

Original

Comparison of clinical body composition methods in people taking weight-inducing atypical antipsychotic medications

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The purpose of this study was to compare the accuracy of clinical methods to estimate body fat (%BF) in people who take weight-inducing atypical antipsychotic medications. Forty-seven people (35 males, 12 females) with previously diagnosed psychotic illness who had been taking atypical antipsychotic medications for more than 6 months took part in this study. Percentage body fat was estimated using bioelectrical impedance analysis (BIA) and anthropometry from previously published prediction equations and compared with that measured using the deuterium dilution technique which served as the criterion measure. Bland-Altman analyses were used to assess the agreement between measures. In the males, %BF determined using BIA with the Lukaski equation was the only clinical method with mean differences that were not significant from criterion values. While in the females, %BF determined from BMI was the only method that was significantly different from the criterion values. All of the methods of estimating %BF except Watson equations provided consistent estimates across the weight range. Therefore, this study suggests that in a group of people who predominantly had schizophrenia and were taking atypical antipsychotic medications, BIA using the equation of Lukaski was the best indicator of %BF, although on an individual basis the accuracy was poor. BMI underestimated %BF to a greater significant extent than BIA. The use of BIA rather than BMI may provide a better indicator of adiposity in people who take weight inducing antipsychotic medications.

Key Words: bioelectric impedance, obesity, deuterium dilution, percentage body fat, atypical antipsychotic medication

INTRODUCTION

Obesity has become a serious worldwide public health problem and is a major contributor to the global burden of chronic disease such as cardiovascular disease and diabetes with serious social, economic and psychological consequences.¹ People with mental illnesses, particularly those with psychotic illnesses such as schizophrenia, have obesity rates which are at least double population rates.²⁻⁷

The underlying reasons for the current increased prevalence of obesity in people with mental illness are likely to be multifactorial. There is some evidence which suggests that obesity in people with mental illness may be associated with factors relating to biology or genetics and/or those that relate to lifestyle behaviours, socioeconomic conditions and the side effects of treatment. Weight gain induced by antipsychotic medication has been the subject of many review articles.⁸⁻¹³ Recently, a study conducted in the United States documented weight change in ninety-eight people who began taking antipsychotic medication following an episode of psychosis.¹⁴ Over a one year period, those taking older style medications gained a mean of 3.7 kg, with 38% gaining more than 7% of their initial weight. Those taking the newer atypical antipsychotic medications gained substantially

more body weight – a mean of 9.5 kg with 59% gaining more than 7% of their initial body weight over the year. The use of the atypical antipsychotic medications is recommended despite their weight inducing potential because of their lower rates of motor side effects and clinical efficacy.¹⁵⁻¹⁷

People with psychotic illness have higher morbidity and mortality rates associated with cardiovascular disease and diabetes and some of this excess has been associated with increased prevalence of excess adiposity.^{4,18,19} Although studies which distinguish between the contributions of fat and fat free mass in this clinical group are relatively sparse, studies have used Dual-Energy X-ray Absorptiometry (DXA) and bioelectric impedance analysis (BIA) to demonstrate that most of the weight gain associated

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with atypical antipsychotic use was due to increases in fat mass, not fat-free mass.^{20,21} Given that it is the excessive accumulation of body fat rather than body size per se that causes the health risk associated with obesity²² and that body composition may be altered in people who take atypical antipsychotic medication,²³ the monitoring of weight gain, particularly of the accumulation of body fat is essential for clinical management of people who take atypical antipsychotic medication.

Currently four compartment models are considered the 'gold standard' for determining body composition. In clinical and some research settings, it is often not possible to use criterion methodologies to determine body composition due to financial constraints, time issues and lack of specialist equipment. There are many different published prediction equations used to determine body composition from simple clinical measures such as anthropometry and BIA. Such predictions of percentage body fat are based on statistical relationships derived against a reference methodology. However the accuracy of such equations is limited by similarities between the characteristics of the group used to develop the equation/s and their similarity with the people that the equation is being applied to, thus for those with altered body composition the extrapolation of clinical measure to estimate percentage body fat may result in greater inaccuracy. The purpose of this research was to compare estimates of percentage body fat derived from simple clinical measures with that derived from deuterium dilution, a criterion body composition methodology in people who take atypical antipsychotic medication.

MATERIALS AND METHODS

Forty-seven people (35 males, 12 females) with psychotic illness were recruited from the West Moreton District Mental Health Services to take part in this research study. Most of the participants had previously been diagnosed with schizophrenia (n=38), while the remaining participants had been diagnosed with – schizoaffective disorder (n=3), bipolar disorder (n=4) and non-specific psychotic illnesses (n=2). All participants had been taking second generation antipsychotic medications as their main antipsychotic therapy [clozapine (n=23), olanzapine (n=8), risperidone (n=8), quetiapine (n=4), aripiprazole (n=4)] for more than four months. Potential participants were excluded from the study if they had a co-morbid condition known to affect body composition or were incapable of giving informed consent. All testing took place in a general practice clinic. This study was approved by the Human Ethics Research Committees of West Moreton Health Services District and the Queensland University of Technology. All participants provided written informed consent prior to their participation in the study.

Deuterium Dilution

Despite the requirement of specialist laboratory equipment for analysis, the deuterium (²H) isotope dilution technique can be used in the clinical setting as a reference method to assess total body water (TBW) and subsequently fat-free mass (FFM) and body fat.²⁴ The principle of isotope dilution techniques is based on the distribution of water in all parts of the body except body fat. The volume of the water pool can be calculated from the concen-

tration of a known dose of isotope following equilibration of the isotope in the body water. This method has been described in detail by Colley et al.²⁵ Briefly, this method measures the dilution in the body of a known dose of the isotope, deuterium (²H₂O). Participants orally consumed a dose equating to 0.05 g·kg⁻¹ body weight of ²H₂O. The enrichment of the ²H₂O in the pre-dose and 5 hour post-dose samples was assessed using isotope ratio mass spectrometry (Hydra 20/20, SerCon, UK). Fat-free mass was calculated from TBW (ie fat-free mass (FFM) = TBW/0.73). Body fat was calculated as body weight minus FFM and from there as a percentage of body weight (%BF). All assays were performed in duplicate, with repeat assays in our laboratory demonstrating a coefficient of variation of less than 2.0% at low enrichment levels and less than 1% for higher values.

Anthropometry

Height was measured to the nearest 0.01cm (Harpden stadiometer, Holtain Ltd, UK) and weight to the nearest 0.01kg (BWB-300, Tanita, Japan). Body mass index (BMI) was calculated as from weight (Wt) and height (Ht) where BMI = Wt (kg) ÷ Ht² (m). Percentage body fat was then estimated using BMI with the regression equations published by Jackson et al²⁶ and is referred to as %BF (BMI). Nilsson et al²³ used regression equations previously published by Watson et al²⁷ to determine total body water in people with schizophrenia using age, weight and height. In the current study, the equations of Watson et al²⁷ were used to estimate percentage body fat with the resultant estimate designated as %BF (WAT).

Bioelectric Impedance Analysis

Body composition was also estimated using an Imp DF50 (Impedimed, Australia) single frequency bioelectrical impedance analyser to determine resistance and reactance at 50 Hz. Standard operating conditions were observed by a trained operator including preparation of the participant, electrode placement and operation of the Imp DF50 bioelectric impedance analyser.²⁸ The measurement using BIA was taken immediately prior to deuterium dosing with participants lying supine, in a rested state. The equations published by Lukaski et al²⁹ and more recently by Sun et al³⁰ were also used to estimate percentage body fat from the resistance and reactance values recorded by the Imp DF50. The estimate of %BF made using the Lukaski equation is referred to as %BF (LUK) while the estimate of %BF made using the Sun equation is referred to as %BF (SUN).

Statistical Analysis

Paired t-tests, correlations and the limits of agreement method as proposed by Bland and Altman³¹ were used to compare criterion %BF (determined by deuterium dilution) and predicted %BF. The limits of agreement method quantifies the variation in between-method differences for individuals.³¹ The bias is the difference between methods with the limits of agreement (\pm 1.96 standard deviation of the mean bias) indicating the spread of the bias. For good agreement between two methods, the mean bias should be close to zero, the limits of agreement within an acceptable range and there should be no systematic variation in the

Table 1. Mean \pm SD of the characteristics of male and female participants

	Male (n=35)	Female (n=12)
Age (years)	34.9 \pm 11.4	38.0 \pm 10.3
Weight (kg)	95.0 \pm 20.1	93.5 \pm 28.7
Height (m)	1.77 \pm 0.07*	1.67 \pm 0.07
BMI (kg/m ²)	30.3 \pm 5.6	33.3 \pm 9.3
TBW (l)	46.3 \pm 8.3*	37.8 \pm 6.3
FFM (kg)	63.6 \pm 11.4*	51.8 \pm 8.6
FM (kg)	31.8 \pm 12.1	41.7 \pm 21.0
%BF	32.6 \pm 7.6*	42.3 \pm 9.2

* $p < 0.05$ independent t tests for significant differences between male and female participants

bias. For body composition assessment, good clinical agreement is usually considered to be $\pm 5\%$ body fat in comparison with a criterion methodology.³² Linear regression analysis was used to determine the presence or absence of a systematic bias between the methods i.e., whether the agreement between the two methods varied as the magnitude of the methods increased or decreased.^{31,33}

RESULTS

The descriptive characteristics for the 47 participants in this study are reported in Table 1. Independent t tests revealed that although the males and females were of similar age and body weight, the males were taller with greater TBW, FFM and %BF. All clinical methods used underestimated %BF in both men and women (see Table 2). In both males and females there were significant correlations between criterion %BF and %BF predicted using the clinical methods. However paired t tests revealed that there was a significant difference between criterion %BF and the methods used to predict %BF in males with the exception of %BF (LUK). In males the bias between criterion %BF and predicted %BF was lowest for %BF (LUK) – mean of 1.2%. However, the limits of agreement were relatively wide at 24.4%. The largest bias and limits of agreement occurred with the prediction of %BF (WAT)

in males. This prediction method also contained a systematic bias where the difference between the criterion %BF increases as the magnitude of %BF increases. It is expressed by the equation $y = 0.40x + 27.5$ ($r=0.47$, $R^2=0.22$, $p=0.004$, $SEE=4.94$).

In the females, paired t tests revealed that there was a significant difference between criterion %BF and %BF (BMI), with no significant difference between criterion %BF and %BF (LUK), %BF (SUN) or %BF (WAT). The bias between criterion %BF and %BF (LUK) and %BF (WAT) were similar – approximately 1%. However, like the males, the prediction of %BF (WAT) contained a significant bias expressed by the equation $y = 1.2x + 40.4$ ($r=0.66$, $R^2=0.43$, $p=0.02$, $SEE=6.1$).

The bias between criterion %BF and the estimates using BMI was significantly greater than the bias for the estimates when using %BF (LUK) in both males (3.3 \pm 6.6%; 95% CI of the difference, 5.5 to 1.0%) and females (2.1 \pm 2.9%; CI of the difference, 4.0 to 0.3%). Figure 1a & b demonstrate that particularly in males, the prediction of %BF in a clinically relevant proportion of participants exceeded $\pm 5\%$ of their body fat measured using deuterium dilution.

DISCUSSION

The current study is the first to assess the accuracy of clinically derived estimates of %BF in people who take weight-inducing atypical antipsychotic medications. Interest in and subsequent use of body composition techniques that distinguish between fat and FFM in this clinical group is growing, stimulated by the high prevalence of obesity and higher weight gain liabilities of antipsychotic medications such as olanzapine and clozapine. The results of this investigation need to be considered against the limiting factors - specifically that the study was conducted using convenience sampling with a relatively small sample. The strengths of this study included the use of deuterium dilution to determine TBW and subsequently %BF. Deuterium dilution is a criterion technique for the determination of TBW. However, using the two-compartment model to determine adiposity from TBW introduces assumptions about the density of FFM that may not be valid in this clinical group. The use of DXA to assess body composition would have provided for the

Table 2. Comparison between measured %BF and %BF predicted using clinical methods

	Males				FEMALES			
	Mean \pm SD	R [†]	Bias [‡]	LOA [§]	Mean \pm SD	R [†]	Bias [‡]	LOA [§]
%BF	32.6 \pm 7.6				42.3 \pm 9.2			
%BF (LUK)	31.4 \pm 9.2	0.74	1.2 \pm 6.2	-11.0 to 13.4	41.4 \pm 7.5	0.85	0.90 \pm 4.9	-8.6 to 10.4
%BF (SUN)	26.7 \pm 7.6*	0.77	5.9 \pm 5.2	-4.2 to 16.0	40.0 \pm 7.9	0.90	2.2 \pm 4.2	-6.0 to 10.5
%BF (WAT)	26.9 \pm 4.9*	0.54	5.7 \pm 6.4 [¶]	-6.9 to 18.3	41.5 \pm 6.6	0.92	0.8 \pm 4.1 [¶]	-7.2 to 8.7
%BF (BMI)	28.1 \pm 6.7*	0.67	4.5 \pm 6.0	-7.3 to 16.2	39.2 \pm 8.1*	0.90	3.0 \pm 4.0	-4.7 to 10.8

%BF, percentage body fat measured using deuterium dilution, %BF (LUK), %BF predicted using BIA with the equations of Lukaski et al (1986), %BF (SUN), %BF predicted using BIA with the equations of Sun et al (2003), %BF (WAT), %BF predicted using anthropometry with the equations of Watson et al (1980), %BF (BMI), %BF predicted using BMI with the equations of Jackson et al (2002)

[†] r, correlation between %BF and %BF predicted by each method

[‡] Bias (mean \pm SD), difference between criterion %BF and %BF predicted by each method

[§] LOA, limits of agreement

* $p < 0.05$, paired t test comparison with %BF

[¶] Systematic bias present, $p < 0.05$

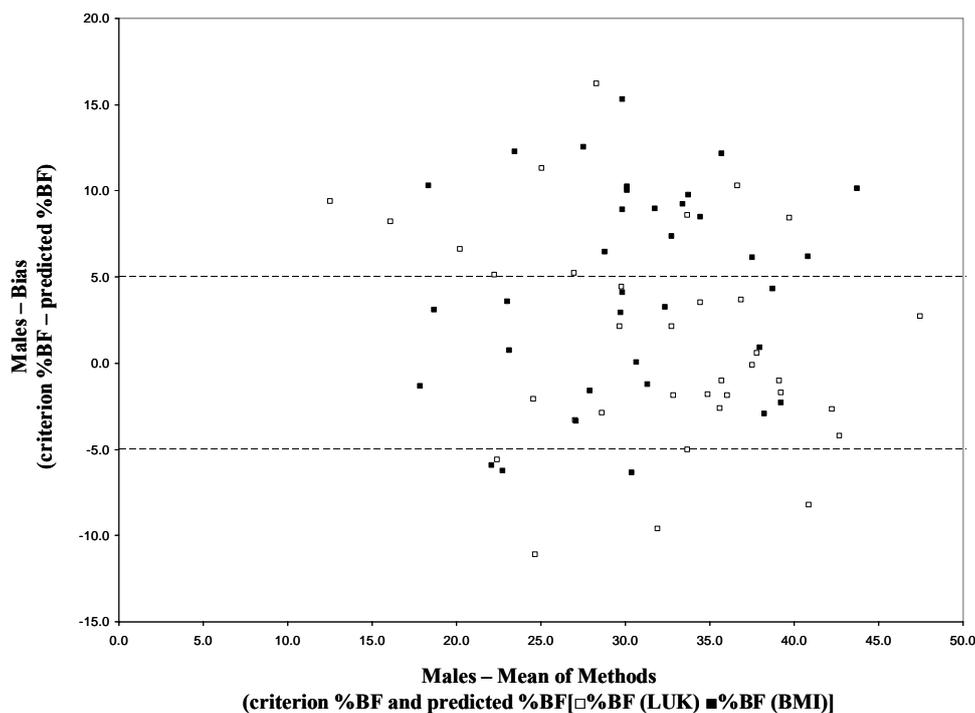


Figure 1a. A scatterplot of the bias between criterion %BF and predicted %BF versus the mean of the methods (criterion %BF and predicted %BF) in males. The values between the dotted lines indicate those predictions of %BF which are within 5% of criterion %BF.

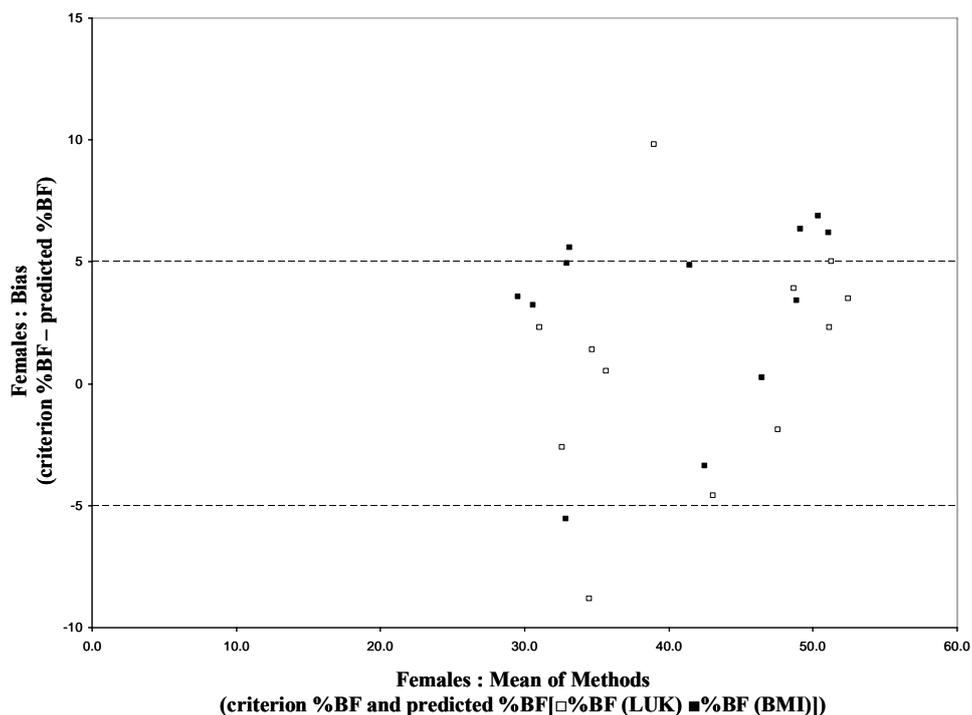


Figure 1b. A scatterplot of the bias between criterion %BF and predicted %BF versus the mean of the methods (criterion %BF and predicted %BF) in females. The values between the dotted lines indicate those predictions of %BF which are within 5% of criterion %BF.

determination of bone mineral content thus allowing the use of a more accurate 3 or, with the measurement of body density, a 4-compartment model to quantify body fat. DXA was not used in this study because of its expense and the requirement of participants to attend a specialist research facility.

It is technically correct to compare estimates of body composition from BIA with TBW or FFM determined

from deuterium dilution. However, in clinical practice and often in research, interest is focused on the ability to predict %BF. The clinical methods used in this study under predicted %BF. BIA was the best predictor of %BF in those who participated in this study. Percentage body fat was under predicted by a mean of 1.1% in the males and 0.8% in the females using the Lukaski et al²⁷ equations. Importantly there was no systematic variation of the bias

between criterion %BF and that predicted using BIA. The limits of agreement were reasonably wide in both males and females. The more recent equations developed by Sun et al²⁸ for use in large population surveys in the United States were less accurate.

The equations of Watson et al²⁵ which use age, weight and height to determine TBW and had been previously used in this clinical group as an indicator of adiposity proved to be unsuitable to predict percentage body fat in this cohort. The current study found that in both males and females, the equations of Watson et al²⁵ increasingly under predicted %BF as the magnitude of %BF increased. Therefore these equations cannot be recommended for use in estimating body composition in people taking atypical antipsychotic medications.

While BMI is measure of relative body size, it is commonly used as an indicator of body fat. The current study suggests that in people who take weight-inducing antipsychotic medications, BMI underestimates %BF across all weight ranges and that the magnitude of this underestimation is greater than when BIA is used. It may be that this cohort is more sarcopenic than the general population, specifically that they have lower relative fat free mass and higher relative body fat at a given body weight.

These results suggest that among people who have schizophrenia or other psychotic illnesses and who take atypical antipsychotic medications, BIA using the equation of Lukaski et al²⁷ provides the best indicator of percentage body fat. BIA has considerable clinical advantages as it is easy to use, inexpensive and non-invasive. However while BIA proved to be a suitable group measure for adiposity, it was less accurate on an individual level as demonstrated by wide limits of agreement. Estimates of %BF could be 10% higher or lower than the actual %BF. Given the health implications of excess adiposity, further comparisons between criterion and clinical methods of assessing body composition are important in this vulnerable cohort of individuals.

AUTHOR DISCLOSURES

The authors report no conflicts of interest

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臨床體組成評估方法比較之—服用體重誘增的非典型抗精神病藥物的族群

此研究目的為比較評估服用體重誘增的非典型精神病藥物的人體脂肪率(%BF)的臨床方法之準確度。47名患者(35名男性、12名女性)被診斷有精神疾病並以非典型抗精神病藥物治療超過6個月以上，參與此研究。體脂肪百分比的評估分別以生物電阻法(BIA)及以體位按照已發表的預測方程式計算而得，並與重氫稀釋法的測量結果當作標準值來相比。使用 Bland-Altman 分析評估測量值之間的一致性。在男性，惟有使用 BIA 及 Lukaski 方程式評估的體脂肪率，與標準值的平均差異沒有顯著性。但在女性，僅有採用 BMI 評估的體脂肪率與標準值有顯著差異性。所有評估體脂肪率的方法，除了 Watson 方程式外，在體重範圍內都提供一致性的評估。因此，此研究建議有精神分裂及服用非典型抗精神病藥物的族群，使用 BIA 及 Lukaski 方程式為體脂肪率的最佳預測指標，雖然應用在個體的準確性不佳。BMI 低估體脂肪率的情形顯著地大於 BIA 的預測。BIA 比起 BMI 可以提供服用體重誘增的非典型抗精神病藥物的人更佳的體脂肪預測值。

關鍵字：生物電阻法、肥胖、重氫稀釋法、體脂肪百分比、非典型抗精神病藥物