

# Frequency of Prediabetes According to Optimal Cut-Points for Body Mass Index in Saudi Population

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## Research Article

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## Abstract

**Background and Objective:** The prevalence and incidence of prediabetes are increasing worldwide. Body mass index (BMI) cut-off for prediabetes can vary. The objective of this study is to identify the optimal BMI cut-off that is associated with prediabetes.

**Methods:** For the present study, we analyzed participants who are equal to or older than 18 years old. A total of 5498 were selected to be enrolled for the present study. All patients were from the population of the primary health and diabetic Centers at King Fahad Armed Forces Hospital. Participants were defined as having prediabetes according to self-report, clinical reports, use of antidiabetic agents and HbA1c (5.7-6.4). All data were collected by personal interview and on the basis of a review of electronic medical data. Weight (kg) and height (cm) were measured by physician and nurse interviewers and recorded. The optimal sensitivity and specificity using different BMI cut-off values to predict the presence of prediabetes were examined by receiver operating characteristic curve analysis.

**Results:** Of the 5498 participants analyzed, 2049 (37.3%) were male and 3449 (62.7%) were female with female to male ratio 1.7:1. Age was  $42.7 \pm 15.8$  (minimum 18 years and maximum 105 years) and males were significantly older than females ( $45.3 \pm 16.6$  vs.  $41.1 \pm 15.1$  respectively,  $p < 0.0001$ ). BMI was  $29.6 \pm 6.9$  where females had higher BMI than males ( $30.1 \pm 7.5$  vs.  $28.8 \pm 5.5$  respectively,  $p < 0.0001$ ). Prediabetes was present in 579 (10.5%), 89 (15.4%) were male and 490 (84.6%) were female with female to male ratio 5.5:1. Diagnostic performance of BMI in detecting prediabetes using optimal BMI cut-off values based on the shortest distance in ROC curve showed BMI values ranged from 28.50 to 29.50 in total population, 27.50 to 28.50 in male and from 28.50 to 29.50 in female. The AUC was 0.560 (95% CI, 0.503-0.617) in male and 0.517 (95% CI, 0.490-0.544) in female. The predictive value of BMI in detecting prediabetes using BMI

cut-off values based on the lowest significant association between BMI and the risk factors from the logistic regression analysis showed that the risk of prediabetes was significantly increased at BMI values as low as 21 kg/m<sup>2</sup> and has not been increased as BMI increased. Applying this criterion to identify the cut-off values resulted in improvements in sensitivity, false negative rate and worsening in specificity and false positive rate. Using these lower BMI cut-offs resulted in a very small false negative rate ranging from 0.07 to 0.09. A significant positive association for total population was observed with BMI values starting at 21 kg/m<sup>2</sup> and non significant association with BMI values for both genders.

**Conclusion:** The diagnostic usefulness of BMI alone in defining obesity as risk for prediabetes is limited among men and women Saudi adults.

**Keywords:** Prediabetes; Body Mass Index

## Introduction

Prediabetes is defined as blood glucose concentrations higher than normal, but lower than established thresholds for diabetes itself [1]. According to the World Health Organization, high risk for developing diabetes relates to two distinct states, impaired fasting glucose defined as fasting plasma glucose of 6.1–6.9 mmol/L (in the absence of impaired glucose tolerance) and impaired glucose tolerance defined as post load plasma glucose of 7.8–11.0 mmol/L based on 2-h oral glucose tolerance test or a combination of both [2]. The American Diabetes Association, although applying the same thresholds for impaired glucose tolerance, uses a lower cut-off value for impaired glucose tolerance (fasting plasma glucose=5.6–6.9 mmol/L) and has additionally introduced HbA1c levels of 5.7–6.4% as a new category of high diabetes risk [1]. Individuals with impaired fasting glucose and/or impaired glucose tolerance were referred as having prediabetes, showing the relatively high risk for the future development of diabetes and associated complications [1,3]. Although complications and target organ disease is more common with hyperglycaemia at the levels associated with diabetes, vascular complications, nephropathy, retinopathy and neuropathies are more common in people with prediabetes than individuals at normal blood glucose levels [4-8]. In addition, previous studies have observed about 35-39% of impaired glucose tolerance was undiagnosed in acute heart attack patients [9-11]. Furthermore, a substantial number of individuals with prediabetes progress to diabetes [12]. In particular, between 5% and 10% of people with prediabetes progress to diabetes each year [13].

Globally, diabetes has been increasing, as has intermediate hyperglycaemia and by 2030, it can rise up to >470 million people suffering from it [14,15]. In the USA, the prevalence of prediabetes has been steadily increasing [15]. The 2010 estimate of prediabetes among adults in the USA was 36.2%. Recent data have shown that in developed countries, such as the United States and the United Kingdom, more than one-third of adults have prediabetes, but most of these individuals are unaware they have the condition [14-16]. The 2010 prevalence of prediabetes among adults in China was even higher at 50.1% [16]. In Saudi Arabia, primary epidemiological diabetes features are not different. Statistics regarding the increasing trend of prediabetes in the world have also been observed in Saudi Arabia. As per the WHO country profile 2015, the prevalence of prediabetics was found to be 9.0% in Jeddah with 9.4% in men [17,18]. Another study conducted in Saudi population revealed that the impaired fasting glucose was 25.5%. Once detected, prediabetes needs to be acknowledged with a treatment plan to prevent or slow the transition to diabetes [19,20]. Treatment of prediabetes is associated with delay of the onset of diabetes [21]. Detection and treatment of prediabetes is therefore a fundamental strategy in diabetes prevention [1].

The most commonly used indicator to evaluate excess body fat and measurement of the degree of Obesity is body mass index (BMI) as a known risk factor of prediabetes [22-24]. Although this index has advantages in clinical and epidemiological practice, as a non-invasive and low-cost method, its predictive value for chronic diseases has been questioned, especially when applied to certain population groups [15-17]. Increasing evidence suggests that the excess body fat in overweight and obese

people might lead to increased degradation of fat, which resulted in the production of large amounts of free fatty acids (FFAs). When the level of FFAs was higher in blood, the capacity of liver tissue for insulin-mediated glucose uptake and utilization was lower, so the blood glucose level was high in circulation [25]. In other words, high FFAs in the blood were one of the important pathogenic factors of obesity caused by insulin resistance [26].

Current recommendations for prediabetes screening by the American Diabetes Association focus nearly exclusively on adults who are overweight or obese as defined by BMI until the patient meets the age-oriented screening at 45 years [1]. Further, the recently released recommendation from the US Preventive Services Task Force regarding screening for abnormal glucose levels limits screening to individuals who are overweight or obese [27]. This focus on obese or overweight individuals, Although obesity and prediabetes have shown trends of increasing prevalence. Although obesity and prediabetes have shown trends of increasing prevalence. Identifying individuals likely to be affected by prediabetes using a simple indicator such as BMI is an important step toward reducing the burden of diabetes in Saudi communities. This focus on obese or overweight individuals, however, may lead to missed opportunities for investigation of undetected disease in healthy-weight individuals. It has not been fully investigated whether a BMI cut-off lower than 25 kg/m<sup>2</sup> is feasible to indicate elevated likelihood of having prediabetes in population of Saudi Arabia. The objective of this study is to identify the optimal BMI cut-off that is associated with prediabetes.

## Methods

For the present study, we analyzed participants who are equal to or older than 18 years old. A total of 5498 were selected to be enrolled for the present study. All patients were from the population of the primary health and diabetic Centres at King Fahad Armed Forces Hospital. Participants were defined as having prediabetes according to self-report, clinical reports, use of antidiabetic agents and HbA1c (5.7-6.4) [1]. All data were collected by personal interview and on the basis of a review of electronic medical data. Weight (kg) and height (cm) were measured by physician and nurse interviewers and recorded and BMI was calculated.

## Statistical Analysis

Univariate analysis of demographic and clinical laboratory was accomplished using unpaired t-test

between variables, to estimate the significance of different between groups where appropriate. Chi square (X<sup>2</sup>) test were used for categorical data comparison. The optimal sensitivity and specificity using different BMI cut-off values to predict the presence of diabetes were examined by receiver operating characteristic curve (ROC) analysis. A greater area under the curve (AUC) indicates better predictive capability. An AUC=0.5 indicates that the test performs no better than chance, and an AUC=1.0 indicates perfect discrimination. An ideal test is one that reaches the upper left corner of the graph (100% true positives and no false positives). To determine the optimal BMI cutoff points, we computed and searched for the shortest distance between any point on the curve and the top left corner on the y-axis. Distance was estimated at each one-half unit of BMI according to the equation: Distance in ROC curve= (1-sensitivity)<sup>2</sup>+(1-specificity)<sup>2</sup> [28,29]. Additional criteria were also used to select cut-offs, including the greater sum of sensitivity and specificity, the smallest misclassification rate, and the significant associations between BMI and risk factors based on the logistic regression. Diagnostic performance of BMI in predicting diabetes was assessed by calculating AUC, sensitivity, specificity, likelihood ratios, false positive, false negative and the total misclassification rate. All results are presented as mean ± standard deviation or percentage, where applicable. Data analysis was performed in men and women separately. BMI was stratified in unit of 0.5 for both men and women. A BMI <15.0 was considered as the reference. Logistic regression analysis was used to examine the independent relationship between the stratified BMI and the odds ratio of having diabetes. All statistical analyses were performed using SPSS Version 22.0. The difference between groups was considered significant when P<0.05.

## Results

Of the 5498 participants analyzed, 2049 (37.3%) were male and 3449 (62.7%) were female with female to male ratio 1.7:1. Age was 42.7 ± 15.8 (minimum 18 years and maximum 105 years) and males were significantly older than females (45.3 ± 16.6 vs. 41.1 ± 15.1 respectively, p<0.0001). BMI was 29.6 ± 6.9Vwhere females had higher BMI than males (30.1 ± 7.5 vs. 28.8 ± 5.5 respectively, p<0.0001), table 1. Prediabetes was present in 579 (10.5%), 89 (15.4%) were male and 490 (84.6%) were female with female to male ratio 5.5:1.

Parameters	Total	Male	Female	P value
n (%)	5498	2049 (37.2)	3449 (62.7)	
Age (years)	42.7 ± 15.8	45.3 ± 16.6	41.1 ± 15.1	<0.0001
Body mass index (kg/m <sup>2</sup> )	29.6 ± 6.9	28.8 ± 5.5	30.1 ± 7.5	<0.0001
Prediabetes	579 (10.5)	89 (15.4)	490 (84.6)	<0.0001

Table 1: Population characteristics (means ± SD or number (%)).

Table 2 displays details of the diagnostic performance of BMI in detecting prediabetes using optimal BMI cut-off values based on the shortest distance in ROC curve. Values ranged from 28.50 to 29.50 in total population, 27.50 to 28.50 in male and from 28.50 to 29.50 in female.

The AUC was 0.560 (95% CI, 0.503-0.617) in male and 0.517 (95% CI, 0.490-0.544) in female, Figure 1. These values were statistically significantly higher than that would be expected by chance alone ( $P < 0.0001$ ).

Parameters	Area under curve (95% CI)	Cut-offs BMI kg/m <sup>2</sup>	Sensitivity	Specificity	False positive rate	False negative rate	Positive likelihood ratio	Negative likelihood ratio	Misclassification rate
<b>Total</b>	0.535 (0.511-0.560)	29.0	0.53	0.54	0.46	0.47	0.98	0.87	0.93
<b>Male</b>	0.560 (0.503-0.617)	28.0	0.52	0.50	0.50	0.48	1.04	0.96	0.98
<b>Female</b>	0.517 (0.490-0.544)	29.5	0.54	0.50	0.50	0.46	1.08	0.92	0.96

Table 2: Diagnostic performance of BMI in detecting prediabetes using optimal BMI cut-off values based on the shortest distance in ROC curves in Saudi adults.

Table 3 displays the predictive value of BMI in detecting prediabetes using BMI cut-off values based on the lowest significant association between BMI and the risk factors from the logistic regression analysis. Regression analysis showed that the risk of prediabetes was significantly increased at BMI values as low as 21

kg/m<sup>2</sup> and has not been increased as BMI increased. Applying this criterion to identify the cut-off values resulted in improvements in sensitivity, false negative rate and worsening in specificity and false positive rate. Using these lower BMI cut-offs resulted in a very small false negative rate ranging from 0.07 to 0.09.

Parameters	Area under curve (95% CI)	Cut-offs BMI kg/m <sup>2</sup>	Sensitivity	Specificity	False positive rate	False negative rate	Positive likelihood ratio	Negative likelihood ratio	Misclassification rate
<b>Total</b>	0.535 (0.511-0.560)	21.0	0.917	0.09	0.91	0.083	1.01	0.92	0.99
<b>Male</b>	0.560 (0.503-0.617)	21.0	0.908	0.102	0.898	0.092	1.03	0.92	0.99
<b>Female</b>	0.517 (0.490-0.544)	21.0	0.966	0.062	0.928	0.072	1.04	0.86	1.00

Table 3: Diagnostic performance of BMI in detecting prediabetes using optimal BMI cut-off values based on the significant association using logistic regression in Saudi adults.

Table 4 shows the odds ratios of the association between prediabetes and BMI in male and female. A significant positive association for total population was

observed with BMI values starting at 21 kg/m<sup>2</sup> and non significant association with BMI values for both genders.

BMI (kg/m <sup>2</sup> )	Total		Male		Female	
	Odd ratio (95% CI)	P	Odd ratio (95% CI)	P	Odd ratio (95% CI)	P
<15.0	0.6 (0.2-2.3)	0.5	-	-	0.6 (0.2-2.4)	0.5
15.0-15.9	-	-	-	-	-	-
16.0-16.9	2.0 (0.6-6.8)	0.3	-	-	1.7 (0.5-5.7)	0.4
17.0-17.9	1.9 (0.7-5.6)	0.2	1.2 (0.1-12.1)	0.9	1.8 (0.5-6.1)	0.4
18.0-18.9	1.3 (0.6-2.9)	0.5	1.4 (0.1-14.6)	0.8	1.1 (0.5-2.6)	0.8
19.0-19.9	1.3 (0.6-2.5)	0.5	2.5 (0.3-25.0)	0.4	0.8 (0.4-1.8)	0.7
20.0-20.9	1.2 (0.6-2.1)	0.6	-	-	0.9 (0.5-1.7)	0.9
21.0-21.9	2.9 (1.4-6.0)	0.005	-	-	1.8 (0.9-3.9)	0.1
22.0-22.9	1.9 (1.0-3.5)	0.05	2.4 (0.4-14.9)	0.3	1.3 (0.7-2.6)	0.4
23.0-23.9	1.2 (0.7-1.9)	0.6	1.7 (0.3-8.9)	0.5	0.9 (0.5-1.5)	0.7
24.0-24.9	1.3 (0.8-2.0)	0.3	1.3 (0.3-5.6)	0.7	1.0 (0.6-1.7)	1.0
25.0-25.9	1.8 (1.1-3.1)	0.03	1.4 (0.3-6.2)	0.6	1.5 (0.8-2.7)	0.2
26.0-26.9	1.4 (0.9-2.2)	0.2	1.7 (0.4-7.1)	0.5	0.8 (0.5-1.4)	0.5
27.0-27.9	1.5 (0.9-2.4)	0.09	0.8 (0.2-2.9)	0.7	1.3 (0.8-2.3)	0.3
28.0-28.9	1.4 (0.9-2.3)	0.1	1.1 (0.3-4.3)	0.9	1.1 (0.7-1.9)	0.7
29.0-29.9	1.5 (1.0-2.5)	0.07	3.3 (0.6-16.6)	0.2	1.0 (0.6-1.7)	0.9
30.0-30.9	1.1 (0.7-1.8)	0.6	1.7 (0.4-7.2)	0.5	0.7 (0.5-1.2)	0.2
31.0-31.9	1.6 (1.0-2.6)	0.06	1.5 (0.4-6.6)	0.6	1.3 (0.7-2.1)	0.4
32.0-32.9	0.8 (0.5-1.2)	0.3	0.7 (0.2-2.9)	0.7	0.6 (0.4-1.0)	0.05
33.0-33.9	1.4 (0.9-2.4)	0.2	1.1 (0.3-4.6)	0.9	1.2 (0.7-2.0)	0.6
34.0-34.9	1.2 (0.7-1.9)	0.5	0.9 (0.2-4.0)	0.9	1.1 (0.6-1.8)	0.8
35.0-35.9	1.3 (0.9-1.8)	0.2	1.0 (0.2-5.1)	0.9	1.1 (0.6-1.9)	0.8
36.0-36.9	1.2 (0.7-2.1)	0.6	1.0 (0.2-5.2)	1.0	1.0 (0.6-2.0)	0.9
37.0-37.9	1.6 (0.8-3.3)	0.2	1.0 (0.2-6.3)	0.3	1.5 (0.7-3.4)	0.3
38.0-38.9	1.2 (0.6-2.4)	0.5	2.1 (0.2-20.7)	1.0	1.0 (0.5-2.0)	0.6
39.0-39.9	1.1 (0.6-2.1)	0.8	-	0.9	0.9 (0.5-1.8)	0.9

Table 4: Risk of prediabetes associated with increasing BMI in Saudi adults based on regression analysis.

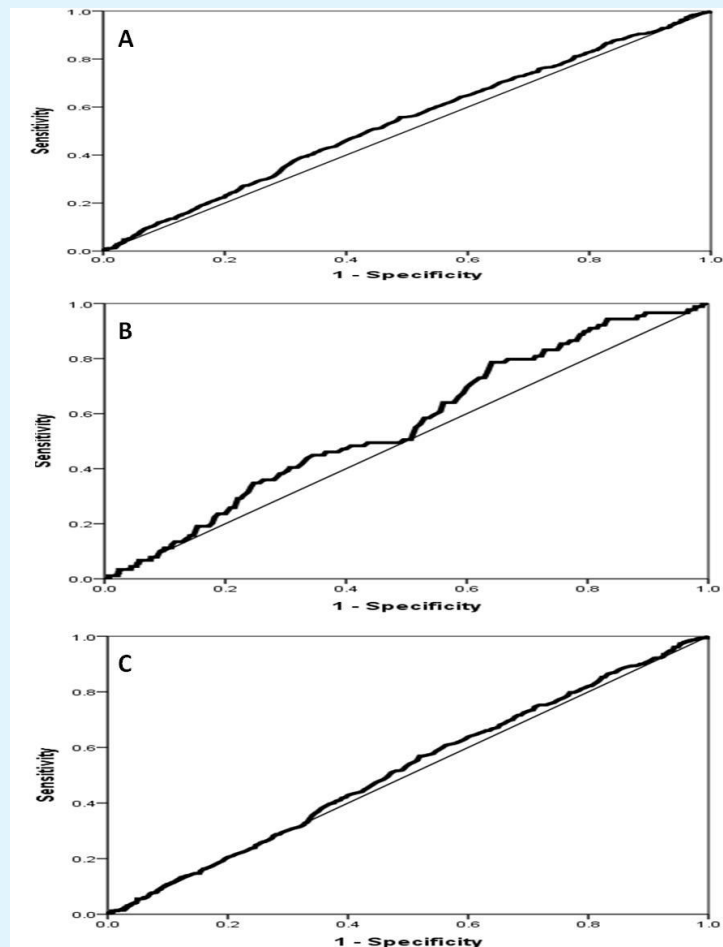


Figure 1: ROC curve showing the performance of BMI in predicting prediabetes (A: prediabetes in total population, B: prediabetes in male, C: prediabetes in female).

## Discussion

In this hospital-based cohort of Saudi adults, we showed that individuals with a BMI of  $\leq 21$  kg/m<sup>2</sup> have been significantly associated with an increased frequency of prediabetes. Report of the Mex Diab study, among the 550 subjects with prediabetes, 16.7% were within normal weight; of these, 51 (9.3%) had impaired glucose tolerance [30]. Around 5–10% of people with prediabetes become diabetic annually although conversion rate varies by population characteristics and the definition of prediabetes [31].

The prevalence of obesity in the world is growing [32]. Obesity is a major concern as it is strongly related to

multiple metabolic disorders [33]. General obesity measured by BMI is a known risk factor for prediabetes and diabetes [33]. The use of a reliable tool with optimal cut-off points for obesity diagnosis is very important to establish consequent public health policies, treatment protocols and to determine the correct optimal cut-off points of BMI for each population. As a known risk factor of diabetes, high BMI ( $> 30$  kg/m<sup>2</sup>) is associated with 3–10 times greater risk of developing diabetes compared to low BMI ( $< 25$  kg/m<sup>2</sup>) [34–41]. The mean BMI of males in this study was significantly lower than that of females which is consistent with findings in other studies [34]. This observation is similar to the findings among report in Saudi Arabia and could be explained by the fact that men are mostly taller than women, especially when the BMI



calculation is mainly dependent on the net body weight and height, regardless of the distribution of muscle and bone mass [35]. We showed the optimal cutoff values for BMI were 28 kg/m<sup>2</sup> for men and 29.5 kg/m<sup>2</sup> for women for identifying the risk of prediabetes which was higher than previously reported [35]. Although BMI has advantages in clinical and epidemiological practice, as a non-invasive and low-cost method, its predictive value for chronic diseases has been questioned, especially when applied to certain population groups [15-17]. Although BMI is often advocated as a simple measure to determine disease risk, it has several limitations. First, lean mass and fat mass could not be differentiated for a given BMI across age, sex and race [42]. Second, fat distribution could not be distinguished by BMI, whilst it has been generally accepted that visceral adiposity plays more important role in developing insulin resistance and diabetes rather than overall adiposity [43-47].

The risk of prediabetes associated with each BMI level was estimated, adjusting for other covariates. To assess the impact of the other covariates, we estimated an unadjusted logistic regression model (with BMI level as the only covariate). The Odd Ratios (OR), which approximate the relative risks in the nested case-control analysis, are listed in Table 4. BMI cut-off of  $\leq 21.0$  kg/m<sup>2</sup> was associated with the highest unadjusted and adjusted prevalence ratio. The unadjusted ORs were slightly higher than the adjusted ORs. This implies that some factors, such as age and gender, are associated with both increased BMI and increased risk of prediabetes, but the impact of these factors on the association between BMI and risk of prediabetes is limited. Moreover, BMI values were clinically measured in the current study, compared with BMI calculated from self reported height and weight in those earlier studies.

Pre-specified anthropometric cut-points serve to standardize comparisons of obesity within and between populations [32]. However, the currently used cut-points are derived from studies among subjects of European ancestry, and may not be applicable to other ethnic groups such as Asians, including Saudis [48]. A recent consultation by a World health organization expert group reviewed the scientific evidence for appropriate cut points for BMI in Asians and suggested that Asians have different associations between BMI, percentage of body fat, health risk of T2DM compared to European populations [48]. In this study, ROC curve analysis and associated sensitivity and specificity showed that, among Saudi men and women respectively, BMI values of 28.0 to 29.5 kg/m<sup>2</sup>, best characterize individuals' optimal cut-

points. Alternatively, the differences in cut-points may reflect real underlying differences in body fat percentages corresponding to a given BMI value between Saudis and Asians or Europe ethnic groups. Thus, the proposed cut-points need to be validated in other Arab populations of the Middle East.

The overall performance of the ROC curve can be quantified by estimating the AUC which ranged from 0.503 to 0.617, Table 3. An area of 1.0 is perfect and an area  $<0.5$  is considered non-informative. Our results indicated that the ROC analysis was close to a non-informative test as shown in the Figure 1. ROC curve analysis showed that the corresponding sensitivities and specificities were poor ( $<0.53$  and  $<0.54$ , respectively). This indicates that the percentage of people identified as having the risk factors and the percentage of people who were identified as not being at risk were less than 53% of total population. Both positive likelihood ratio and negative likelihood ratio were close to 1.0, indicating a minimal increase in the likelihood of the presence of the risk factor if the test is positive and a minimal decrease in the likelihood if the test is negative. The false positive and false negative rates were high and close to each other in both women and men. Several reasons may explain the weakness of BMI as a tool to classify obesity in the Saudi Arabian population. First, BMI does not reflect fatness uniformly in all populations and different ethnic groups [49]. This may suggest the importance of including a measure of abdominal obesity in classifying obesity in Saudi populations. Second, the short stature of Saudi women could be limiting the usefulness of BMI in this population [50].

The overall misclassification was high and exceeded 90% of the total population across all the selected BMI cut-off points. Most of the other previous studies that have been conducted in non-Caucasian populations did not assess the misclassification rate [51-58]. However, one study conducted in Asian Indians indicated a high overall misclassification rate, particularly in women [49]. Those authors concluded that the BMI did not accurately predict overweight in that population. This is not the first study to suggest the presence of a significantly increased risk of prediabetes at BMI values less than 25. However, the use of such low cut-offs would lead to large misclassification of healthy people as being at risk, as indicted by the high values of sensitivities and false positive rates. This fact that could cause unnecessary and costly diagnostic testing. Overall the total misclassification rate was unacceptably high, even with the use of different BMI cut off points. These findings

illustrate the significant limitations in using BMI alone for obesity diagnosis in the Saudi Arabian population.

Our results should be interpreted in light of the study's limitations. First, and foremost, the use of a retrospective cohort design prevented us from understanding the causal effect of BMI on the risk of developing prediabetes. Selection bias due to the healthy volunteer effect may have affected this study. Another limitation of the present study was having considered only overall obesity (assessed by BMI) and not abdominal obesity (measured by waist circumference), which is known to bear a close relationship with the target diseases. Prospective studies should be done to identify the causes of the incidence of these diseases and explain the role of genetic, nutritional, and/or metabolic factors in the appearance of these diseases in Saudis. Our sample was drawn from a hospital based patients, therefore this study may not be comparable to other population studies and cannot strictly be generalized to the whole older Saudi population. Finally, generalization of these findings is limited, because the data are predominantly from those of Jeddah ancestry. Considering the goal population, a larger cohort would have probably provided a greater power of the statistical analyses.

## Conclusion

The diagnostic usefulness of BMI alone in defining obesity as risk for prediabetes is limited among men and women Saudi adults.

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