

# Normal body mass index (BMI) can rule out metabolic syndrome

## An Israeli cohort study

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### Abstract

The aim of the study was to assess whether body mass index (BMI) can be used as a simple and reliable survey test for metabolic syndrome.

The study is an observational cohort study among patients who visited the Rambam Periodic Examinations Institute (RPEI). We analyzed the correlation between obesity indices and presence of metabolic syndrome. We identified the ideal value of BMI for identification of patients at risk for metabolic syndrome. We also described the correlation between different BMI values and its negative predictive value (NPV) for metabolic syndrome.

During the study years, 23,993 patients visited the RPEI, and 12.5% of them fulfilled the criteria for metabolic syndrome. Women with metabolic syndrome had higher proportion of obesity, when compared with men (89.9% vs 52.6%;  $P < .0001$ ). Normal BMI had very high NPV to rule out metabolic syndrome among men and women (98% and 96%, respectively). Using receiver-operating characteristic curve, we found BMI 27 to be the ideal value for identification of metabolic syndrome for the entire cohort (area under the curve [AUC] 0.767, 95% confidence interval [CI] 0.758–0.775,  $P < .0001$ ), for men (AUC 0.726, 95% CI 0.715–0.738,  $P < .0001$ ), and for women (AUC 0.843, 95% CI 0.831–0.855,  $P < .0001$ ). BMI below 30 provided NPV of 91.1% to rule out metabolic syndrome.

The BMI as single survey measurement of obesity offers high NPV for metabolic syndrome and can be used by physician and patients for this purpose.

**Abbreviations:** AUC = area under the curve, BAI = body adiposity index, BMI = body mass index, HDL = high-density lipoprotein, NPV = negative predictive value, PPV = positive predictive value, RHCC = Rambam Health Care Campus, ROC curve = receiver-operating characteristic curve, RPEI = Rambam Periodic Examinations Institute, WC = waist circumference, WHR = waist-to-hip ratio, WHtR = waist-to-height ratio.

**Keywords:** abdominal obesity, BMI, metabolic syndrome, waist circumference

### What Is Already Known On This Subject

- metabolic syndrome carries substantial cardiovascular risk.
- BMI is a simple to use measurement, however it is unknown whether it can be used to rule out metabolic syndrome

### What This Study Adds

- among anthropometric indices, BMI offers the highest negative predictive value to rule out metabolic syndrome.
- Even BMI of 30 offers NPPV over 90%.

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## 1. Introduction

Obesity is a recognized risk factor for various cardiometabolic diseases, and several indices are used clinically to assess overall cardiometabolic risk.<sup>[1]</sup> The metabolic syndrome, which is associated with increased cardiovascular risk, was defined by the Adult Treatment Panel III (ATP III) as at least 3 of the 5 conditions—central obesity (as defined by men waist circumference >40 inch or women waist circumference >35 inch), raised triglycerides (above 150 mg/dL or on treatment), reduced high-density lipoprotein (HDL) (below 40 mg/dL for men or 50 mg/dL for women), raised blood pressure (above 130/85 mm Hg or on treatment), and abnormal fasting plasma glucose (above 110 mg/dL or on treatment).<sup>[2]</sup>

The prevalence of metabolic syndrome varies in different regions of the world. Most studies found that over one-third of the adults suffer from metabolic syndrome, and its prevalence is increasing with the years. It is estimated that around 50% of those aged over 60 in the United States have metabolic syndrome. Metabolic syndrome is somewhat more common among Hispanic than whites and black, and more common among

women than men.<sup>[3–8]</sup> Previous studies found lower prevalence of metabolic syndrome in Israel (9.7%–15.7% of adults and 25% of those over 60).<sup>[9,10]</sup> Metabolic syndrome is an independent risk factor for coronary heart disease, peripheral artery disease, stroke, and total mortality among various populations.<sup>[8,11–13]</sup>

The definition of increased waist circumference (WC), as part of metabolic syndrome diagnosis, requires the use of sex and ethnic specific values, and is less intuitive, hence not used in common practice. Furthermore, there is still no uniformly accepted protocol regarding the anatomic site of WC measurement,<sup>[14,15]</sup> resulting in increased variability and bias of the measurement, and this makes its use more complicated. WC has further disadvantages, which make its use more challenging for both patients and physician. First, WC measurement requires that patients fast before the examination, to have an empty bladder and to be minimally dressed. Unlike body mass index (BMI), it cannot be measured by the person itself. Additionally, WC tends to feel more intimate and even invasive in some cultures.<sup>[16]</sup>

The best adiposity measure to help predict cardiovascular risk factors has remained controversial. BMI is traditionally the most widely used measure of obesity; it is also used by some as part of the criteria for metabolic syndrome.<sup>[17,18]</sup> It is simple to use both by clinicians and patients; however, the BMI is unable to differentiate between lean mass and fat mass, nor does it consider body fat distribution. The cut-off value of BMI above which metabolic syndrome should be suspected is yet to be determined. Other measures of adiposity, which consider body fat distribution, like WC, waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) have been developed. Recently, neck and wrist circumference were also shown to correlate central obesity but are not commonly used.<sup>[19,20]</sup>

The measure WHtR seems to be a good predictor of cardiometabolic risk, mainly in the Asian population.<sup>[21]</sup> In Western populations, however, WC tends to serve as a better predictor of cardiovascular risk.<sup>[22]</sup> Recently, body adiposity index (BAI), which is calculated using hip circumference and height, was proposed,<sup>[23]</sup> but was not consistently proved as a better predictor.<sup>[24]</sup>

The Israeli population has diverse ethnical origins which makes the use of the WC even more challenging. In our study, we aimed to assess the prevalence and the characteristics of metabolic syndrome among adults in Israel; to assess whether BMI can serve as a survey test to rule out metabolic syndrome in the Israeli population; and to estimate the appropriate BMI threshold above which metabolic syndrome should be suspected.

## 2. Methods

The study is a retrospective, observational, cohort-based study, performed at the Rambam Health Care Campus (RHCC) Periodic Examinations Institute, between the years 2008 and 2016. RHCC is a primary and tertiary care university-affiliated hospital in northern Israel and operates an outpatients' Periodic Examinations institute. The study was approved by the hospital's ethics committee, with a waiver of consent.

The Rambam Periodic Examinations Institute (RPEI) is an independent institute which operates within RHCC. It provides service of comprehensive medical examination for patients, including physical examination, blood tests, exercise test (when indicated), and so on.

We included any adult patient who underwent medical testing at the RPEI. Patients are instructed to fast before their visit to the Periodic Examinations Institute; hence, all blood tests done

during the visit are fasting blood tests. Patients were identified using RHCC's electronic patient data file. RHCC operates a full electronic patient register that includes clinical, laboratory, and radiological data. It also has access to medical summary reports and diagnoses from other healthcare providers.

Each patient file was scanned to determine if they fulfil the American Heart Association criteria for metabolic syndrome. The exposure variables, anthropometric indices, were extracted from the medical record.

Waist circumferences (abnormal above 40 inch for men or 35 for women), and also BMI (abnormal above 25), WHR (abnormal above 0.85 for women, 0.9 for men), WHtR (abnormal above 0.5 for women, 0.53 for men), and BAI (abnormal above 0.23 for men, 0.35 for women) were based on measurements done during medical examination at RPEI.

Hypertriglyceridemia (above 150 mg/dL), reduced HDL (below 40 mg/dL for men or 50 mg/dL for women), and impaired fasting glucose (above 110 mg/dL) were assessed by the blood test results during the visit, or the presence of appropriate diagnosis or treatment in the patient history.

Hypertension was assessed by the blood pressure measurement, above 130/85 mm Hg during the examination at RPEI, a confirmed diagnosis of hypertension, or chronic use of antihypertensive medications.

All the above mentioned cut-off values are in accordance with the metabolic syndrome definition of the ATP III.<sup>[2]</sup>

To examine the hypothesis that BMI can serve as an independent marker for cardiovascular risk, we also used a "modified" metabolic syndrome, which was defined as the presence of at least 3 of the 4 nonobesity criteria (hypertension, impaired fasting glucose, low HDL, and hypertriglyceridemia).

### 2.1. Statistical analysis

Descriptive statistics in terms of mean, SD, and ranges were presented to the whole parameters in the study. Categorical variables were compared using the Fisher exact test, and continuous variables were compared using the *t* test.

Diagnostic parameters (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) were calculated related to occurrence of metabolic syndrome.

A receiver-operating characteristic (ROC) curve with area under the curve (AUC) and 95% confidence interval (CI) was demonstrated to describe the relationship between the sensitivity and the false positive rate for different value of BMI in identification of patients at risk for MS. Youden index was used for describing the best cut-off for identification.

$P < .05$  was considered as significant. SPSS version 25 was used for the statistical analysis.

## 3. Results

During the study period, of 23,993 patients who underwent medical examination at the RPEI, 2996 (12.5%) fulfilled the criteria for metabolic syndrome. The prevalence of metabolic syndrome was similar among men and women. As expected, patients with metabolic syndrome were older, more obese, and had more comorbidities (see Table 1). When stratified by aged, the prevalence of metabolic syndrome among men and women aged over 60 was significantly higher than under 60 (men 19.3% vs 10.2%;  $P < .0001$ ; women 22.1% vs 10.1%;  $P < .0001$ ).

Most of the patients (72%) who fulfilled the criteria for metabolic syndrome had 3 of the 5 criteria. Majority of the

**Table 1****Demographics and past medical history of patients with and without metabolic syndrome, by sex.**

	Male, n=16713			Female, n=7101		
	No metabolic syndrome, n=14,605	With metabolic syndrome, n=2108	P	No metabolic syndrome, n=6213	With metabolic syndrome, n=888	P
Age, y	50.9±11.6	56.9±9.4	<.0001	50.2±10.4	56.1±8.68	<.0001
BMI, mean	26.9±3.8	30.0±3.9	<.0001	25.3±4.3	31.4±4.7	<.0001
DM, n (%)	675 (4.6%)	642 (30.5%)	<.0001	80 (1.3%)	172 (19.4%)	<.0001
Hypertension, n (%)	2524 (17.3%)	1310 (62.1%)	<.0001	433 (7.0%)	410 (46.2%)	<.0001
Dyslipidemia, n (%)	6026 (41.3%)	1375 (65.2%)	<.0001	1934 (31.3%)	554 (62.4%)	<.0001
Beta-blocker use	922 (6.3%)	639 (30.3%)	<.0001	207 (3.3%)	206 (23.2%)	<.0001
ACE/ARB use	1887 (12.9%)	1117 (53.0%)	<.0001	303 (4.9%)	328 (36.9%)	<.0001
Statin use	3299 (22.6%)	1036 (49.1%)	<.0001	835 (13.4%)	329 (37.0%)	<.0001

ACE/ARB=angiotensin-converting-enzyme/angiotensin II receptor blockers, BMI=body mass index, DM=diabetes mellitus.

women with metabolic syndrome (89.9%) fulfilled the obesity (waist) criteria, whereas only 52.6% of the men fulfilled it. Women with metabolic syndrome had higher proportion of obesity, when compared with men (Table 2), regardless of the anthropometric indices used, whereas men had higher prevalence of hypertension, diabetes, and dyslipidaemia.

We compared different anthropometric indices and its correlation with metabolic syndrome in men and women (Table 3). Normal BMI (lower than 25, the accepted threshold for overweight) had the highest NPV to rule out metabolic syndrome among men and women (96% and 98%, respectively), whereas WC had the higher PPV (29% in men, 35% in women). BMI over 25 was also found to have the highest specificity for metabolic syndrome among men (94%) with relatively high sensitivity (53%). Abnormal BAI was very specific among women for metabolic syndrome (97%), but had relatively low sensitivity (10%) and showed no advantage among men when compared with WC (sensitivity 36% for both, specificity 75% for BAI vs 85% for WC). WHtR and WHR had no specific advantage over other indices. When stratified by age, in those aged over 60, BMI was the only index to provide NPV higher than 90% for both men and women (92.1% and 96.9%, respectively). In the younger group, BMI still provided the highest NPV (98.7% for women, 97.2% for men). Compared with BMI, WC had higher PPV in all subgroups.

We also examined whether BMI or WC can serve as an independent marker for cardiovascular risk using a “modified” metabolic syndrome, which was defined as the presence of at least 3 of the 4 nonobesity criteria (hypertension, impaired fasting glucose, low HDL, and hypertriglyceridemia). WC had higher specificity and PPV for the presence of modified metabolic

syndrome among both men and women. BMI (using the cut-off value of 25), however, had higher sensitivity and very high NPV (Table 4).

Using ROC curves, we tried to describe the relationship between the sensitivity and the false positive rate for different values of BMI in identification of patients at risk for metabolic syndrome. Using Youden index, BMI of 27 was found to be the ideal value for identification of metabolic syndrome for the entire cohort with AUC of 0.767 (95% CI 0.758–0.775,  $P < .0001$ ), the sensitivity and specificity of BMI 27 are 79.5% and 59.8%, respectively. When we performed the same analysis by sex, 27 was consistent as the ideal BMI value both for men (AUC 0.726, 95% CI 0.715–0.738,  $P < .0001$ , sensitivity 77.2%, specificity 55%) and for women (AUC 0.843, 95% CI 0.831–0.855,  $P < .0001$ , sensitivity 84.7%, specificity 70.1%) (Fig. 1).

We also described the relationship between BMI value and its NPVs. As expected, an inverse ratio was noted with higher NPVs for women than for men. BMI below 30, which defines obesity (rather than overweight), provide NPV of 91.1% for the entire cohort, 93% for women and 90.2% for men.

#### 4. Discussion

The question of which obesity marker should be used by the primary physician is still open. WC, as part of the diagnostic criteria for metabolic syndrome, has a solid body of evidence for the usefulness of its use.<sup>[2]</sup> On the contrary, it has multiple disadvantages that make its use less intuitive and practical. Not surprisingly, as WC is part of the diagnostic criteria for metabolic syndrome, it had the highest PPV for metabolic syndrome among all anthropometric indices we examined. We aimed to examine the role of BMI as a survey measurement to rule out the presence of metabolic syndrome. Our findings suggest that normal BMI have high NPV to rule out metabolic syndrome both in men and women in all age groups. However, compared with WC, BMI has a relatively low PPV (slightly higher among women than men). We concluded that BMI can serve as a good survey for the primary physician. A patient without known metabolic disturbances and normal BMI may not need to undergo WC measurement or other survey tests. When we examined different BMI values and its relationship with NPV for men and women, we found that even BMI of 30 can provide NPV over 90%. Using ROC curves, we tried to find the ideal BMI to identify metabolic syndrome, which was found to be 27 for the entire cohort, for men and for women.

We also examined the correlation of abnormal BMI (with the traditionally accepted value of 25) and WC to a “modified

**Table 2****Characteristics of patients with metabolic syndrome, by sex.**

	Female, n=888	Male, n=2108	P
Abnormal Waist circumference	772/859 (89.9%)	1036/1968 (52.6%)	<.0001
Hypertension	387 (43.6%)	1246 (59.1%)	<.0001
Hypertriglyceridemia	520/868 (59.9%)	1611/2096 (76.9%)	<.0001
Low-HDL	709 (79.8%)	1883 (89.3%)	<.0001
DM/impaired fasting glucose	685 (77.1%)	1948 (92.4%)	<.0001
Abnormal BAI	1086 (51.5%)	306 (34.5%)	<.0001
Abnormal WHR	431 (48.5%)	708 (33.6%)	<.0001
Abnormal WHtR	843 (94.9%)	1724 (81.8%)	<.0001
Mean BMI	31.4±4.7	30.0±3.9	<.0001
BMI >25	839 (94.4%)	1954 (92.5)	.048

BAI=body adiposity index, BMI=body mass index, DM=diabetes mellitus, HDL=high-density lipoprotein, WHR=waist-to-hip ratio, WHtR=waist-to-height ratio.

**Table 3**

**Different anthropometric indices and its correlation with metabolic syndrome, stratified by age.**

	Entire Cohort				Under 60				Over 60			
	NPV	PPV	Sensitivity	Specificity	NPV	PPV	Sensitivity	Specificity	NPV	PPV	Sensitivity	Specificity
Waist, men	89.2%	29.2%	36.6%	85.5%	91.1%	26.9%	34.7%	87.7%	82.9%	33.3%	39.7%	78.7%
Waist, women	88.6%	35.1%	27.3%	91.8%	90.9%	31.4%	29.3%	91.7%	81.9%	44.9%	24.3%	92.0%
BMI, women	98.4%	23.9%	94.5%	53.2%	98.7%	20.5%	94.0%	55.3%	96.9%	34.3%	95.5%	43.7%
BMI, men	96.1%	18.2%	92.4%	31.3%	97.2%	15.8%	92.6%	34.1%	92.1%	23.4%	92.1%	23.4%
BAI, women	88.3%	34.3%	10.2%	97.2%	90.5%	28.5%	9.5%	97.3%	81.4%	46.2%	11.4%	96.7%
BAI, men	89.1%	17.4%	36.2%	75.2%	91.3%	14.9%	33.7%	78.2%	81.3%	22.3%	40.2%	65.1%
WHR, women	88.3%	22.2%	14.4%	92.7%	90.7%	19.3%	16.1%	92.4%	81.0%	32.9%	11.7%	94.0%
WHR, men	89.2%	27.1%	23.6%	90.9%	91.1%	24.8%	19.7%	93.3%	82.5%	30.0%	29.7%	82.7%
WHtR, men	91.7%	20.3%	57.5%	67.5%	93.4%	18.4%	54.7%	72.7%	84.0%	23.6%	61.9%	50.0%
WHtR, women	89.0%	20.2%	28.1%	84.0%	91.4%	17.3%	29.9%	83.9%	81.9%	28.9%	25.4%	84.4%

BMI = body mass index, NPV = negative predictive value, PPV = positive predictive value, WHR = waist-to-hip ratio, WHtR = waist-to-height ratio.

**Table 4**

**BMI and WC correlation to “modified” metabolic syndrome.**

	NPV, %	PPV, %	Specificity, %	Sensitivity, %
BMI, men	96	17	31	92
BMI, women	99	11	50	90
WC, men	92	27	85	42
WC, women	89	14	89	13

BMI = body mass index, NPV = negative predictive value, PPV = positive predictive value, WC = waist circumference.

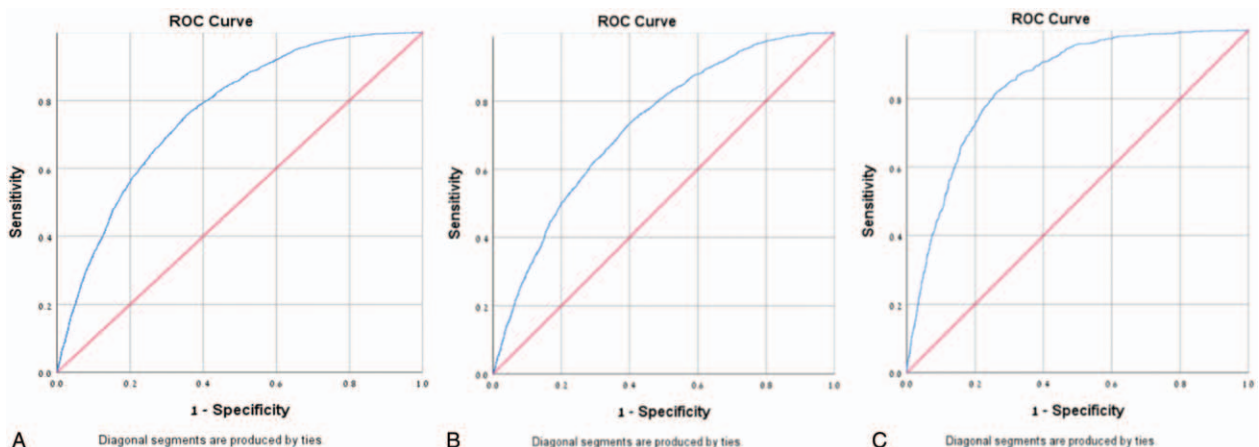
metabolic syndrome,” as a marker of high cardiovascular risk. Again, WC offered higher PPV and specificity in both men and women. BMI, however, offered higher NPV to rule out any 3 nonobesity criteria for metabolic syndrome.

Over the course of 8 years, we identified 2996 patients with metabolic syndrome, which represents 12.5% of the population screened. The prevalence of metabolic syndrome in our cohort lower than most of the previous studies in the western world.<sup>[3–8]</sup> However, a study in Taiwan found a national prevalence of metabolic syndrome among adults as low as 16%,<sup>[25]</sup> and previous studies found prevalence of metabolic syndrome in Israel between 10% and 15%.<sup>[9,10]</sup> We may interpret, according to our results and previous published data, that the prevalence of metabolic syndrome in Israel is relatively low. However, our trial may not reflect the true prevalence of metabolic syndrome in Israel. This study results may be influenced by selection bias, as

attendants of the periodic examination institute are probably more aware of their health. Furthermore, the mean age of the patients in our cohort was 51.4 years, and the relationship between age and prevalence of metabolic syndrome is well established and was proven in other results too.<sup>[4,10]</sup> Therefore, the overall prevalence of metabolic syndrome in Israel cannot be concluded according to our results.

In our cohort, we found similarity in the prevalence of metabolic syndrome in men and women, and similar mean age of men and women with metabolic syndrome (men 50.9 years, women 50.2years). Over the age of 60, the prevalence of metabolic syndrome was higher regardless of sex (men 19.3% vs 10.2%;  $P < .0001$ ; women 22.1% vs 10.1%;  $P < .0001$ ). However, women and men had different characteristics of metabolic syndrome. Among women with metabolic syndrome abdominal obesity, as represented by abnormal WC, was more common than among men (89.9% vs 52.6%;  $P < .01$ ). Other obesity markers as BMI, BAI, waist-to-hip circumference, and WHtR, were all significantly more common among women with metabolic syndrome than men. Among men, diabetes mellitus was the most common factor of metabolic syndrome (92.4% vs. 77.1% of women;  $P < .001$ ). Low HDL was the second most common factor among men and women (79.8% among women, 89.3% among men;  $P < .01$ ).

Only 43% of the women with metabolic syndrome suffered from hypertension (vs 59.1% in men;  $P < .01$ ). Differences in the characteristics of metabolic syndrome among men and women



**Figure 1.** Receiver-operating characteristic (ROC) curves for BMI 27 of the entire cohort (A), men (B), and women (C). BMI = body mass index.



were previously described in other populations as well.<sup>[26]</sup> The lower prevalence of other metabolic disturbances among women may suggest that due to differences in fat distribution in women, they may need higher degree of obesity for the same level of metabolic disturbances.

Our study, however, has some limitations; first, it was done on a specific group—Israeli adults who visited the RPEI during study years. On the contrary, the large number of patients allowed us to achieve statistical significance for our findings. Another limitation is the relatively low prevalence of metabolic syndrome in our cohort. The question whether it reflects a truly low prevalence of metabolic syndrome in Israel or it is secondary to our cohort characteristics discussed above, and yet to be determined. We have considered different endpoints to our study; the character of our study did not enable us to use mortality as the endpoint. As metabolic syndrome is an independent risk factor for coronary heart disease, peripheral artery disease, stroke, and total mortality,<sup>[8,11–13]</sup> we decided to use it as our target disease. Further, longer follow-up trial on our or other cohorts may reveal mortality differences and should be considered.

## 5. Conclusions

In conclusion, normal BMI provides a very high NPV to rule out metabolic syndrome in men and women both over and under age of 60. We believe that this study adds to the body of evidence regarding the usefulness of BMI, we suggest using the same cut-off value of 25 in men and women, over and under the age of 60. Using the same cut-off in both sexes and in all age groups makes BMI simple and easy to use and interpret. However, BMI in any level below 30 has a very high NPV to rule out metabolic syndrome. BMI of 27 was found to be ideal for identification of metabolic syndrome in men and women. Furthermore, normal BMI offered an excellent NPV to rule out any other 3 nonobesity cardiovascular risk factors. A survey measurement should not only provide high NPV, but also be easy to use, and intuitive and comfortable both for the patients and the physician. As BMI is such a measurement that can also be done by the patients himself, and offers a very high NPV, we believe that it can be the first single survey measurement to rule out metabolic syndrome in the Israeli population and perhaps in other populations.

## Author contributions

**Conceptualization:** Avizohar Ophir, Karban Amir.

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