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# Comparison of predictive equations for resting metabolic rate in obese psychiatric patients taking olanzapine

Maria Skouroliakou, Ph.D.[a,b,*], Ifigenia Giannopoulou, Ph.D.[b,c], Christina Kostara, M.Sc.[b], and Melanie Vasilopoulou, B.Sc.[b]

[a] *Harokopio University, Athens, Greece*
[b] *Dietetic Department, Iaso Hospital, Athens, Greece*
[c] *Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom*

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**Abstract**

**Objective:** The prediction of resting metabolic rate (RMR) is important to determine the energy expenditure of obese patients with severe mental illnesses (SMIs). However, there is lack of research concerning the most accurate RMR predictive equations. The purpose of this study was to compare the validity of four RMR equations on patients with SMIs taking olanzapine.

**Methods:** One hundred twenty-eight obese (body mass index >30 kg/m$^2$) patients with SMIs (41 men and 87 women) treated with olanzapine were tested from 2005 to 2008. Measurements of anthropometric parameters (height, weight, body mass index, waist circumference) and body composition (using the BodPod) were performed at the beginning of the study. RMR was measured using indirect calorimetry. Comparisons between measured and estimated RMRs from four equations (Harris-Benedict adjusted and current body weights, Schofield, and Mifflin-St. Jeor) were performed using Pearson's correlation coefficient and Bland-Altman analysis.

**Results:** Significant correlations were found between the measured and predicted RMRs with all four equations ($P < 0.001$), with the Mifflin-St. Jeor equation demonstrating the strongest correlation in men and women ($r = 0.712$, $P < 0.001$). In men and women, the Bland-Altman analysis revealed no significant bias in the RMR prediction using the Harris-Benedict adjusted body weight and the Mifflin equations ($P > 0.05$). However, in men and women, the Harris-Benedict current body weight and the Schofield equations showed significant overestimation error in the RMR prediction ($P < 0.001$).

**Conclusion:** When estimating RMR in men and women with SMIs taking olanzapine, the Mifflin-St. Jeor and Harris-Benedict adjusted body weight equations appear to be the most appropriate for clinical use. 

*Keywords:* Resting metabolic rate predictive equations; Obese psychiatric patients; Males; Females; Diet

## Introduction

Weight gain is a complex process influenced by societal factors, such as cultural and ethnic patterns of life, individual lifestyle practices, and biological factors [1]. Excessive weight gain often leads to obesity, which is associated with a number of health problems such as hypertension, heart disease, type 2 diabetes, gallbladder disease, and certain types of cancer [2]. It is commonly thought that obesity is often due to a lower resting metabolic rate (RMR). More specifically, there is evidence that people with a lower RMR tend to gain more weight than those with a normal RMR [3]. A number of factors can contribute to a lower RMR including genetics, age, sleeping habits, reduced muscle mass, poor nutrition, and sedentary lifestyle [4].

Patients with severe mental illnesses (SMIs) such as bipolar disorder, depression, and schizophrenia are often prescribed medications for prolonged periods. The majority

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* Corresponding author. Tel.: +30-694-414-7897; fax: +30-210-618-4158.

*E-mail address:* diatrofi@hygeia.gr (M. Skouroliakou).

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of these psychotropic drugs, especially clozapine and olanzapine, have been shown to cause significant weight gain, which can lead to obesity and thus adversely affect their health and subsequently their treatment [5,6]. Hence, management of weight gain for patients with SMIs has become a crucial component of their treatment and needs to be instituted as soon as the problem is identified. Nutritional interventions, exercise, and behavioral treatments have been shown to effectively counteract the antipsychotic medication-induced weight gain [5]. However, to design an appropriate weight-loss intervention for this population, it is essential to accurately assess their energy needs. This assessment is best accomplished by measuring the RMR of each patient [3]. The RMR can be measured using devices such as direct and indirect calorimeters and respiratory chambers but the operation of these devices requires trained personnel and it is very expensive and time consuming. For this reason, calculation of RMR by mathematical equations was adopted as a major method of assessing the energy needs of individuals [3]. Despite extensive research in the field of dietetics concerning the applicability and accuracy of RMR predictive equations in healthy populations [7–10], there is a considerable lack of research concerning the applicability of these equations on patients with SMIs. To our knowledge, only one study by Sharpe et al. [11] has been published in this area and has found that the commonly used RMR predictive equations of Harris-Benedict and Schofield systematically overestimated RMR in eight men with SMIs taking the atypical antipsychotic clozapine. No studies have been published on the use of these predictive equations on female patients with SMIs, a population that has a high prevalence of obesity. Hence, the purpose of this study was to measure RMR in a group of male and female patients with SMIs taking the antipsychotic medication olanzapine and to determine whether RMR can be accurately estimated using previously published predictive equations. In accordance with previous research [11], we hypothesized that the predictive equations would overestimate the actual RMR value in men and women.

## Materials and methods

### *Subjects*

A total of 156 subjects were recruited for the study from 2005 to 2008. The study was part of a large 5-y research project that began in 2005 and will be completed in 2010. This research project provides free nutritional support to the population of psychiatric patients of Athens, Attika region. Subjects were referred to the project by the clinical psychologists who collaborate in the 5-y research project. From the 156 subjects, 128 patients agreed to participate in the study. The final sample included 41 men and 87 women with *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, mood or psychotic disorder diagnoses obtained from psychiatrists of the psychiatric clinics and private practices of Athens. All subjects were on the stable antipsychotic medication olanzapine for a minimum of 6 mo and all were obese (body mass index $>30$ kg/m$^2$). Participants who had a medical condition known to affect RMR (e.g., hypertension, diabetes) were excluded from the study. Before participation in the study, all subjects signed an informed consent form approved by the institutional review board of the ethical committee of Iaso Hospital, Athens, Greece.

### *Experimental measurements*

All subjects were required to come to the hospital for two separate visits. At visit 1, subjects participated in a 1-h interview for the evaluation of eating habits, dietary preferences, and medical history. At visit 2, subjects were asked to come in the laboratory after refraining from eating for 12 h and exercising for the previous 24 h. Anthropometric measurements of body weight, height, and waist circumference were performed. Body weight was measured without shoes on a standing scale that was calibrated to 0.1 kg. Body height was measured without shoes on a wall-mounted stadiometer. Waist circumference was measured at the narrowest part of the subjects' waist in addition to waist–hip ratio. In addition, measurement of body composition (body fat and fat-free mass) was performed on each patient with the use of the BodPod (Life Measurement Inc., Concord, CA, USA) according to the manufacturer's instructions.

Measurement of RMR was performed in the supine position after the subject had rested for 10 min before the beginning of the test. The measurement lasted for 20 min. The first 5 min of the measurement was discarded. Steady-state data (15 min of data at which the coefficient of variation in the minute-by-minute oxygen consumption data and carbon dioxide production was $<10\%$) was used for the analysis of RMR. The RMR measurement was performed using indirect calorimetry with the Kosmed metabolic cart (Kosmed, Trieste, Italy).

### *Predictive RMR equations*

The predictive regression equations of Harris and Benedict [12] for adjusted body weight (ABW) and current body weight (CBW) [12], Schofield [13], and Mifflin et al. (Mifflin-St. Jeor) [14] were used to calculate RMR. These equations were chosen because they are commonly used by practitioners for obese populations [3]. Adjusted body weight was calculated as the average of ideal body weight and CBW.

### *Statistical analysis*

Statistical analysis was performed with SPSS 15 for Windows (SPSS, Inc., Chicago, IL, USA). All values are presented as mean ± standard deviation. Descriptive statistics were used to calculate the baseline characteristics for male and female patients with SMIs. Pearson's correlation coefficient ($r$) was calculated to observe the association between the measured and predicted RMRs for each of the predictive regression equations used. Bland-Altman analysis [15] was performed to assess the accuracy of RMR prediction with each equation. The threshold for significance in all tests was set at $P = 0.05$. Prediction accuracy of each predictive RMR equation was defined as the percentage of subjects in the study whose RMR was predicted to within ±10% of measured RMR. Linear regression analysis was performed to compute the root mean square prediction error (RMSE) of each predictive RMR equation.

## Results

### *Subject characteristics*

Characteristics of the subjects at the beginning of the study are listed in Table 1. Significant differences were found between men and women in anthropometric measurements such as body weight, height, percentage of body fat, waist circumference, and fat-free mass. Moreover, men were found to have significantly higher measured and predicted RMRs compared with women (Table 1).

### *Correlations*

The measured RMR correlated most strongly with fat-free mass ($r = 0.65$, $P < 0.01$) and body weight ($r = 0.51$, $P < 0.01$) in all subjects, with no significant differences found between male and female patients. A statistically significant correlation was found between the measured RMR and the predictive regression equations used. More specifically, a significant correlation was found between the measured RMR and the equations of Mifflin-St. Jeor ($r = 0.712$, $P = 0.001$), Schofield ($r = 0.678$, $P = 0.001$), Harris-Benedict CBW ($r = 0.697$, $P = 0.001$), and Harris-Benedict ABW ($r = 0.502$, $P = 0.001$). No significant gender differences were found in the correlations between the measured and predicted RMRs.

### *Linear regression*

Linear regression analysis revealed that the Mifflin-St. Jeor equation had the lowest RMSE and thus the best accuracy of prediction of all equations (RMSE = 373.19, $R = 0.624$, $P < 0.001$), followed by the Schofield equation (RMSE = 374.10, $R = 0.623$, $P < 0.001$), the Harris-Benedict CBW equation (RMSE = 375.68, $R = 0.618$, $P < 0.001$), and the Harris-Benedict ABW equation (RMSE = 397.17, $R = 0.556$, $P < 0.001$). All four predictive equations were found to reliably predict the measured RMR ($P < 0.001$).

### *Prediction accuracy of each RMR equation*

In men, the Mifflin-St. Jeor equation demonstrated the highest percent RMR prediction accuracy, with 63% of the subjects falling within ±10% of measured RMR. The Harris-Benedict ABW, Schofield, and Harris-Benedict CBW equations had 59%, 56%, and 51% of the cases falling within ±10% of measured RMR, respectively. All four equations demonstrated a great tendency for overestimation of RMR.

In women, the Schofield equation demonstrated the highest percent RMR prediction accuracy, with 64% of the subjects falling within ±10% of measured RMR. The Mifflin-St. Jeor, Harris-Benedict ABW, and Harris-Benedict CBW equations had 56%, 55%, and 48% of the cases falling within ±10% of measured RMR, respectively. All four equations demonstrated a great tendency for overestimation of RMR.

Table 1
Anthropometric characteristics and RMR of subjects

| | Men ($n$ = 41) | Women ($n$ = 87) | All subjects ($n$ = 128) | $P$ |
|---|---|---|---|---|
| Age (y) | 38.18 ± 11.09 | 42.61 ± 11.07 | 41.19 ± 11.22 | 0.038* |
| Height (cm) | 173.78 ± 6.19 | 160.70 ± 6.59 | 164.89 ± 8.89 | 0.001* |
| Weight (kg) | 106.16 ± 16.32 | 86.56 ± 18.83 | 92.91 ± 20.18 | 0.001* |
| Body mass index (kg/m$^2$) | 35.07 ± 4.49 | 33.60 ± 7.20 | 34.07 ± 6.47 | 0.161 |
| Waist circumference (cm) | 114.49 ± 11.43 | 102.31 ± 14.52 | 106.21 ± 14.71 | 0.001* |
| Fat mass (%) | 37.01 ± 6.71 | 45.31 ± 7.08 | 42.65 ± 7.95 | 0.001* |
| Fat-free mass (kg) | 66.19 ± 7.95 | 46.13 ± 7.25 | 52.56 ± 11.99 | 0.001* |
| RMR measured (kcal/d) | 1961.10 ± 463.20 | 1422.99 ± 375.19 | 1595.35 ± 475.86 | 0.001* |
| RMR Harris-Benedict ABW (kcal/d) | 2028.34 ± 273.72 | 1510.10 ± 196.38 | 1676.10 ± 329.61 | 0.001* |
| RMR Harris-Benedict CBW (kcal/d) | 2136 ± 280.37 | 1585.62 ± 198.84 | 1762.20 ± 343.83 | 0.001* |
| RMR Schofield (kcal/d) | 2115.13 ± 267.84 | 1558.82 ± 193.21 | 1737.01 ± 340.27 | 0.001* |
| RMR Mifflin-St. Jeor (kcal/d) | 1959.72 ± 215.52 | 1501.52 ± 213.40 | 1648.28 ± 302.54 | 0.001* |

ABW, adjusted body weight; CBW, current body weight; RMR, resting metabolic rate
* Significant difference between genders.

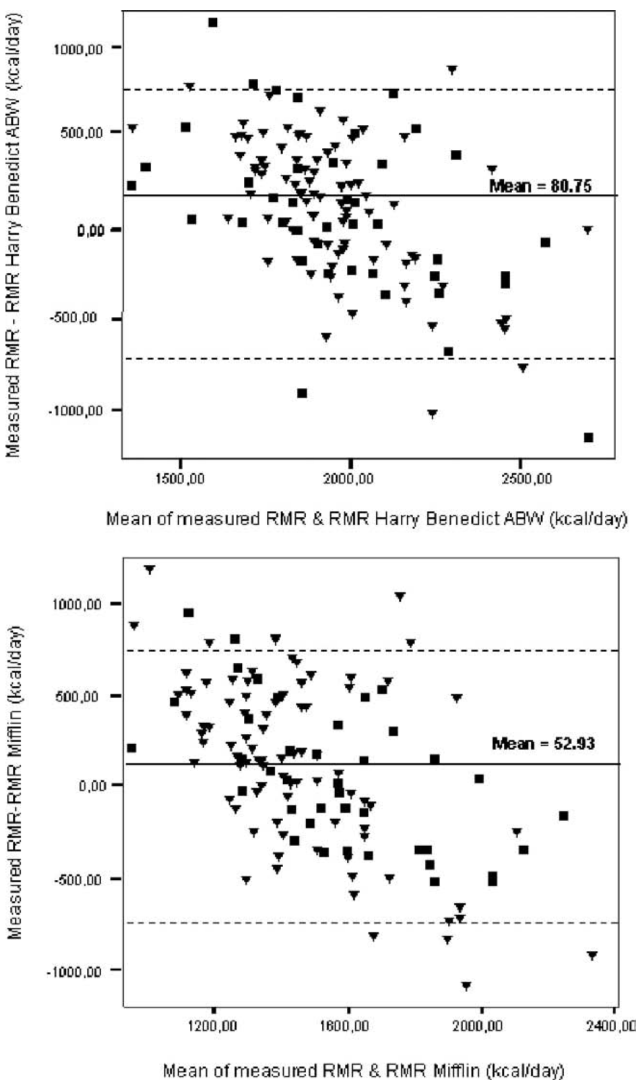


Fig. 1. Bland-Altman plot of measured RMR and predicted RMR using the Harris-Benedict ABW and Mifflin equations in male (squares) and female (triangles) patients with severe mental illnesses. The solid line represents the mean bias and the dashed lines represent the limits of agreement (mean ± 2 SD). ABW, actual body weight; RMR, resting metabolic rate.

*Bland-Altman analysis*

In both genders, the Bland-Altman analysis revealed that only the Mifflin-St. Jeor predictive equation did not show a significant bias in the prediction of RMR (52.93 ± 385.93 kcal/d; Fig. 1). For the other three equations, the Bland-Altman analysis showed significant mean biases of 80.75 ± 416.40 kcal/d for the Harris-Benedict ABW equation, −166.85 ± 395.51 kcal/d for the Harris-Benedict CBW equation, and −141.66 ± 387.35 kcal/d for the Schofield equation (Figs. 1 and 2).

In men, the Bland-Altman analysis revealed that only the Mifflin-St. Jeor predictive equation and the Harris-Benedict ABW equation did not show a significant bias in the prediction of RMR. Specifically, the Mifflin-St. Jeor equation had a mean bias of −10.38 ± 432.97 kcal/d, and the Harris-Benedict ABW a mean bias of +67.25 ± 460.44 kcal/d. For the other two equations, the Bland-Altman analysis showed significant mean biases of −175.32 ± 450.33 kcal/d for the Harris-Benedict CBW equation and −154.05 ± 421.62 kcal/d for the Schofield equation.

In women, similar to the male patients with SMIs, the Bland-Altman analysis revealed that only the Mifflin-St. Jeor predictive equation and the Harris-Benedict ABW equation did not show a significant bias in the prediction of RMR. Specifically, the Mifflin-St. Jeor equation showed a mean bias of +78.53 ± 338.89 kcal/d, and the Harris-Benedict ABW of +87.11 ± 372.35 kcal/d. In contrast, the Bland-Altman analysis showed significant mean biases of −162.63 ± 340.69 kcal/d for the Harris-Benedict CBW equation and −135.83 ± 353.07 kcal/d for the Schofield equation.

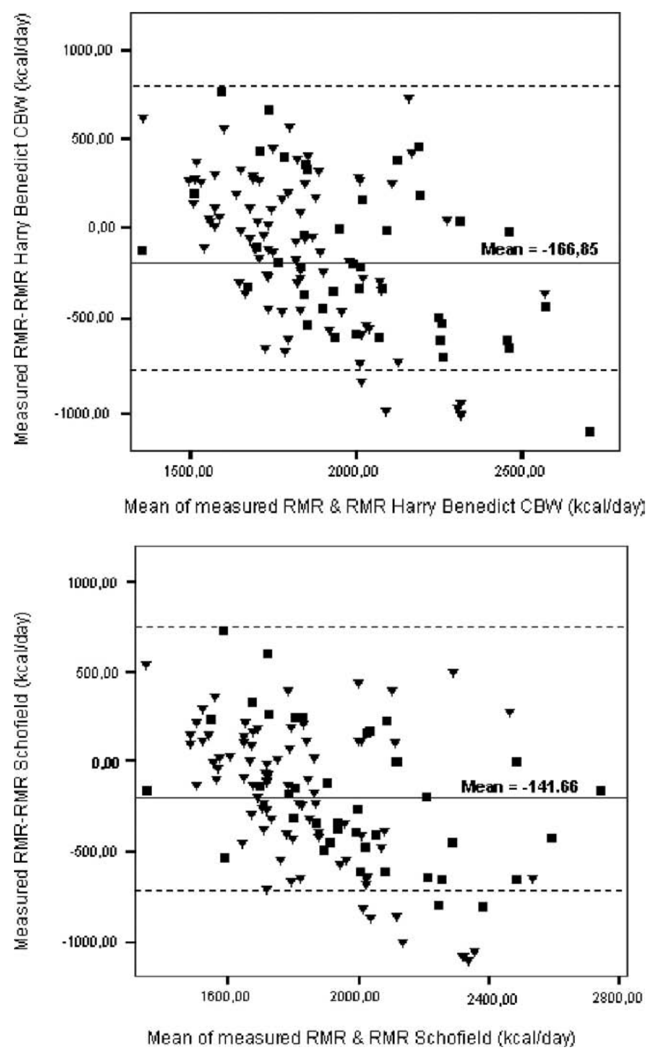


Fig. 2. Bland-Altman plot of measured RMR and predicted RMR using the Harris-Benedict CBW and Schofield equations in male (squares) and female (triangles) patients with severe mental illnesses. The solid line represents the mean bias and the dashed lines represent the limits of agreement (mean ± 2 SD). CBW, current body weight; RMR, resting metabolic rate.

## Discussion

Patients with SMIs are often prescribed medications such as olanzapine and clozapine for prolonged periods that have been shown to induce significant weight gain [6]. As a result there is an increased incidence of obesity in this population, a factor that adversely affects their healthy and their overall treatment. To appropriately treat obesity in this population there is a great need for an accurate assessment of their energy requirements. However, there is paucity of research on the measurement of energy expenditure and the use of appropriate predictive equations of RMR in patients with SMIs and particularly in female patients. Hence, the purpose of our study was to assess the predictive value of the commonly used RMR predictive Harris-Benedict ABW and CBW, Schofield, and Mifflin-St. Jeor equations in a large sample of male and female patients with SMIs and to observe the variability in measurement resulting from each equation. We found that in male and female patients with SMIs, the Mifflin-St. Jeor and Harris-Benedict ABW equations accurately estimated the energy needs of the patients with very small, clinically insignificant prediction error.

To our knowledge this is the first study comparing the actual and predicted RMR measurements in a large population of male and female patients with SMIs. Previous studies have investigated their association only in a small sample ($n = 8$) of male patients with SMIs [11], with no research being conducted on women with SMIs. Our results show that the Mifflin-St. Jeor equation and the Harris-Benedict ABW equation are the most appropriate equations to be used in male and female patients with SMIs, because they have an insignificant mean bias very close to zero. More specifically, the Mifflin-St. Jeor equation was found to be the most accurate equation in our study because it produced estimation errors of only 78 kcal/d in women and −10 kcal/d in men, with the lowest prediction error and the highest percentage of patients (~60%) falling within the ±10% estimation error of all four RMR equations. No other study has investigated the use of this predictive equation in this population. Our results are in accordance with the research conducted in healthy obese populations [3], where the Mifflin-St. Jeor equation was found to have the highest percentage of patients (~80%) falling within the ±10% prediction error. Similarly to the Mifflin-St. Jeor equation, the Harris-Benedict equation that adjusts a subject's body weight produced very small clinically insignificant errors of 87 kcal/d in women and 67 kcal/d in men. Furthermore, using this equation resulted in a high percentage of patients (~57%) falling within the ±10% of measured RMR. However, in both genders these two predictive equations demonstrated great variability between the measured and predicted RMRs and, hence, despite their low estimation error need to be used with care in patients with SMIs.

In our study, the predictive Harris-Benedict CBW and Schofield equations were found to greatly overestimate the real energy needs of male and female patients with SMIs. More specifically, in men the Harris-Benedict CBW equation overestimated the measured RMR by 175 kcal/d. This error in the prediction of RMR is in accordance with the sole published study in patients with SMIs by Sharpe et al. [11], where the researchers also found an overestimation error in the prediction of RMR by 284 kcal/d. The mean bias of the RMR predicted using the Schofield equation in men was also very similar to the prediction of RMR by the Harris-Benedict CBW equation by overestimating RMR by 154 kcal/d. The study by Sharpe et al. [11] also found an overestimation error of RMR by 287 kcal/d with this specific equation in men. No other studies have investigated the use of the Harris-Benedict CBW and Schofield predictive equations in female patients with SMIs. In our study, both equations overestimated RMR by 162 and 135 kcal/d, respectively, in our female patients. Hence, our findings suggest that these two commonly used RMR predictive equations in healthy populations are not appropriate for the population of male and female patients with SMIs taking olanzapine and, if used, corrections of the predicted RMR by approximately −165 kcal/d for men and −150 kcal/d for women should be performed.

Possible reasons for the high overestimation error in the prediction of RMR with equations such as the Harris-Benedict and Schofield that have been widely used in the clinical nutrition field are the specific characteristics of this population such as the effects of the mental disease, antipsychotic medication use, mood changes, and lifestyle changes. Also, daily variations in the energy expenditure of the patients might have played a role [16]. However, due to a lack of research in this population it is very difficult to find the specific parameters that might have played a role. Future studies should be conducted to establish the predictive value of these equations in a larger sample of this population taking different antipsychotic drugs and to possibly create new equations specifically on the characteristics of the population of patients with SMIs.

## Conclusion

The findings of this study suggest the use of the Mifflin-St. Jeor and Harris-Benedict ABW equations as the most appropriate means of estimating RMR of male and female patients with SMIs taking olanzapine. These two equations can predict the energy needs with a low estimation error and low cost.

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