Do Advanced Statistical Techniques Really Help in the Diagnosis of the Metabolic Syndrome in Patients Treated With Second-Generation Antipsychotics?

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ABSTRACT

Objective: Metabolic and cardiovascular diseases in patients with schizophrenia have gained a lot of interest in recent years. Developing an algorithm to detect the metabolic syndrome based on readily available variables would eliminate the need for blood sampling, which is considered expensive and inconvenient in this population.

Method: All patients fulfilled *DSM-IV* diagnosis of schizophrenia or schizoaffective disorder. We used the International Diabetes Federation criteria (European population) to diagnose the metabolic syndrome. We used logistic regression and optimized artificial neural networks and support vector machines to detect the metabolic syndrome in a cohort of schizophrenic patients of the University Psychiatric Center Kortenberg, KU Leuven, Belgium. Testing was done on one-third of the included cohort (202 patients); training was performed using a 10-fold stratified cross-validation scheme. The data were collected between 2000 and 2008.

Results: All 3 methods yielded similar results, with satisfying accuracies of about 80%. However, none of the advanced statistical methods could improve on the results obtained using a very simple and naive model including only central obesity and information on blood pressure.

Conclusions: Although so-called pattern recognition techniques bear high promise in improving clinical decision making, the results should be presented with caution and preferably in comparison with a less complicated technique.

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Recently, metabolic and cardiovascular diseases in patients with schizophrenia have become a major focus in both clinical care and research.[1–3] The cause of metabolic and cardiovascular comorbidity in these vulnerable patients, though not fully understood, is a complex interplay between environmental (lifestyle, diet, substance use), genetic, and illness-related factors, such as specific symptoms, as well as effects of treatment. Furthermore, accumulating evidence demonstrates that adverse effects of antipsychotic medications, especially second-generation antipsychotics (SGAs), also contribute to the metabolic syndrome (MetS), especially in vulnerable populations, such as first-episode and drug-naive patients as well as in children and adolescents.[4–6]

Although weight gain and metabolic disorders might occur in patients treated with any antipsychotic, individual agents differ markedly in their propensities for inducing these abnormalities and can be roughly classified into 3 groups.[7–10] The first group, causing the highest elevation in weight, cholesterol, and glucose, includes olanzapine and clozapine. The second group, including quetiapine, risperidone, sertindole, and iloperidone, has been shown to cause intermediate weight and metabolic elevations (although the levels in this group, with exception of quetiapine regarding cholesterol, were closer to the third group than to the first). The third group, which has proven to have the lowest elevations, includes aripiprazole, amisulpride, ziprasidone, paliperidone, asenapine, and asenapine and lurasidone, with lurasidone seeming to have the least metabolic risk.

The need for screening, monitoring, and prevention of cardiovascular disease risk factors has been acknowledged in the psychiatric literature.[11–14] The term *metabolic syndrome* was thus concerned in the clinical psychiatry. MetS brings together a constellation of predictive factors for cardiovascular disease, generally including central obesity, hypertension, dyslipidemia, and glucose intolerance or insulin resistance, though there is continuing debate around the use of the term.[15]

The most common definitions for the MetS are the working criteria of the International Diabetes Federation (IDF) Task Force,[16] the Adult Treatment Panel III of the National Cholesterol Education Program,[17] and the adapted Adult Treatment Panel proposed by the American Heart Association.[18] Considering the IDF definition of the MetS, a patient should be considered centrally obese (waist > 94 cm for men or > 80 cm for women) and fulfill any 2 of the following criteria: an elevated blood pressure (systolic blood pressure> 130 mm Hg or diastolic blood pressure > 85 mm Hg), a decreased high-density lipoprotein cholesterol level (men < 40 mg/dL, women < 50 mg/dL), an elevated triglycerides level (> 150 mg/dL), and a raised fasting plasma glucose (> 100 mg/dL).

According to Hanley et al,[19] who studied 822 adults aged between 40 and 69 years during 5 years, the IDF definition of the MetS is associated with an odds ratio of 3.4 considering the development of diabetes.

Clinical Points

- The accuracy in detecting the metabolic syndrome using criteria by the International Diabetes Federation in a schizophrenic patient population highly depends on the number of patients without central obesity, as these patients were easily classified by all classifiers used in this study.
- The accuracy obtained by a very simple model that included only blood pressure outperformed more advanced classification schemes in the subset of patients without central obesity.
- The accuracy of this simple model also depends highly on the number of patients with prediabetes and diabetes. If diabetic status is known, blood sampling can be omitted in the prediabetic and diabetic group but not in the nondiabetic group.

Studies in patients with schizophrenia using even different MetS criteria consistently show the prevalence of MetS is 2- to 3-fold higher compared to that in the general population, as confirmed by several studies and meta-analyses.[20–24]

However, in clinical practice, metabolic monitoring is considered a low priority in people prescribed antipsychotic medication, and although guidelines can increase monitoring, most patients still do not receive adequate testing.[25,26] One reason for this might be that patients are lacking knowledge about the additive burden of cardiometabolic complications. A further possible explanation for poor monitoring practices, at least in part, is that laboratory tests are time consuming and invasive and the patients may reject blood drawing and laboratory tests. Convenient, noninvasive, and acceptable assessment tools that do not require laboratory work would be useful in first-step screening of MetS.

Anthropometric indices (waist circumference, body mass index, and waist-hip ratio), whether single or combined, were evidenced as simple and effective predictors of the MetS in many studies in the general population,[27–29] especially in children and adolescents[30,31] and in children treated with SGAs.[32] Lin et al[33] developed an artificial neural network model and a logistic model by inputting only demographic and anthropometric data as well as antipsychotic medication data without any biochemical parameter. Both quantitative assessment tools were reported to yield relatively satisfactory results on an external dataset (accuracy: 81.2% and 79.7%; sensitivity: 85.2% and 96.3%; specificity: 78.6% and 69.1%).[33]

In this study, we aimed to replicate the methods applied by Lin et al[33] in a fairly large and independent European patient population and to test whether these kinds of models are really useful in clinical practice. Finally, we compared these models to a very simple decision tree based on only 2 variables (central obesity and elevated blood pressure) that are included in the definition of the MetS but do not involve blood sampling. This latter tree was constructed using simple logic and does not require complicated statistical procedures. These algorithms allow us to assess the quality with which a prediction on the IDF status can be made based on solely readily available clinical variables.

METHOD

Patients and Procedure

The data were collected between 2000 and 2008 at the University Psychiatric Center Kortenberg, KU Leuven, Belgium. All patients fulfilled the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, diagnosis of schizophrenia or schizoaffective disorder. The severity of symptoms was assessed by the treating psychiatrists and was rated using the Global Assessment of Functioning (GAF) Scale, which has a score range from 0 (worst) to 100 (best). According to previously published guidelines,[34] a 75-g glucose load oral glucose tolerance test (OGTT) was performed (see, eg, Manu et al[35] for a more complete description).

The presence of the MetS was assessed using the criteria proposed by the IDF.[16] Body weight and height were assessed by a trained research nurse, with the patients wearing light clothing and weight measured to the nearest 100 g and height to the nearest 1 mm. Waist circumference was assessed when the patients were standing upright with their hands by their sides and measured to the nearest cm at the level of the umbilicus and at the end of the expiration. Patients attained by the MetS according to the IDF criteria are denoted as IDF+, whereas patients who did not fulfill the IDF criteria are denoted as IDF–.

Heart rate and diastolic and systolic blood pressure were collected when the patients were lying down for about 5 minutes. Other clinical variables were age, gender, body mass index (BMI), hip circumference, and waist-hip ratio. Smoking behavior was assessed as the number of cigarettes smoked per day, alcohol as the number of alcohol units per day.

The study procedure was approved by the Scientific and Ethical Committee of the University Psychiatric Center of the Catholic University of Leuven, Belgium, in accordance with the principles of the Declaration of Helsinki. All participants gave their informed consent.

Statistics and Validation

We divided our patient group into 2 parts, a training set and a test data set. The first set (403 patients) was used for calculating the regression equation and selecting the relevant variables, whereas the latter data set (202 patients) was used as an independent test set.

To simplify the optimization procedures, we provided the models with 2 extra Boolean variables. The first one denotes the status of central obesity as defined by the IDF criteria, the other on a patient's blood pressure status, ie, a variable that denotes that the patient either has an elevated blood pressure or receives medication to suppress his or her blood pressure. All clinical variables that were collected entered the models together with the 2 extra Boolean variables.

Logistic Regression

The training data are used both for calculating the regression coefficients and for optimizing the cutoff in the final model. Backward stepwise elimination was used based on the Akaike information criterion (AIC) as implemented in the step function of R.[36]

A logistic regression model is a model that takes a linear combination of the input features and applies the logistic function to the outcome of this linear combination. It can also be seen as an artificial neural network (see following section) with 1 hidden node. The general idea is that if the linear combination for a new test example returns a negative value, the example belongs to one class, and if it is greater than 0, the example belongs to the other class.

Artificial Neural Networks

Artificial neural networks are computational models inspired by the human brain. An artificial neural network typically consists of 3 layers of nodes, the input layer, the hidden layer, and the output layer. At every hidden node, a linear combination of the input variables is calculated and subjected to a transfer function (the logistic function was used for this article). Another linear combination of these hidden nodes finally returns the output, which can be used for classification. A training set has to be provided to optimize the weights of the different linear combinations involved. As a typical artificial neural network has an enormous amount of parameters, it can easily overfit the training data; therefore, a cross-validated procedure to optimize the weights and the parameters is necessary. For our calculations, we used the neuralnet toolbox for R.[37]

The parameters of the neural network that were optimized were learning method (backpropagation, resilient backpropagation), thresholds, the error function used (sum of squared errors, cross-entropy), and the number of hidden units (1, 2, 3, 4, 5, 10). The set of parameters that yielded the highest accuracy in the cross-validation data was used to calculate the performance on the independent test set (202 patients).

Support Vector Machines

We constructed support vector machines using the e1071 package for R.[38] We used radial basis functions and optimized the cost and γ parameter using a fixed grid search through 10-fold cross-validation.

A higher value for γ makes the support vector machines more prone to overfitting. A low value of γ makes the radial basis function–support vector machines behave like a linear support vector machine. The grid chosen for the optimization of γ was taken between E-5 and E-1 and, for the cost parameter, between E-1 and E-4, with a uniform logarithmic scaling. In total, 25 grid points were calculated.

Model Performance

We used 2 outcome measures to evaluate model performance: *accuracy*, defined as the percentage of correctly classified individuals, and maximal sensitivity at a predefined specificity level. The minimal specificity level was set to 70%. This second outcome parameter allowed us to optimize the detection properties of the constructed classifier.

RESULTS

Patient Population

We have summarized the most important clinical variables and the results of the blood sampling in Table 1.

Modeling

A very simple and naive model. A very simple tree can be easily constructed by taking into account readily available clinical data such as status of central obesity and whether a patient has high blood pressure. This model results in the tree structure as depicted in Figure 1.

We can construct 2 classifiers based on this tree. The first is one in which we denote all patients with central obesity as IDF+ (Table 2, naive model A). In a second classifier (model B), we used blood pressure information to denote only patients with central obesity and high blood pressure as IDF+. In model C, we applied model B to the subset of patients with central obesity. This model produced the results shown in Table 2.

Using this simple model, we obtained an accuracy of 83.9%, with acceptable sensitivity (78.8%) and specificity (86.8%) levels. Following this approach, it is also obvious that any result obtained in a general population of schizophrenic patients highly depends on the number of patients without central obesity, as these patients are—of course—perfectly classified in this model. However, as we will see, this patient group is easily classified by most classifiers (especially as central obesity is included as an input feature).

In the same table under naive model C, we report the results obtained when including only patients with central obesity. Although the accuracy dropped, the results were still acceptable.

Validation of the Lin et al Logistic Regression Model

Lin et al[33] report the following logistic regression model:

Logit(odds of MetS) = 0.193 * waist circumference (cm) + 0.109 * diastolic blood pressure (mm Hg) + 1.47 * female

The optimal cutoff Lin et al[33] found was 25.7, ie, when the outcome of the classifier is greater than this cutoff, a patient is classified as IDF+; if not, a patient will be classified as IDF–. This specific cutoff may seem large, but note that Lin et al[33] have omitted the constant in the model.

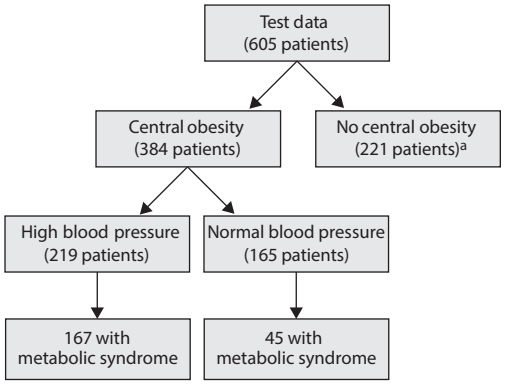
As a first attempt to validate their results in our patient population, we applied this model to our data with and without adjusting for the different definition of central obesity in a European population (for men, waist circumference > 0.94 m instead of 0.9, and for women, waist circumference > 0.8).

Table 1. Comparison of the General Characteristics and the Blood Sampling Data[a]

Characteristic	IDF– (n = 393)		IDF+ (n = 212)		Effect Size[b]	*P* Value[c]
Clinical data						
Gender, n						
Male	271		133			
Female	122		79			
	Mean	SD	Mean	SD		
Age, y	34.7	11.5	39.8	11.7	−0.44	< .001
BMI (kg/m^2)	24.6	3.90	29.8	5.02	−1.16	< .001
Length, m	1.74	0.10	1.74	0.10	0.03	NS
Weight, kg	74.6	12.9	90.0	16.2	−1.06	< .001
Waist-hip ratio	0.92	0.09	0.98	0.09	−0.64	< .001
Waist, cm	89.7	11.2	105.5	11.8	−1.36	< .001
Hip, cm	97.6	9.4	108.3	11.4	−1.02	< .001
Diastolic blood pressure, mm Hg	75.3	11.6	81.8	10.7	−0.58	< .001
Systolic blood pressure, mm Hg	120.9	14.8	129.8	14.7	−0.60	< .001
Heart rate, bpm	80.0	13.3	81.9	12.5	−0.14	NS
GAF	57.0	12.5	58.1	10.6	−0.10	NS
Alcohol, units/d	0.74	2.25	0.6	1.81	0.07	NS
Smoking, cigarettes/d	15.5	15.6	16.8	17.2	−0.08	NS
Glucose data						
Fasting plasma glucose, mg/dL	87.6	8.9	99.5	18.6	−0.87	< .001
Glucose in OGTT at 30 min, mg/dL	144.6	35.1	175.7	44.8	−0.78	< .001
Glucose in OGTT at 60 min, mg/dL	125.8	43.1	177.1	65.6	−0.94	< .001
Glucose in OGTT at 120 min, mg/dL	92.3	34.6	126.3	58.3	−0.73	< .001
Glycosylated hemoglobin, %	5.37	0.46	5.60	0.65	−0.44	< .001
Insulin data						
Insulin fasting, µU/mL	9.59	7.56	15.3	11.4	−0.60	< .001
Insulin in OGTT at 30 min, µU/mL	71.8	47.0	89.9	56.7	−0.35	< .001
Insulin in OGTT at 60 min, µU/mL	65.6	45.0	104.5	69.9	−0.68	< .001
Insulin in OGTT at 120 min, µU/mL	33.7	44.9	65.2	59.9	−0.60	< .001
Lipid data						
High-density lipoproteins, mg/dL	54.3	15.7	44.8	13.3	0.65	< .001
Low-density lipoproteins, mg/dL	113.3	37.0	123.9	37.9	−0.27	< .01
Cholesterol, mg/dL	191.8	42.4	210.4	48.9	−0.41	< .001
Triglycerides, mg/dL	123.0	70.8	204.9	89.9	−1.01	< .001

[a]Patients attained by the MetS according to the IDF criteria are denoted as IDF+, whereas patients who did not fulfill the IDF criteria are denoted as IDF–.
[b]The effect size reported was Cohen *d* and is defined as (mean [MetS = 0] – mean [MetS = 1])/(mean standard deviation).
[c]*P* values calculated through *t* test.
Abbreviations: BMI = body mass index, bpm = beats per minute, GAF = Global Assessment of Functioning, IDF = International Diabetes Federation, MetS = metabolic syndrome, NS = nonsignificant, OGTT = oral glucose tolerance test.

Figure 1. Illustration of the Naive Tree Model, Based on Central Obesity (waist > 94 cm for men or > 80 cm for women) and Blood Pressure Status (systolic blood pressure > 130 mm Hg or diastolic blood pressure > 85 mm Hg or medication against high blood pressure)



[a]Patients without central obesity cannot fulfill diabetes criteria of the International Diabetes Federation; therefore, there is no terminal node to this branch.

When optimizing the cutoff value of the logistic regression model, we obtained a similar accuracy (78.5%) as reported by Lin et al[33] (79.7%).

Applying Artificial Neural Networks, Logistic Regression, and Support Vector Machines

To reduce calculation time, we divided our patient group into 3. We trained a model on two-thirds of the data and tested it on the remaining part. The results obtained on this test set are shown in Table 3A. For every method in Table 3, 2 results are shown. Lines starting with an A denote the results when the method's cutoff of hyperparameters have been optimized for maximized accuracy in the validation set; lines starting with B denote the results when sensitivity was maximized, ie, the maximal possible sensitivity for a low but still acceptable specificity (arbitrarily set to 70%). The optimization of the cutoff and hyperparameters was performed using a 10-fold cross-validation scheme. All results are reported on the independent test set.

In Table 3B, we assessed the performance of the trained classifier omitting the group without central obesity. Although the classifiers in Table 3A and 3B were exactly the

Table 2. Comparison of the Naive and Lin et al Models

Model	N	True Negatives, n	True Positives, n	False Negatives, n	False Positives, n	Accuracy	Sensitivity	Specificity
Naive model[a]								
A	605	221	212	0	172	71.6	100	56.2
B	605	341	167	45	52	83.9	78.8	86.8
C	384	120	167	45	52	74.7	78.8	69.8
Lin model[b]								
A	69	…	…	…	…	79.7	96.3	78.6
B	605	205	191	202	7	65.5	96.7	48.6
C	605	228	196	16	165	70.1	92.5	58.0
D	605	275	178	34	118	78.5	66.0	85.2

[a]The naive model is built by including only the factors central obesity and high blood pressure as shown in Figure 1. Model A included all patients with central obesity who were classified as having the metabolic syndrome; all patients without central obesity were classified as not having the metabolic syndrome. In model B, patients with central obesity and high blood pressure were classified as having the metabolic syndrome. In model C, only patients with central obesity were included.

[b]The Lin model is the application of the model constructed by Lin et al[33] on our data set. Line A depicts the results Lin et al[33] obtained in an independent test set; line B depicts the results obtained on our data set without adjustment for waist; line C depicts results adjusted for waist circumference; and line D depicts the results obtained on our data set, with adjustment for waist and with an optimized cutoff.

Symbol: … = Data not provided by Lin et al.[33]

Table 3. Results Obtained on the Independent Test Set for Logistic Regression, Artificial Neural Networks, and Support Vector Machines[a]

Model	True Negatives, n	True Positives, n	False Negatives, n	False Positives, n	Accuracy	Sensitivity	Specificity
A. Training and testing including the complete set of patients							
Logistic regression							
A	117	43	26	16	79.2	62.3	88.0
B	95	63	6	38	78.2	91.3	71.4
Artificial neural networks							
A	101	54	15	32	76.7	78.3	75.9
B	95	63	6	38	78.2	91.3	71.4
Support vector machines							
A	108	48	21	25	77.2	69.6	81.2
B	93	64	5	40	77.7	92.8	69.9
B. Training performed on the complete data set, results obtained in the subset of data with central obesity							
Logistic regression							
A	36	43	26	16	65.3	62.3	69.2
B	14	63	6	38	63.6	91.3	26.9
Artificial neural networks							
A	22	54	15	30	62.8	78.3	42.3
B	16	63	6	36	65.3	91.3	30.8
Support vector machines							
A	27	48	21	25	62.0	69.6	51.9
B	18	64	5	34	67.8	92.8	34.6
C. Both training of the classifier and testing on the subset of patients with central obesity							
Logistic regression							
A	38	48	21	21	67.2	69.6	64.4
B	37	48	21	22	66.4	69.6	62.7
Artificial neural networks							
A	35	41	28	24	59.4	59.4	59.3
B	18	58	41	11	59.4	84.1	30.5
Support vector machines							
A	31	54	15	28	66.4	78.3	52.5
B	27	54	15	32	63.3	78.3	45.8

[a]All algorithms were optimized for maximal accuracy (lines starting with A) or for maximal sensitivity at a predefined specificity (lines starting with B).

same, the accuracy dropped, as it is a lot more difficult to classify patients without central obesity. Finally, one could reason that the performance of the classifier would improve when only training on this subset of patients. However, as one can clearly see in Table 3C, the performance was quite poor.

Although the accuracy of the total group of patients was rather satisfying (77%–79%), the results changed dramatically when the subgroup with central obesity was assessed. The best accuracy (67.8%) was still a lot worse than the accuracy that was obtained using our naive and simple tree model depicted in Figure 1. We hope that these results show that the reported accuracies on this particular type of problem highly depend on the sample composition.

Finally, we stress that these results were obtained by including all clinical variables into the model (age, gender, BMI, length, weight, waist-hip ratio, hip, waist, GAF, alcohol, smoking, central obesity flag, blood pressure flag, diastolic blood pressure, systolic blood pressure, and heart rate). The

results did not improve when including the major applied antipsychotic—the antipsychotic with which the patient was treated most—in the model.

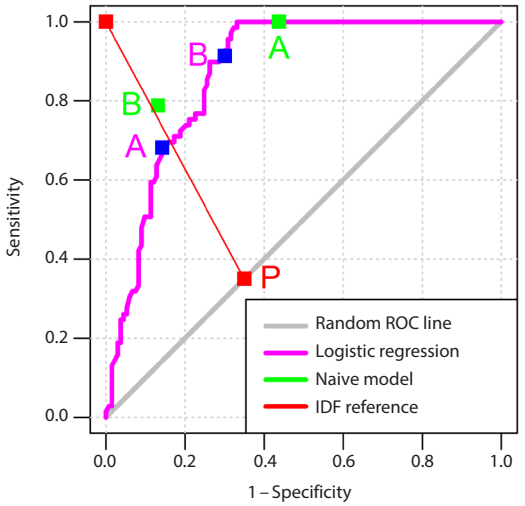
Receiver Operating Characteristic Analysis

A more visual assessment of the different results is shown in Figure 2, which shows the random receiver operating characteristic curve (ROC curve) in gray. On this curve, the probability of being classified as positive is the same for those with or without the MetS. The magenta line denotes the ROC curve obtained by the logistic regression model. The 2 points depicted as A and B denote the different choices we made: point A refers to the model with maximized accuracy, whereas B refers to the model with maximal sensitivity (at an acceptable specificity level).

Next, the sensitivity-specificity pairs obtained by the 2 naive models A and B (compare with Table 2) are shown in green. The IDF reference line is depicted in red. For more information on how to obtain this reference line, see Kraemer.[39]

As Figure 2 clearly illustrates, the bias is the lowest for logistic regression model A and naive model B. In the case of logistic regression (and the other more advanced classifiers), it is logical that the bias is minimized. These models aim at maximal accuracy. The other variant (eg, logistic regression model B) aims at maximizing the sensitivity (while still maintaining an acceptable level of specificity). Therefore, these models have—by design—more bias. However, as Kraemer[39] notes in a recent review, bias does not always mean the model is without merit.

Figure 2. Receiver Operating Characteristic Curve[a]



[a]The gray line denotes the "random ROC line"; the magenta line is the ROC curve for the logistic regression models; point A denotes the point of maximized accuracy (Table 3A, logistic regression model, line A); point B denotes the point of optimized sensitivity. The green points denote the 2 versions of the naive model (Table 2). The red line is the IDF reference line.
Abbreviation: IDF = International Diabetes Federation, ROC = receiver operating characteristic.

DISCUSSION

Recent research in clinical sciences devotes an increasing amount of attention to the application of advanced statistical techniques to clinical data in hopes of being able to pick up data structures that are not linear and that cannot be extracted with a mere correlation analysis. The idea is that techniques like support vector machine classification or artificial neural networks improve the prediction of a clinical outcome beyond the results obtained by, eg, logistic regression.

In this study, we aimed at replicating the results obtained by Lin et al[33] who propose an easy and low-cost classification scheme to detect the MetS in a psychiatric population treated with SGAs without the use of blood sampling. The clinical relevance of this research is obvious, as blood sampling is expensive and rather inconvenient in a psychiatric population.

We have optimized support vector machines, artificial neural networks, and a logistic regression scheme to detect the MetS solely based on readily available clinical data (like diastolic and systolic blood pressure, heart rate, central obesity). In this specific case, it is important to note that many variables used in the definition of the MetS are readily available. Although deviant blood values are necessary to meet the criteria of MetS, central obesity is a sine que non condition, without which a patient cannot be classified as being affected by the MetS according to the IDF criteria. Therefore, we compared our results obtained using advanced statistical techniques with the results obtained by a manual classification scheme, taking into account central obesity and blood pressure.

The accuracy we obtained on the complete dataset using this very simple and naive model was 83.9% with a high sensitivity (78.8%) and high specificity (86.8%). These results are slightly better than the results obtained by Lin et al,[33] who report an overall accuracy of 79.7%, although with a very high sensitivity (96.3%) and a high specificity (78.6%). A high sensitivity is an important feature for a screening algorithm, as patients suspected of a certain symptom can be further investigated, but it is desirable to reduce as much as possible the number of patients who are actually affected by the syndrome and who test negative on the sentinel test (false negatives).

The 3 artificial intelligence techniques applied in this article return comparable accuracies of about 77%–79% and sensitivities and specificities. These results are comparable with the accuracy reported in the Asian population by Lin et al.[33] However, as central obesity is a necessary condition and can be easily measured, we have assessed the results on the subgroup of patients diagnosed with central obesity. In this subgroup, our results were substantially worse (62%–68%), and high sensitivities (>90%) could be obtained only at the cost of very low specificity (<35%). Training the classifiers using only these data did not help either, and the results were still worse than the results obtained by our proposed naive model using blood pressure as the only feature.

The results obtained by the naive model, ie, the accuracy of 74.7% on the patient group without central obesity, are remarkable. We analyzed these results further by assessing the patients' diabetic status. In total, 45 patients (7.4%) were diagnosed with diabetes mellitus and 136 patients (22.5%) were diagnosed with prediabetes. Testing the naive model (version B) on the patients with diabetes mellitus and prediabetes produced very high accuracies (> 93%). This result is also logical, since patients with diabetes mellitus and prediabetes—by definition—have elevated fasting glucose values. Therefore, an elevated blood pressure for patients with central obesity almost automatically classifies them as IDF+. The accuracy of this model on nondiabetic patients with central obesity drops to 63%. However, as we did not want to take any information of blood sampling into account (ie, the diabetic status is unknown), we can still state that the naive model outperforms the more complicated ones.

One possible limitation of this study is the fact that all patients were treated at the same psychiatric center. We could also expect that the results would worsen if we had acquired 2 separate data sets: eg, all clinical and blood-sampling variables needed for IDF criteria at day 1 and all readily available clinical variables at day 2. This would imply 2 measurements of central obesity and blood pressure. As both measurements would not have a perfect test-retest reliability, we expect some deterioration of the results if that set-up was chosen.

Another possible limitation to this study design is the fact that we considered the IDF definition as the gold standard of the MetS. Therefore, one should be careful when interpreting these results. If we obtain a certain accuracy, that accuracy is based on detecting the IDF criteria of the MetS and does not give direct evidence of the accuracy of the prediction of cardiovascular diseases or diabetes.

The goal of this study was to detect the MetS in a schizophrenic population using only readily available clinical variables. However, the definition yielded by the IDF does include 2 readily available clinical variables (central obesity and blood pressure). This fact inspired us to classify our patient group based on these variables.

The results obtained by applying a simple model to these readily available parameters outperformed the results obtained by the more advanced statistical techniques both in the total group and in the subset of patients with central obesity. The results on the total of patients also highly depended on the amount of patients without central obesity who were easily classified by every method.

CONCLUSION

Although so-called pattern recognition techniques bear high promise in improving clinical decision making, the results should be presented with caution and preferably in comparison with a less complicated technique.

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Drug names: aripiprazole (Abilify and others), asenapine (Saphris), clozapine (Clozaril, FazaClo, and others), iloperidone (Fanapt), lurasidone (Latuda), olanzapine (Zyprexa and others), paliperidone (Invega and others), quetiapine (Seroquel and others), risperidone (Risperdal and others), ziprasidone (Geodon and others).

Author contributions: Both senior authors (Drs De Hert and Nagels) contributed equally to the presented work.

Potential conflicts of interest: **Dr De Hert** has been a consultant for, has received grant/research support and honoraria from, and has been on the speakers/advisory boards of AstraZeneca, Lundbeck JA, Janssen-Cilag, Eli Lilly, Pfizer, Sanofi-Aventis, Bristol-Myers Squibb, and Takeda. **Drs Van Schependom**, **Keyser**, and **Nagels**; **Ms Yu**; and **Messrs Gielen** and **Laton** declare no conflicts of interest related to this study.

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