

# Detection of High Risk People for Diabetes by American Diabetes Association Risk Score in PERSIAN Guilan Cohort Study

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## Research

**Keywords:** ADA, Diabetes Mellitus, Risk score, Guilan cohort study

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# Abstract

**Background:** To determine prevalence of high risk individuals for diabetes mellitus (DM) and pre DM based on American Diabetes Association (ADA) risk score among Iranian people.

**Methods:** Present study was based on 7989 non diabetic subjects aged 35–70 years from 10520 PERSIAN Guilan Cohort Study (PGCS) participants. ADA risk score was calculated for every individual through online calculator. Receiver operating characteristic (ROC) curves was used to study diagnostic accuracy of the anthropometric indices for detecting individuals with high risk ADA score for developing DM, represented by area under the curve (AUC).

**Results:** From 7989 study subjects, ADA risk score found 3874 (48.5%) and 19122 (23%) at risk for developing PreDM and DM, respectively. The results of ROC curve analyses showed the highest diagnostic value was related to waist circumference (WC) followed by Body Mass Index (BMI) (0.695 and 0.693, respectively). The cut-points of WC and BMI for identifying high risk people for DM were 97 and 29, respectively.

**Conclusions:** A large number of our participants had high ADA risk score for developing DM and PreDM that provide the importance of prevention strategies. WC seems to be highest diagnostic value in identifying people (men and women) with DM.

## Introduction

Diabetes mellitus (DM) is one of the most prevalent chronic diseases in the world with high cost of medical services due to complications of the disease [1]. Over the past decade, the prevalence of diabetes has risen due to aging, urbanization and increased unhealthy behaviors like bad dietary habits, physical inactivity[2]. According to International Federation of Diabetes (IDF) Atlas for Diabetes, middle east region and Iran was known as one of the countries with the high prevalence of diabetes. It is estimated 9.2 million Iranian individuals will have diabetes by the year 2030[3]. Hence, this dramatic increase in the diabetes prevalence results the high economic cost for management of disease and its complications [4]. In spite of genetic susceptibility, environmental factors like unhealthy diet habit and sedentary lifestyle play an important role in the development of diabetes [5]. Evidence from studies has clearly shown early identification and behavioral intervention to lose weight, increase physical activity and choose healthy diet can significantly decrease the incidence of diabetes and prediabetes [6, 7]. To decrease the burden of DM, several guidelines and World Health Organization (WHO) recommended strategies for early detection of individuals are at risk of diabetes [8–10]. Till now, several non invasive and easily practical risk prediction model have been developed to identifying those with high risk for the diabetes including FINDRISK (Finnish Diabetes Risk Score)[11], AUSDRISK (Australian Type 2 Diabetes Risk Assessment Tool)[12], ADA (American Diabetes Association) RISK SCORE [13, 14], and a risk score had been developed in Thailand [15]. In a recent study [16] the validity of the ADA risk prediction models had been confirmed for identifying high risk individuals for type 2 diabetes in a large sample of Iranian population related to

the Tehran Lipid and Glucose Study (TLGS). In the recent report, over the 70% of Guilan population were found to be overweight or obese [17] and consequently at risk of non communicable disease. Hence, identifying high risk people and implementing prevention community based program seems to be substantial. The aim of present study was to assess the prevalence of high risk individuals for diabetes or prediabetes among Iranian individuals according to ADA risk score.

## Materials And Methods

### Study design and population

This is a cross sectional study on PGCS participant (PERSIAN Guilan Cohort Study), a prospective, population-based cohort study in Guilan has been described in detail elsewhere[17-19]. Briefly, The Guilan cohort study(GCS) was conducted on 10 520 participants aged between 35-70 years in Guilan province, northern Iran, between October 8, 2014 and January 20, 2017 as part of the Prospective Epidemiological Research Studies in Iran (PERSIAN). Eligible subjects were contacted through phone by trained interviewers who can spoke the native language of the region and invited to participate the study. After signed informed constant all study data including demographic characteristics, socio-economic status, lifestyle and sleep habits, Anthropometric indices and blood pressure were recorded by a trained research assistants. Also biological samples were collected. In phase 2, annually active follow up was planed for next 15 years for all participants according to the PERSIAN cohort protocol [18]. Present study data included 7989 non diabetic participants of the GCS study. Diabetic subjects were excluded. Subjects with DM in the GCS were defined as 1) history of diagnosed DM 2) history of anti diabetic medication consumption 3) fasting blood sugar (FBS)>126 in the initial cohort laboratory data [17].

### Data collection and measurement

For every participant, we retrieved data from GCS database that were collected through interviews, physical examinations, and laboratory tests according to cohort protocol [19]. For the present study, data included demographic factors like age, sex, living location (city or rural), Marital status, Occupation (employed, unemployed), anthropometric indices including weight, height, hip and waist circumference, waist to hip ratio (WHpR) and waist to height ratio (WHtR), history of hypertension (HTN), gestational DM in women subjects and any history of DM in their first degree family like father, mother, sister or brother and finally information about physical activity. All anthropometric indices including weight, height, Hip Circumference (HC), Waist Circumference (WC), WHpR, and WHtR were measured by trained research assistants according to GCS protocol. Body mass index (BMI) was categorized as underweight (BMI<18.5 kg/m<sup>2</sup>), normal weight (BMI= 18.5-24.99 kg/m<sup>2</sup>), overweight (BMI= 25-29.9 kg/m<sup>2</sup>) and obese (BMI≥30 kg/m<sup>2</sup>). The level of Physical activity was reported as metabolic equivalent rates (METs) based on self reported daily activity PERSIAN cohort questionnaire.

The risk of developing DM or prediabetes was calculated for every individual based on ADA risk prediction model through online calculator [13] the ADA risk prediction model was developed based on American population higher than 20 years without DM to identify high risk individuals for DM or prediabetes. ADA risk score included 7 questions like age, sex, race, weight, height, family history of DM, history of gestational DM, history of HTN and physical activity. Total score was calculated between 0-11. The higher score represent higher risk of diabetes. The cut point 5 or higher shows the high risk for DM and cut point 4 shows the high risk for prediabetes [20]. All required data for calculating ADA risk were extracted from cohort study. Family history of DM in ADA risk score was defined any history of diabetes in mother, father, sister or brother. Gestational diabetes in PERSIAN cohort was considered yes if women answered yes to the question “did you have a history of diabetes in pregnancy or did you have given birth a baby with  $\geq 4$  kg?” For race, all participants were defined as white. For physical activity, the question in ADA risk score tool was “are you physically active? Yes or no” Low level of physical activity in PERSIAN cohort was defined as less than mean METs rates of participants (41 METs/hour/day) that have been previously described in details [17].

## Ethics

This research project was approved by the Ethics Committee of the Gastrointestinal and Liver Disease Research Center and Guilan University of Medical Sciences (code number IR.GUMS.REC.1398.241). All participants expressed their consent for participation in the research.

## Statistical analysis

In this study, continuous variables were expressed as mean  $\pm$  standard deviation (SD) and categorical variables as frequency (percentage). One-way ANOVA and Chi-square test were used to compare demographic characteristics and anthropometric indices among normal, prediabetes, and diabetes groups. Receiver operating characteristic (ROC) curves were used to study diagnostic accuracy of the anthropometric indices for detecting patients with diabetes, represented by area under the curve (AUC). An AUC value of 0.5 indicates an entirely random classifier and an AUC value of 1 indicates perfect classifier. The best cut-off value was defined as the value with the highest accuracy that maximizes you den’s J statistic, i.e.  $J = \text{sensitivity} + \text{specificity} - 1$ . Data analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA), and a  $P < 0.05$  was considered statistically significant.

## Result

### Characteristics of the participants

Totally, of 10520 participants, 7989 non diabetic individuals were included in the study. Prevalence of DM in PERSIAN Guilan Cohort Study (PGCS) was 2531 (24.1%) [20]. Demographic characteristics and

anthropometric indices of the participants are presented in Table 1. The geographic distributions of study participants according to ADA score category (normal, high risk for preDM, high risk for DM) are presented in Fig. 1. The mean age of the participants was  $50.52 \pm 8.75$  years. More than, 51% were female, 91.2% were married, 54.9% were resident in rural area, and 27.5% had normal BMI, 53.6% had a family history of diabetes.

Table 1

Demographic and clinical characteristics of adult participants based on ADA risk scores in the PERSIAN Guilan Cohort Study (n = 7989)

	Total(N)	Normal (N)	Prediabetes (P)	Diabetes (D)	<i>P</i>	
Age (y)	50.52 ± 8.75	44.62 ± 5.83	48.59 ± 7.48	54.84 ± 8.40	< 0.001	N < P < D
Sex						
Male	3898 (48.8)	990 (25.4)	913 (23.4)	1995 (51.2)	< 0.001	
Female	4091 (51.2)	1213 (29.7)	999 (24.4)	1879 (45.9)		
Marital status					< 0.001	
Single	259 (3.2)	129 (49.8)	53 (20.5)	77 (29.7)		
Married	7282 (91.2)	1969 (27.0)	1772 (24.3)	3541 (48.6)		
Widowed	348 (4.4)	65 (18.7)	68 (19.5)	215 (61.8)		
Divorced	100 (1.3)	40 (40.0)	19 (19.0)	41 (41.0)		
Occupation					< 0.001	
Employed	3372 (42.2)	793 (23.5)	785 (23.3)	1794 (53.2)		
Unemployed	4617 (57.8)	1410 (30.5)	1127 (24.4)	2080 (45.1)		
Place of residence					< 0.001	
Urban	3601 (45.1)	893 (24.8)	868 (24.1)	1840 (51.1)		
Rural	4388 (54.9)	1310 (29.9)	1044 (23.8)	2034 (46.4)		
Height (cm)	162.94 ± 9.35	163.38 ± 9.29	163.07 ± 9.29	162.62 ± 9.39	0.008	N > D
Weight (kg)	73.91 ± 13.54	67.49 ± 11.23	72.96 ± 12.75	78.03 ± 13.61	< 0.001	N < P < D
BMI (kg/m <sup>2</sup> )	27.90 ± 4.97	25.34 ± 4.08	27.49 ± 4.62	29.56 ± 4.94	< 0.001	N < P < D
Underweight	119 (1.5)	64 (53.8)	31 (26.1)	24 (20.2)		

	Total(N)	Normal (N)	Prediabetes (P)	Diabetes (D)	<i>P</i>	
Normal	2200 (27.5)	1063 (48.3)	545 (24.8)	592 (26.9)		
Overweight	3177 (39.8)	850 (26.8)	825 (26.0)	1502 (47.3)		
Obese	2493 (31.2)	226 (9.1)	511 (20.5)	1756 (70.4)		
Family history of diabetes						
No	3703 (46.4)	1435 (38.8)	904 (24.4)	1364 (36.8)		
Yes	4286 (53.6)	768 (17.9)	1008 (23.5)	2510 (58.6)		
Hip Circumference (cm)	102.92 ± 9.65	99.07 ± 8.16	102.14 ± 9.07	105.50 ± 9.91	< 0.001	N < P < D
Waist Circumference (cm)	97.98 ± 12.32	91.64 ± 11.04	96.79 ± 11.23	102.18 ± 11.84	< 0.001	N < P < D
Waist/Hip Ratio	0.95 ± 0.06	0.92 ± 0.07	0.95 ± 0.06	0.97 ± 0.05	< 0.001	N < P < D
Waist/Height Ratio	0.60 ± 0.09	0.56 ± 0.08	0.60 ± 0.08	0.63 ± 0.09	< 0.001	N < P < D

## Distribution of ADA risk score

Figure 2 presents the frequency of ADA risk scores among participants. The mean ADA risk score for all respondents were 4.48 (SD = 1.55), and using a recommended cut-off values, the prevalence of high risk subjects for preDM and DM were, 23.9% (n = 1912) and 48.5% (n = 3874), respectively.

## Comparison of groups

As presented in Table 1, all of the anthropometric indices (i.e., BMI, HC, WC, WHpR, and WHtR) in diabetes group were higher than those in prediabetes and normal groups. In addition, all anthropometric indices in prediabetes group were also higher than in normal group.

## ROC curve analysis

The results of ROC curve analyses to examine the diagnostic accuracy of the anthropometric indices for detecting patients with diabetes based on ADA risk score are presented in Table 2. Based on the AUC values, the anthropometric indices that had the highest diagnostic value was “Waist Circumference” followed by “BMI” in differentiating patients with diabetes and healthy subjects. Figure 3

Table 2  
Diagnostic accuracy of anthropometric indices for detecting participants with diabetes using ROC curve analysis

	<b>Cut-Point</b>	<b>Sensitivity (%)</b>	<b>Specificity (%)</b>	<b>AUC</b>
<b>Weight</b>	73	62.1	63.0	0.670
<b>BMI</b>	29.16	52.8	77.2	0.693
<b>Hip Circumference</b>	103	55.1	67.6	0.653
<b>Waist Circumference</b>	97.1	66.1	63.4	0.695
<b>Waist to Hip Ratio</b>	0.94	73.8	50.0	0.663
<b>Waist to Height Ratio</b>	0.59	66.1	56.8	0.666
AUC: Area under the Curve				

## Discussion

Finding from PGCS showed that, near to half of non diabetic participants (48%) were high risk for developing DM and also more than 23% were high risk for preDM. In a large survey (National Health and Nutrition Examination Survey) conducted from 1999 to 2006, ADA risk score found 35% of subjects were high risk for DM [20]. In a recent descriptive large study conducted in central of Iran, prevalence of DM and preDM was 16.1% and 24.5%, respectively [21]. Evidence shows an increase of 35% in DM prevalence in 2011 compared to 2005. In parallel with our prediction, a Meta analysis modeling study estimated 9.2 million Iranian people will have diabetes by the year 2030(3). This significant increase in DM prevalence and also in DM complications, implementation of prevention and control programs seems to be substantial. Finding from Iranian National Surveys (2007–2016) on 7665 and 93,733 adults with and without known diabetes showed secondary prevention in individual level was effective to control of FBS level but primary prevention in non diabetic people had no positive effect [22].

According to our study, frequency of high risk subjects for DM were superior in male when compared to female as well as in urban area rather than rural area. Although, more subjects of GCS population lived in rural area. In primary analysis of GCS, diabetes was more prevalent in females (27.3%) rather than males (20.2%)(17). The finding of PERSIAN Kharameh cohort study showed that subjects living in urban areas were more likely to display metabolic syndrome and DM than those living in rural areas [23]. Contrary to our study in Kharameh cohort study, prevalence of impaired fasting glucose in females was higher than



males. On the other hands, according to International Diabetes Federation, there were about 14 million more men than women with diabetes (198 million men vs 184 million women) in 2013 and it seems the difference increases to 15 million (303 million men vs 288 million women) by 2035[24].Furthermore, in a cross sectional study among adults aged 20–80 years in northern part of Iran was observed DM were most prevalent in males than females [25].

In present study, subjects with high risk for DM had higher waist and hip circumference, waist/hip ratio and waist/height ratio compared to those with low risk group and also to preDM group. Correlation of obesity and risk of developing DM was reported in previous evidence [25–28]. According to our finding, WC followed by BMI had highest diagnostic value in identifying high risk men and women for developing DM. Although, a prospective study on Iranian adult men in 2006 indicated WHtR is better than BMI and WC in detecting urban men population who was at risk of diabetes [29]. On the other hands, according to a study based on Isfahan Cohort Study (ICS), WC compared to other anthropometric indices was better indicator of metabolic syndrome in Iranian women and men population [30]. Furthermore, previous researches showed WC is strongly related to all-cause and cardiovascular mortality with or without adjustment for BMI [31, 32]. Recent review indicated waist circumference is associated with health outcomes within all BMI categories in every sex and age [33].

In the present study, cut-points of WC and BMI for identifying high risk people for developing DM were 97 and 29, respectively which were higher than the recommended cutoff for major CVD risk factors in previous studies [30, 34, 35]. First Iranian study on anthropometric indices proposed WC and BMI cut-offs for detecting DM, between 82–95 cm and 25–29 in women and men, in various age groups [34]. Iranian National Committee of Obesity reported people with WC of  $\geq 90$  cm are at high risk for CVD event [35].

Cut-points of WHpR to identify high risk individual for developing DM in the present study were 0.94 that somewhat close to the recommended cut point in other studies. For example, P Mirmiran et al found cut-points of WHR between 0.86 and 0.97 for men and between 0.78 and 0.92 for women were high risk for various CVD risk factors [34]. In our study, the diagnostic values of WHpR and WHtR in identifying high risk people for DM were relatively similar. The diagnostic value of WHtR in Chinese cohort study was reported 0.679 that was in parallel with our finding(AUC: 0.666)[36].A recent study in middle east region showed WHtR can better predict the risk of DM and also HTN[37]. Finding from a population based study of 1852 Iranian males aged  $\geq 20$  years showed WHtR was a strong predictor for developing type 2 diabetes in the future [29].

In total, finding high risk people in individual and community level may help people and policy makers to develop and plan prevention strategies. We detect a considerable numbers of Iranian adult lived in northern part of Iran were high risk for developing DM and PreDM. Hence, note to lifestyle modification in individual and community level seems to be substantial. Our study was based on PG Cohort Study with large sample size and accurate data collection. Data collection and measurement were based on Persian cohort study standards that increase the precision of the finding. However, this study involves some limitation. First, due to cross sectional nature of present study design, we couldn't define the actual risk of

study subjects and compare to their calculated risk. However, the validity and sensitivity of ADA risk score among GCS population could be assessed in the future years using long term follow up duration. Furthermore, some study variables like physical activity, history of gestational diabetes were measured based on self-reported that increases the probability of recall bias.

## **Conclusion**

In conclusion, present study showed that a large number of people in northern part of Iran were in high risk category of ADA risk score for developing DM and PreDM. High risk group were more prevalent in male rather than female and also urban residents. According to our finding, among abdominal obesity variables, waist circumference appears to be stronger than others in identifying high risk people for developing DM in the future.

## **List Of Abbreviations**

DM: Diabetes Mellitus; ADA: American Diabetes Association; PGCS: PERSIAN Guilan Cohort Study; ROC: Receiver operating characteristic; AUC: Area Under the Curve; WC: Waist Circumference; WHO: World Health Organization; TLGS: Tehran Lipid and Glucose Study; GCS: Guilan cohort study; WHpR: Waist to Hip Ratio; WHtR: Waist to Height Ratio; HTN: History of Hypertension; HC: Hip Circumference; METs: Metabolic Equivalent Rates; BMI: Body Mass Index

## **Declarations**

## **Ethics approval and consent to participate**

The informed consent and study design were reviewed and approved by vice-chancellor for research of Guilan University of medical science according to Helsinki declaration (research number: (IR.GUMS.REC.1398.241)).

## **Consent for publication**

Not applicable

## **Availability of data and materials**

Datasets used during the study are available from the corresponding author on reasonable request.

## **Competing interests**

The authors declare that they have no competing interests

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## Authors' contributions

TH and FJ and FM-G were involved in the study design. SM and MN data analysis. SS data collection and contributed to data interpretation. SS and TH literature searched. TH, FJ, FM-G and MN wrote the initial draft of the manuscript, TH and FJ and FM-G contributed toward its final version. FJ generated of figures. All authors were involved in writing the paper and had final approval of the submitted and published versions

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## Authors' information (optional)

Not applicable.

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## Figures

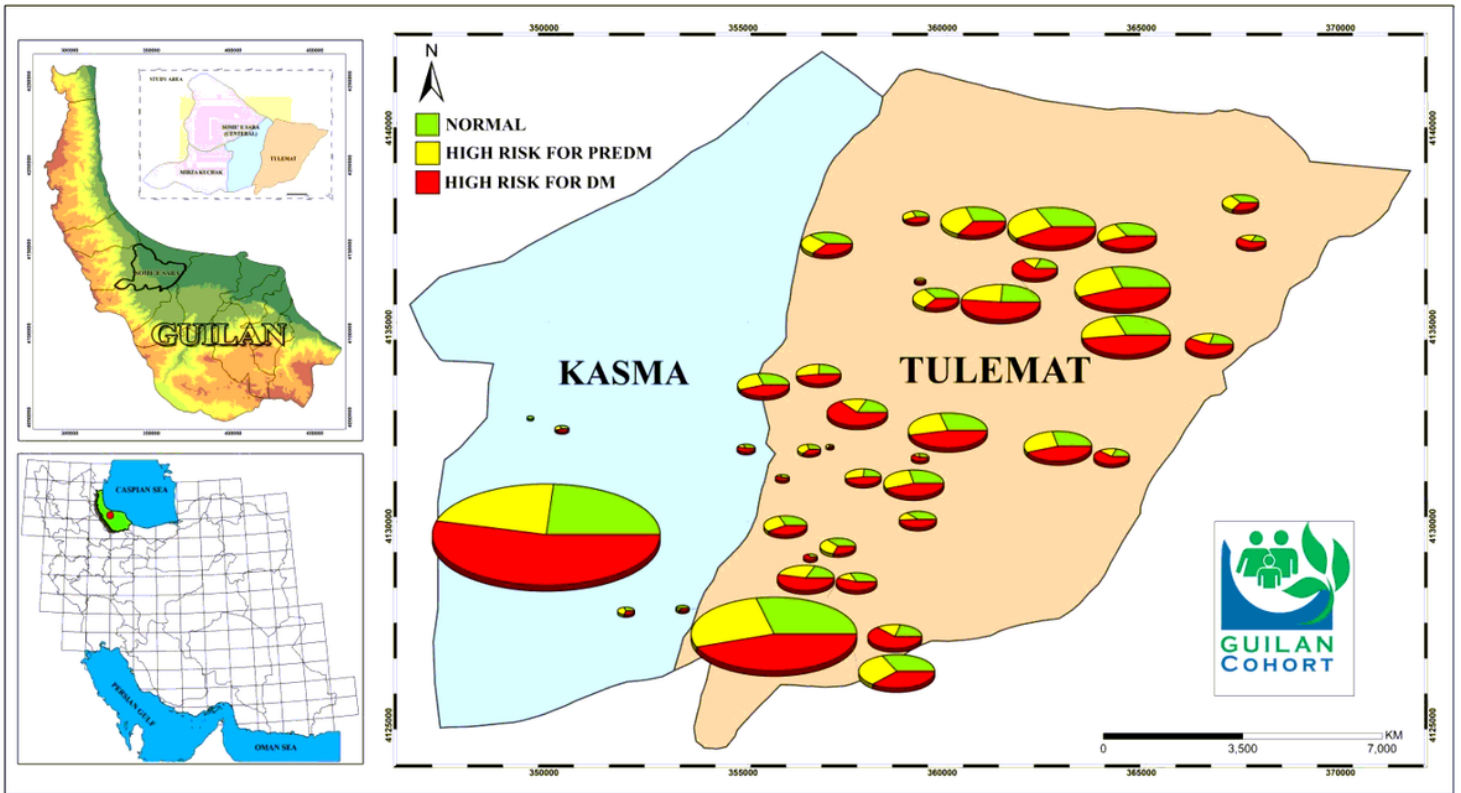
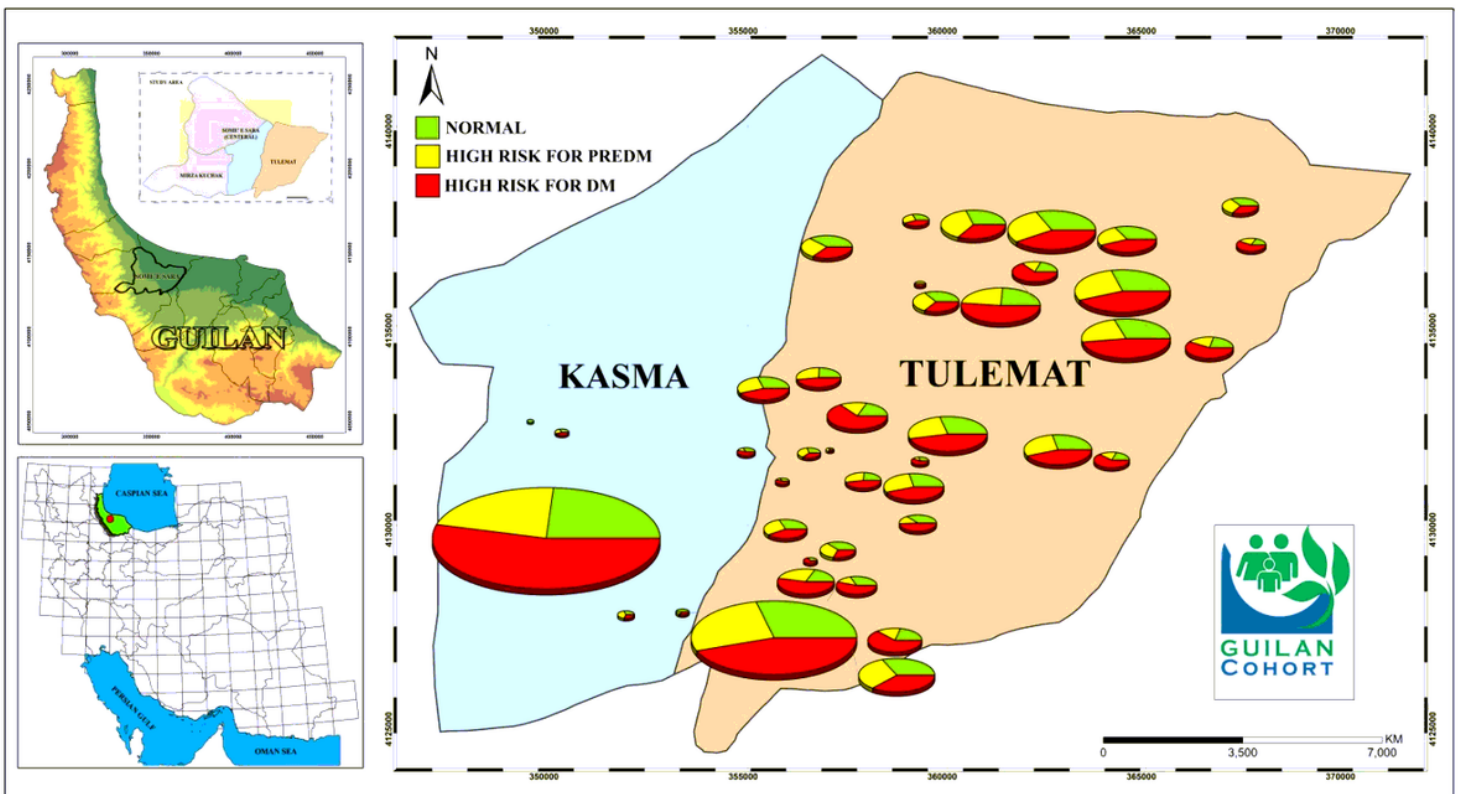


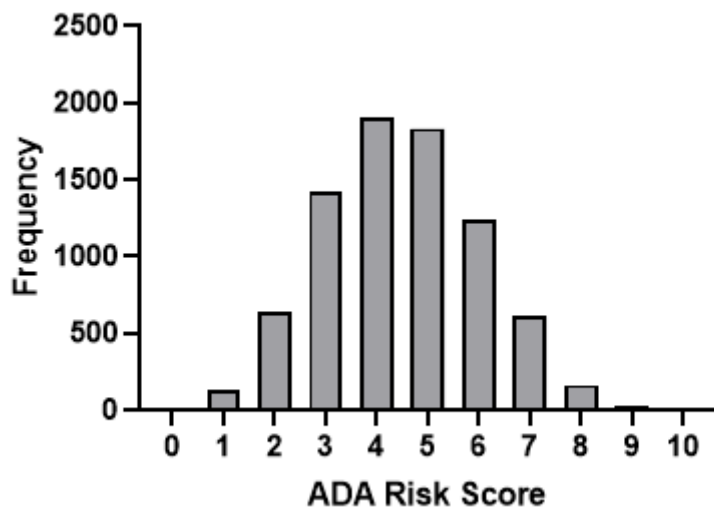
Figure 1

The geographic distributions of study participants according to ADA score category (normal, high risk for preDM, high risk for DM)



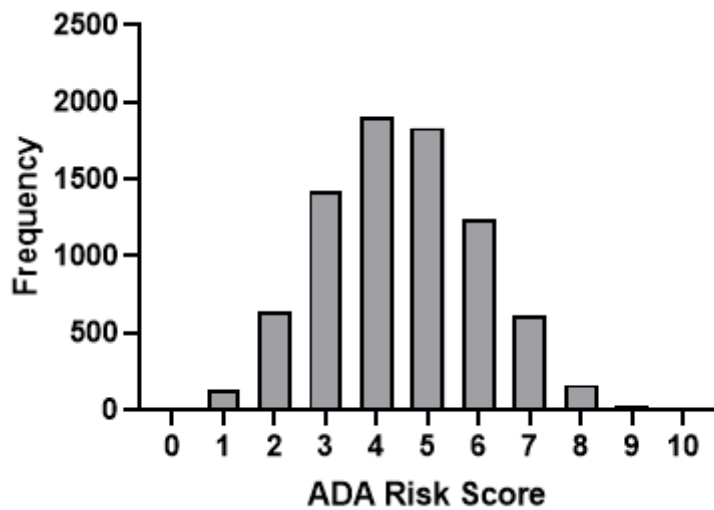
**Figure 1**

The geographic distributions of study participants according to ADA score category (normal, high risk for preDM, high risk for DM)



**Figure 2**

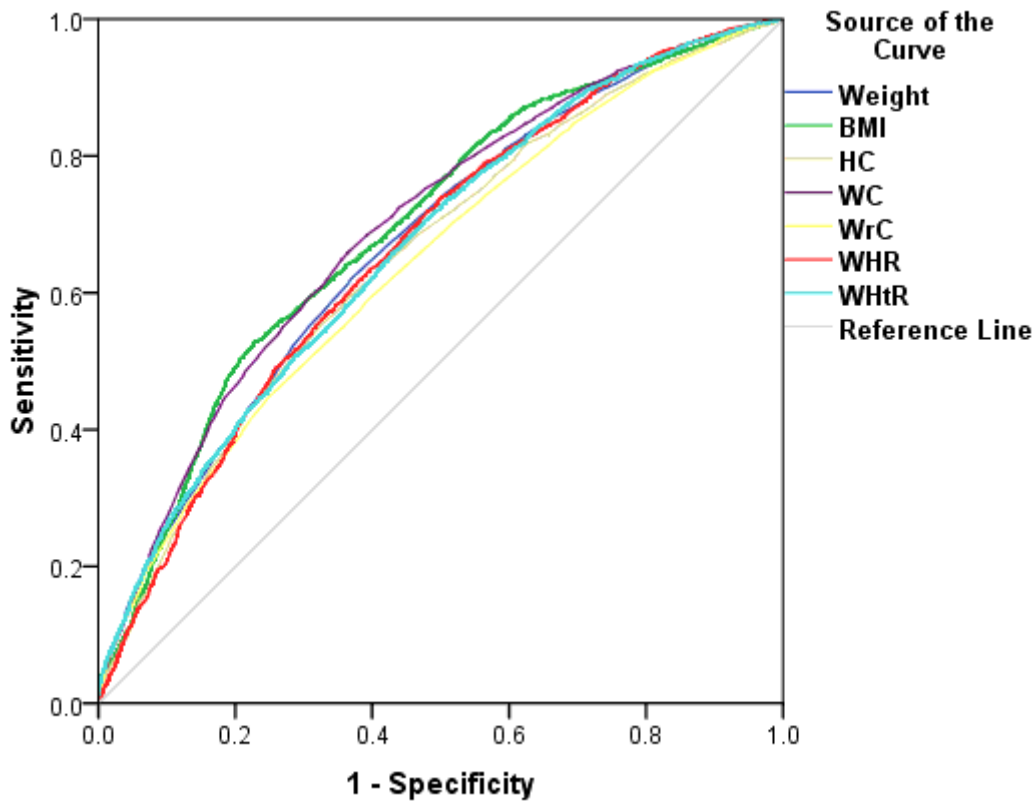
Distribution of ADA risk score among adults participants without diagnosed DM in the Persian Guilan Cohort Study (n=7989)



**Figure 2**

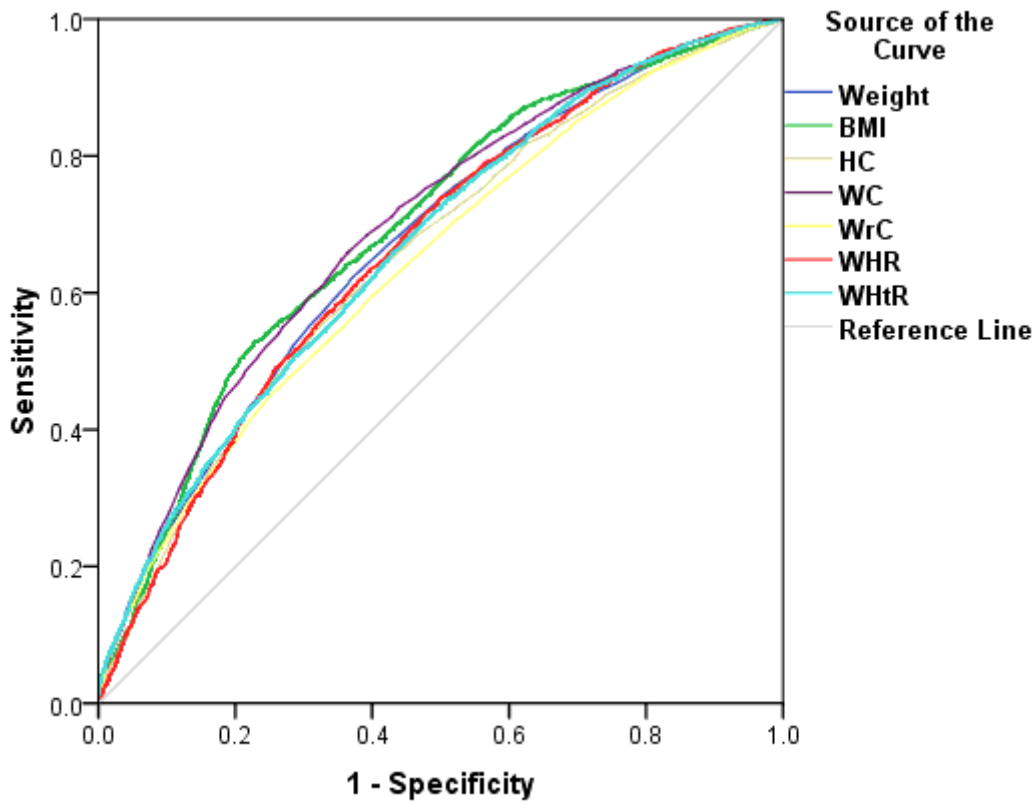
Distribution of ADA risk score among adults participants without diagnosed DM in the Persian Guilan Cohort Study (n=7989)





**Figure 3**

Diagnostic accuracy of anthropometric indices for detecting participants with diabetes using ROC analysis



**Figure 3**

Diagnostic accuracy of anthropometric indices for detecting participants with diabetes using ROC analysis