an Iranian Adult Population	Golesatn province	Cohort	2004-07	Adults 30-87 years old	50044	Poisson regression
	Determinant	**Outcome, adjusted prevalence (PR)**					
	Age	Adjusted PR of diabetes increased 21% for every 10 years increase in age.					
	Ethnicity	No-Turkmen ethnicity compared to Turkmen ethnicity; 1.6 (95%CI: 1.5, 1.8)					
	Residence	Urban compared to rural; 1.1, (95%CI: 1, 1.2)					
	Education	15% decrease in people with higher education than illiterate people, *p* value < 0.0001.					
	Wealth score	37% decrease in people with high wealth score than low wealth score					
	Smoking	30% decreased in smoker than never smokers. It was not significant in abstainers compared to never smokers.					
	Hypertension	Hypertension compared to normotensive; 1.82 (95% CI: 1.70-1.96)					
	Leanness, obesity, overweight	Overweight and obese compared to normal BMI; 1.83 (95%CI: 1.66-2.01) and 1.95 (1.75, 2.16) Increased 20% in extreme leanness and 32% in extreme obesity in childhood					
	Physical activity	Decrease 42% in people who do physical activity at work compare to people don't do it.					
	Opium use	No difference					
Harati 2009	Population-based incidence of Type 2 diabetes and its associated risk factors: results from a six-year cohort study in Iran	Tehran	cohort	1999-2008	non diabetic more than 20 years old	3307	Logistic regression
	Determinant	**Outcome, OR (95% CI)**					
	Age	1.2 (1.1, 1.3)					
	Family history	2.4 (2.6, 7.5)					
	History of cardiovascular diseases	1.3 (0.7-2.3)					
	Smoking (Ref. never)	current: 1(0.7, 1.6), past: 0.7(0.4, 1.2)					
	Education (Ref. Illiterate or primary school)	secondary school: 0.8 (0.5-1.2), diploma or higher: 0.5 (0.4, 0.8)					

	Hypertension	1.9 (1.4, 2.6)				
	Obesity	Overweight: 1.7 (1.1, 2.5), Obese: 4.0 (2.7, 5.8)				
	Abdominal obesity	1.4 (1.3, 1.5)				
	High TG	2 (1.5, 2.6)				
	Low HDL	1.4 (1.0, 1.19)				
	Glucose tolerance category	IFG: 8.3 (4.2-16.5), IGT: 7.1(5.1, 9.8), IFG/IGT: 42.2 (25.8, 75.7)				
Azimi-Nezhad 2008	Prevalence of type 2 diabetes mellitus in Iran and its relationship with gender, urbanization, education, marital status and occupation	Khorasan province	cross-sectional	Adults 30-87 years old	3778, 1923 women	Logistic regression
	Determinant	Outcome, OR (95% CI)				
	Age	1.052 (95%CI: 1.029, 1.074)				
	Education	Not significant				
	Residence	Urbanization OR; 2.73 (95% CI: 1.89, 3.92)				
	Occupation	It was not significant in multivariate analysis, but diabetes was more prevalent in retired group.				
	WC	1.031 (95% CI: 1.012, 1.052)				
	TG	not significant				
	Marital status	not significant.				
Aram-Ahmadi 2014	Predicting Type Two Diabetes and Determination of Effectiveness of Risk Factors Applying Logistic Regression Model	Kerman Province	cross-sectional	Aged more than 15	5357	Logistic Regression
	Determinant	Outcome, OR (95% CI)				
	weight	1.118 (95%CI: 1.064, 1.175)				
	Height	0.932 (95%CI: 0.897, 0.969)				
	BMI	1.054 (95%CI: 0.937, 1.186)				

	WC	1.127 (95%CI:1.029, 1.235)					
	Hip	1.025 (95%CI: 0.953, 1.102)					
	age	1.047 (95%CI: 1.036, 1.58)					
	sex (Ref. females)	2.028 (95%CI: 1.897, 2.119)					
	Primary school (Ref. MSc)	1.931 (95%CI: 1.787, 2.205)					
	Elementary (Ref. MSc)	1.958 (95%CI: 1.795, 2.216)					
	Post diploma	1.906 (95%CI: 1.683, 1.986)					
	Diastolic BP	1.044 (95%CI:1.007, 1.082)					
	Systolic BP	1.054 (95%CI: 1.030, 1.77)					
	HDL	0.925 (95%CI: 0.899, 0.952)					
	LDL	1.001 (95%CI: 0.99, 1.006)					
	Cholesterol	1.003, (95%CI: 099, 1.0007)					
	TG	1.011 (95%CI: 1.006, 1.015)					
	Never Opiume user (Ref. former user)	0.957 (95%CI:0.920, 0.986)					
	Current Opium user (Ref. former user)	1.019 (95%CI: 0.956, 1.21)					
	Intense work activity	0.602 (95%CI: 0.498, 0.766)					
	Not Walking and cycling	1.146 (95%CI:1.113, 1.250)					
	Not having intense Physical activity	1.083 (95%CI: 1.005, 1.153)					
Kalantar-Hormozi 2006	Risk factors of Diabetes in shiraz city	Shiraz city	Case-Control	2007	400 diabetic adults and 400 non diabetic adult	800 (293 females in diabetic and 288 females in non-diabetic group)	T Test
	Determinant	Outcome, prevalence					
	Family history of diabetes	39.9% higher in case group, P< 0.05					
	Hypertension history (more than 140/90)	22.9% higher in case group, P< 0.05					
	Hyperlipidemia	30% higher in case group, P< 0.05					
	PCOD	3.1% in diabetic and 0 in non-diabetic, P< 0.05					

	Hirsutism	6.1% higher in case group, P< 0.05				
	still birth history	3.4% higher in case group, P< 0.05				
	Irregular menstruation	6.1% higher in case group, P< 0.05				
	abortion	not significant				
	Delivery more than one	not significant				
	height	not significant				
	weight	not significant				
	WC	8 cm more in case group, P< 0.05				
	Hip	5 cm more in case group, P< 0.05				
	WHR	0.04 more in case group, P< 0.05				
	BMI	not significant				
	HDL-C	3 mg/dL less in case group, P< 0.05				
	TG	48 mg/dL more in case group, P< 0.05				
	Total Cholesterol	21 mg/dL less in case group, P< 0.05				
Kohan 2013	Association of G-2548A Polymorphism in the Promoter of Leptin Gene with Plasma Leptin Level and Risk of Type 2 Diabetes	Fars Province	Case-Control	100 known diabetic and 100healthy people without risk factors	200	Logistic Regression
	Determinant	Outcome, OR (95% CI)				
	G-2548A Polymorphism, GG genotype	3.26 (95%CI: 1.5, 7.2)				
Hasani 2009	Association of CXCL5 with Type 2 Diabetes	Rafsanjan city	Case-Control	230 known diabetic and 120 healthy people	450	Chi Square
	Determinant	Outcome, OR (95% CI)				
	CXCL5 -156 G/C polymorphism, GC or CC genotype	2.17 (95%CI: 1.27, 3.8)				

Horri 2008	Association of number of important stressful events in the life and prevalence of Impaired Gloucose Tolerance or Diabetes in first degree relatives of type 2 diabetic patients	Esfahan city	Cross sectional		First degree relatives of diabetic patients; 288 normal, 146 IGT, 43 Diabetic	477, 379 females	Logistic regression, chi square
	Determinant	Outcome, OR (95% CI)					
	Stress response	IGT or DM prevalence in people experienced stressful events was 14.7% higher than people who didn't experienced. *P* value = 03					
		IGT or DM prevalence in people experienced eight or more stressful events was 11.4% higher than people who experienced less than eight. OR = 3.8, 95%CI:1.44, 10.05, P value=0.008					
Ahmadi 2009	Family history of diabetes in type 2 diabetic patients in Chaharmhal Bakhtiari province	Chaharmahal o Bakhtiari Province	Cross sectional	2008	Diabetic patients	254, 150 females	Chi square
	Determinant	Outcome, OR (95% CI)					
	Family history	Father; 2.36, 95%CI: 10.3, 5.48					
		Sister; 37.69, 95%CI: 13.45, 114.06					
		Brother; 4.91, 95%CI: 1.66, 15.5					
		Daughter; 1.87, 95%CI:1.04, 3.38					
		Son; was not significant					
Bahreini 2011	Association of SNP-43 of Calpain 10 gen with Type 2 Diabetes in east Azarbayejan province	Azarbayejan Province	Case-control		102 diabetic and 100 non diabetic	202	Chi square, Logistic Regression
	Determinant	Outcome, OR (95% CI)					
	SNP-43 of Calpain 10 gen, Allele G	2.61, 95%CI: 1.06, 6.45					

Farzadfar 2012	Effectiveness of diabetes and hypertension management by rural primary health-care workers (Behvarz workers) in Iran: a nationally representative observational study	National	Case-control		individuals aged 25 years or older	50202	Regression analysis
	Determinant	Outcome					
	primary health care workers	Each addition primary health care worker is associated with 0.09 mmol/L (CI95%: 0.01, 0.18) decrease in mean fasting plasma glucose in district level					
Amini 2007	Diabetes and Impaired Glucose Regulation in First-Degree Relatives of Patients with Type 2 Diabetes in Isfahan, Iran: Prevalence and Risk Factors	Isfahan	cross sectional	2003-2005	first-degree relatives (FDR)of type 2 diabetes outpatients aged 30-60 years	2,368 FDR, (614 men and 1754 women)	T-test, chi squared and binary logistic regression
	Determinant	Outcome, OR (95% CI)					
	Family history	Type 2 diabetes was more prevalent significantly in first degree relatives than general population (Type 2 diabetes in FDRs, 10.3% (9.1-11.5) and in general population 6.0% (5.7-6.2))					
	Age	1. 05 (1. 03 - 1. 08)					
	Waist circumference (cm)	1. 05 (1. 03 - 1. 07)					
	Cholesterol (mg/dl)	1. 01 (1. 00 - 1. 01)					
	Triglyceride (mg/dl)	1. 00 (1. 00 - 1. 01)					
	Systolic BP (mmHg)	1. 35 (1. 17 - 1. 56)					

Hosseinpanah 2007	Population attributable risk for diabetes associated with excess weight in Tehranian adults: a population-based cohort study	Tehran	Cohort	from 1997 with 3.6-years follow-up	aged 3 years and over, from urban district 13 of Tehran	4638 (women: 2716)	T-test, chi squared and binary logistic regression
	Determinant	Outcome					
	Obesity	The ORs for incident diabetes were 2.57 (95% CI 1.60 to 4.13) for overweight and 5.79 (95% CI 3.63 to 9.23) for obesity when compared to normal BMI					
Esteghamati 2014	Trends in the prevalence of diabetes and impaired fasting glucose in association with obesity in Iran: 2005–2011	Iran	cross sectional	2005–2011	Iranian individuals, 6–70 years-	56,225	Chi squared test and logistic regression
	Determinant	**Outcome, OR (95% CI)**					
	BMI	Overweight : 1.05 (1.01–1.10) Obese 1.06 (1.01–1.11) Morbidly obese 1.12 (0.06–1.17)					
	WC ≥ 90cm	1.07 (1.04–1.11)					
		Outcome, Prevalence (95% CI)					
	Residence	**rural:** 7.62 (5.73–9.50), **urban:** 12.69 (10.94–14.43)					
	Sex	**men:** 9.90 (7.72–12.06) 0.0216 **, women:** 12.86 (11.20–14.53)					
	Age	**25–34**: 3.27 (1.92–4.61), **35–44:** 9.20 (6.54–11.85), **45–54:** 19.05 (15.38–22.71), **55–64:** 25.32 (22.74–27.91), **65-70**: 29.18 (25.44–32.91) p<0.0001					
Aghayi meybodi 2008	Assessment of relation between changes in body weight and fat distribution with diabetes incidence in a group of residents of district 13 of Tehran after three years (Tehran Lipid and Glucose Study)	Tehran	cohort	1998-1999 and 2002-2003	3-69 years	15005	Regression analysis

	Determinant	**Outcome, relative risk of diabetes or pre-diabetes according to BMI, OR (95% CI)**					
	BMI in first year	**<18.5** : 0.6 (0.22- 1.63) , **18.5- 24.9:** 1, **25- 29.9**: 1.7(1.36- 2.40), **≥ 30:** 2.02 (1.55- 2.63)					
	Changes in weight after three years	weight loss >4% of : 0.4(0.27-0.65), no change in weight :1, weight gain 4%- 10% 1.2(1.01-1.53), weight gain> 10%:1.3(1.04-1.86)					
Ghaderpanahi 2011	Association of Physical Activity with Risk of Type 2 Diabetes	Tehran	cross sectional		aged 25-64 yr	1552	multivariate model, χ 2 test, Linear and logistic regressions
	Determinant	Outcome					
	aerobic physical activity ≥150 minuets/week	Significantly associated with decreased risk of type 2 diabetes in all and non-obese subjects [OR= 0.56; 95%CI: 0.35-0.91 and OR= 0.50; 95%CI: 0.26-0.94, respectively], it was not significant in obese subjects [OR=0.64; 95%CI: 0.30-1.39].					
Harati 2010	Reduction in Incidence of Type 2 Diabetes by Lifestyle Intervention in a Middle Eastern Community	Tehran	cluster-controlled trial	1999–2001, 2002- 2005	aged >20 years	intervention group:1754 and control groups: 2993,	Regression analysis, T , Mann–Whitney, and chi-square tests
	Determinant	Outcome					
	life style modification: including diet improvement, higher levels of physical activities, and decrease smoking	Results after 3.6 year follow up showed the relative risk declined of 65% significantly, (95% CI: 30%, 83%, p <0.003). The incidence of diabetes was 12.2 (10.3, 14.6) in control group and 8.2 (6.5, 10.6) per 1000 person-years in intervention group.					