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Article type : Regular Article

## **Monitoring children and adolescents with severe obesity: BMI, BMI z-score or %IOTF-25?**

Short title: Monitoring children with severe obesity

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/apa.14898

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## ABSTRACT

**Aim:** Body mass index (BMI)-metrics are widely used as a proxy for adiposity in children with severe obesity. The BMI expressed as the percentage of a cutoff percentile for overweight or obesity has been proposed as a better alternative than BMI z-scores when monitoring children and adolescents with severe obesity.

**Methods:** Annual changes in BMI, BMI z-score and the percentage above the International Obesity Task Force overweight cutoff (%IOTF-25) were compared with dual-energy X-ray absorptiometry (DXA) derived body fat (%BF-DXA) in 59 children and adolescents with severe obesity.

**Results:** The change in %BF-DXA was correlated with the change in %IOTF-25 ( $r=0.68$ ) and BMI ( $r=0.70$ ), and somewhat less with the BMI z-score ( $r=0.57$ ). The Cohen's Kappa statistic to detect an increase or decrease in %BF-DXA was fair for %IOTF-25 ( $K=0.25$ ;  $p=0.04$ ) and BMI ( $K=0.33$ ;  $p=0.01$ ), but not for the BMI z-score ( $K=0.08$ ;  $p=0.5$ ). The change in BMI was positively biased due to a natural increase with age.

**Conclusion:** Changes in the BMI-metrics included in the study are associated differently with changes in %BF-DXA. The BMI z-score is widely used to monitor changes in adiposity in children and adolescents with severe obesity, but the %IOTF-25 might be a better alternative.

## Keywords

Childhood obesity, monitoring, body mass index

## Key notes

- The percentage above the International Obesity Task Force overweight cutoff (%IOTF-25) has been suggested as an unbiased alternative with respect to age for the body mass index (BMI) or BMI z-score in children and adolescents with severe obesity.
- Changes in BMI, BMI z-scores and %IOTF-25 were compared with dual-energy x-ray absorptiometry of body composition
- The %IOTF-25 might be a better alternative to BMI z-scores to monitor changes in adiposity.

## BACKGROUND

Pediatric obesity is a worldwide public health challenge with major consequences for both the individual and the society (1, 2). While effective interventions for prevention and treatment of obesity in children are highly needed, there is currently no consensus on the outcome parameter that should be used for the evaluation of weight status in large-scale intervention studies or in routine clinical practice. Adiposity is commonly assessed by calculating the body mass index (BMI;  $\text{kg}/\text{m}^2$ ) as a proxy of body fatness (3). However, the BMI is a crude index that does not discriminate between fat and fat-free mass. In contrast, dual-energy x-ray absorptiometry (DXA) measures the amount and distribution of fat and fat-free mass. DXA is an accepted reference method for assessment of body composition in children and adolescents (4), but cannot be used on a large scale nor in routine practice due to limited availability and higher costs.

Based on a systematic review, Bryant et al. recommended both the BMI and dual-energy X-ray absorptiometry (DXA) as primary outcome measures when evaluating childhood treatment interventions (5). Because the BMI typically changes during the childhood and adolescent growth phases and also differs between sexes, a correct interpretation of the pediatric weight status requires the use of age- and sex-specific BMI reference charts (3). This is particularly true when monitoring children over long periods of time, or in studies that include children of different ages. The chart can be population specific or an international BMI reference such as the International Obesity Task Force (IOTF) (6, 7) and World Health Organization BMI charts (8).

The number of standard deviations from the mean, the z-score, is a common tool to assess anthropometry (e.g. height, weight). The z-score positions a child on the growth reference chart, and thus adjusts the measurement for age and sex. However, BMI z-scores have been shown to be an inadequate and possibly biased measure of adiposity in children with severe obesity because a wide range of high BMI values corresponds to a relatively narrow range of BMI z-scores in an age

dependent way (9-12). Despite this well documented shortcoming, BMI z-scores are still widely used to evaluate the response of obesity treatment in children with severe obesity (13-15). The BMI expressed as a percentage of a particular BMI cut-off has been proposed as a more appropriate outcome parameter than BMI z-score in children with obesity. Examples are the percentage relative to the 95<sup>th</sup> percentile of the Centers for Disease Control and Prevention (%CDC95) BMI chart (11) or relative to the IOTF overweight cut-off (%IOTF-25) (12). These studies usually focused on cross sectional data, e.g. when comparing children with different degrees of obesity, but only a few addressed the use of such measures for monitoring the weight status during longitudinal follow-up of children or adolescents with obesity (16).

The aim of the current study was to assess the ability of the %IOTF-25, BMI and BMI z-score to measure change in adiposity in children and adolescents with severe obesity, using percentage body fat measured by DXA (%BF-DXA) as a common reference.

## **METHODS**

### **Subjects**

Longitudinal data were retrospectively extracted from the clinical files of 59 children and adolescents (31 boys) aged 5-17 years at baseline who enrolled in an obesity treatment program at the Obesity Outpatient Clinic, Haukeland University Hospital, Bergen, Norway. Criteria for admission to the clinic were an age below 18 years and a BMI above the IOTF threshold for severe obesity (BMI  $\geq$  IOTF-35) or obesity (IOTF BMI-30 to 34.9) with weight-related comorbidity. Additional criteria for the current study were the availability of a DXA measurement at baseline and after a follow-up period of at least 12 months, and anthropometric assessment within three months of these. Not all the children enrolled in the current study were complying with the treatment program provided by the outpatient clinic.

### **Anthropometry**

Height was measured to the nearest 0.1 cm with a wall-mounted electronic stadiometer (Seca 264, Seca, Hamburg, Germany), and weight was measured to the nearest 0.1 kg using a digital scale (InBody 720, Biospace, Seoul, Korea). Participants were measured in underwear without shoes or socks by trained staff members. The BMI was calculated as weight divided by height squared ( $\text{kg}/\text{m}^2$ ). Three metrics of BMI were used in the analyses: BMI, BMI z-score and %IOTF-25. The

%IOTF-25 is the BMI expressed as percentage relative to the age- and sex- specific IOTF cut-off for overweight (IOTF-25), calculated as:  $100 * (BMI/IOTF-25)$  (12). The choice of the IOTF-25 cutoff as baseline has been addressed in a previous publication (12). In brief, results for %IOTF-30 and %CDC95 are highly comparable with those of %IOTF-25, but the latter was chosen because it is based on a widely used international upper limit for a “healthy” BMI, and sets a clear target for clinical practice. BMI z-scores were derived from Norwegian Growth Charts based on data from the Bergen Growth Study (17).

#### Dual-energy X-ray Absorptiometry

Whole-body DXA scans were performed by trained technicians at the Department of Rheumatology, Haukeland University Hospital. A Lunar Prodigy scanner (GE Medical Systems Lunar, Madison WI, USA) was used until November 2014, and a Lunar iDXA scanner (GE Medical Systems Lunar, Madison WI, USA) from November 2014. These scanners were calibrated against each other, limiting the risk of interference. The DXA equipment was calibrated daily by the technicians and once a week against a calibration phantom spine. The DXA measurements were performed with the participants lying in a supine position in light clothing and without shoes or metal containing items such as jewelry or a wrist watch. The %BF, fat mass and lean mass were derived using a software package from the manufacturer (Lunar, version 16).

#### Statistical analyses

Paired samples t-tests were used to test the statistical significance of changes in anthropometry and body composition between baseline and follow-up. To account for individual differences in the duration of follow-up, changes between baseline and follow-up were annualized prior to further processing by subtracting the baseline from the follow-up measurement and dividing by the time interval in years. The association between the annual change in %BF-DXA and the annual change in %IOTF-25, BMI and BMI z-score were assessed with scatterplots and with Pearson product moment correlation coefficients because the plots showed a linear trend. Correlation coefficients were compared with Zhou’s confidence intervals using the cocor package in the statistical program R (18). The ability of the BMI metrics to detect a reduction or increase in %BF was expressed by the sensitivity, specificity and predictive values of a positive (reduction in %BF-DXA) or negative test (increase in %BF-DXA).

Agreement between the change in the BMI metrics and the change in adiposity (%BF-DXA) was assessed with Cohen's Kappa using a dichotomized treatment response that indicated reduction or increase. Agreement analysis of the numerical response (e.g. Bland-Altman plots) was not possible because the units of measurement of the different variables were not interchangeable.

Analyses were performed with IBM SPSS Statistics version 24.0 (2016, International Business Machines Corporation, Statistical Package for the Social Sciences, Armonk, NY, USA) and R version 3.2 (R Foundation for Statistical Computing, Vienna, Austria, 2015). Age- and sex dependent z-scores and %IOTF-25 were calculated using R. P-values less than 0.05 were considered statistically significant.

#### Ethical considerations

The study has been approved by the Regional Committee for Medical and Research Ethics (REC number 2016/1913). Written informed consent was obtained from all participants and/or one of the parents, depending on the age of the participant.

## RESULTS

The median age was 11.5 (range 5.7-17.7) years at baseline and 13.9 (range 8.0-19.3) years at follow-up. Data on age, anthropometry and body composition at baseline and follow-up are listed in Table 1. The median (range) time of follow-up was 2.1 (1.0 – 4.5) years.

The annual change in %BF-DXA was found correlating somewhat stronger with the annual change in %IOTF-25 ( $r = 0.68$ ;  $p < 0.001$ ) and BMI ( $r = 0.70$ ;  $p < 0.001$ ) than with the annual change in BMI z-score ( $r = 0.57$ ;  $p < 0.001$ ). The 95% confidence interval of the difference between these correlations was statistically significant for BMI z-score vs. %IOTF-25 (0.02 – 0.23;  $p = 0.02$ ), and vs. BMI (0.03 – 0.26;  $p = 0.01$ ). The stronger correlations were partly due to the children with a large reduction ( $n = 4$ ) or large increase ( $n = 2$ ) in %BF-DXA. In children with a modest (<4%) annual change in %BF-DXA the correlation was still significant but lower for the annual change in %IOTF-25 ( $r = 0.34$ ;  $p = 0.01$ ) and BMI ( $r = 0.35$ ;  $p = 0.01$ ), and not statistically significant for the BMI z-score ( $r = 0.07$ ;  $p = 0.6$ ).

Corresponding scatterplots (Figure 1) indicate a comparable and more or less linear relation between the BMI metrics and %BF-DXA, albeit also visually influenced by children that responded well or not at all to the treatment, and a wider variability near the zero line that indicate no change.

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The percentages in the graphs indicate the sensitivity, specificity and predictive values of the corresponding variable to detect a decrease in %BF-DXA. The %IOTF-25 showed the highest sensitivity and true negative rate when compared with %BF-DXA, while the BMI had a higher specificity and true positive rate.

Cohen's Kappa of agreement between dichotomized variables of treatment success (a reduction in %BF and reduction in the BMI metric) was 0.25 for %IOTF-25 ( $p = 0.04$ ), 0.33 for the BMI ( $p < 0.01$ ), and 0.08 for the BMI z-score ( $p = 0.5$ ).

## DISCUSSION

The BMI metric %IOTF-25 has previously been suggested as a better tool to measure change in weight status among children with severe obesity (12). In the current study changes in %IOTF-25 showed somewhat better correlation and agreement with changes in %BF-DXA than BMI z-scores when analyzing longitudinal data of treatment seeking children and adolescents with severe obesity. Although the BMI ( $\text{kg}/\text{m}^2$ ) scored comparably in terms of correlation and agreement with %BF-DXA, the positive association between BMI and age makes this parameter unsuitable for the long-time follow up of growing children.

The change in absolute BMI showed the highest specificity, but this comes at the cost of a lower sensitivity. Because the BMI increases with age, the point of no change (the "zero" line) in BMI should not be 0, but a higher (age dependent) number that reflects natural growth. This natural growth is also evident from the mean annual change which is positive for the BMI and negative for the other metrics. Using an age specific BMI baseline to indicate "no change", which is basically what the %IOTF-25 corrects for, will however also decrease the specificity. For this reason, the BMI is not considered as a good outcome measure for routine monitoring of obesity treatment over long periods of time in children, but it can be used to study treatment response in studies in children with a limited age range (5).

Changes in %IOTF-25 showed a slightly higher correlation compared to changes in BMI z-scores, and also a higher sensitivity and true negative rate and better agreement (Cohen kappa), when using %BF-DXA as a common reference. Taken together, this suggests that %IOTF-25 might represent a more preferable metric for the clinical assessment of weight status in children with

severe obesity.

None of the relevant statistics were shown to be best for the BMI z-scores. This is due to the known limitation of BMI z-scores as a measure of weight status in children and adolescents with severe obesity. Several authors have addressed this issue (9-12, 19-23), and found that the BMI z-score has a poor sensitivity to detect changes in adiposity in subjects with severe obesity. Due to a skew distribution, in combination with a relatively high variability, a large range of very high BMI values corresponds to a small range of BMI z-scores (12). This is a major limitation of BMI z-scores in obesity management settings, as children or adolescents may thus change their adiposity status without a comparable change in BMI z-scores. Despite these limitations, changes in BMI z-scores are still widely used to evaluate the response in obesity treatment programs, both in clinical and research settings (13-15).

Expressing the BMI as a percentage of a certain BMI cut-off, such as %CDC95 and %IOTF-25, has been proposed as a better alternative than z-scores to assess and monitor change in adiposity over time in children with overweight or obesity (9, 11, 12, 22, 24). There is however no reason to assume that %CDC95, proposed by Flegal et al. (11), should be better or worse than %IOTF-25, but the latter is based on a widely used international overweight criterion, which enables a direct comparisons of studies.

Data on the ability of different BMI metrics to measure adiposity change is limited and inconsistent in terms of study design, statistical procedures, and duration of follow-up and study population (9, 11, 12, 19, 21-23). The present study is based on a sample of children and adolescents with severe obesity who had a broad age range (5-17 years) at baseline and were followed up for at least 12 months. The amount of change in adiposity was determined with DXA, which is a well-accepted reference method for the assessment of body composition, also in individuals with overweight or obesity (4, 25, 26).

The present study has some limitations that should be considered. We allowed an interval of up to three months between DXA and the anthropometric measurements, which potentially impairs the comparison of the BMI metrics and %BF-DXA. However, we can safely assume that the magnitude of such an impairment would similarly affect the different BMI metrics, and the comparison thus remains valid. It should also be noted that two different DXA scanners were used to measure body composition. Since these were calibrated against each other, the risk of interference is limited. The current study was not designed to evaluate the effect of the lifestyle treatment. All patients with a %BF-DXA measurement at baseline and at follow-up were included, although some of these only partially adhered to the treatment program, or were readmitted because of a negative

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weight development. This is however not important for the present analysis, since we wanted to study change in weight status irrespective of treatment success. Furthermore, we did not correct for puberty in the analysis because the pubertal stage was not systematically registered. Nevertheless, our results are applicable to clinical practice and research because the references used to interpret the BMI metrics only account for age and sex. No further adjustment for age, sex and origin of the child was considered in the analysis because of the small sample size and consequently loss of power. The presence of a few outliers may also have had large leverage on the statistical tests due to the small sample size. Without further research in larger patient groups we can therefore not rule out that relevant differences for the interpretation of the parameters might exist. Finally, although DXA is a widely used and accepted reference method for measuring body composition, there are some limitations when measuring individuals with obesity as results can be influenced by body size and pubertal progression. However, the change in fat or lean mass over time was found unbiased (27).

## **CONCLUSION**

The current study found changes in %IOTF-25 to be an overall better indicator to measure changes in %BF-DXA in children and adolescents with severe obesity when compared with BMI and BMI z-scores. Although the BMI is a measure of body mass and %BF-DXA a measure of body composition, which is a related but distinct characteristic, the BMI-metric that most closely reflects body fat should be preferable when monitoring this group of patients. Because the BMI increases naturally with age and BMI z-scores have been shown to be of limited use in this patient group, the %IOTF-25 or similar cutoff based indices have been proposed as useful alternatives. In the present study we have documented that the %IOTF-25 performs equally well, if not better, to detect changes in %BF over time. However, since cutoff based indices like the %IOTF-25 are fairly recent propositions, more research is needed to confirm our findings.

## **ACKNOWLEDGEMENTS**

We acknowledge the contribution of the staff at the Obesity Outpatient Clinic – the child section, Haukeland University Hospital, for their persistent data collection efforts.

## ABBREVIATIONS

%IOTF-25 – percentage above the International Obesity Task Force definition of overweight; BMI – body mass index; DXA – dual-energy x-ray absorptiometry; %BF – percentage body fat.

## FUNDING

No external funding was secured for this study.

## CONFLICT OF INTEREST

The authors declare no conflict of interests.

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## Table

**Table 1** Characteristics at baseline and at follow-up for 59 children (31 boys) and adolescents with obesity or severe obesity

		Baseline	Follow-up	Annual Change <sup>1</sup>	
	n	Mean ± SD	Mean ± SD	Mean ± SD	p-value*
Age (years)	59	11.6 ± 3.3	13.7 ± 3.3		<0.001
<b>Anthropometry</b>					
Weight (kg)	59	76.6 ± 25.3	88.0 ± 25.2	5.3 ± 4.3	<0.001
Weight z-score <sup>2</sup>	59	3.06 ± 0.60	3.03 ± 0.82	-0.01 ± 0.26	0.7
Height (cm)	59	153.6 ± 16.2	162.5 ± 13.4	4.2 ± 2.9	<0.001
Height z-score <sup>2</sup>	59	0.68 ± 1.26	0.53 ± 1.27	-0.07 ± 0.21	0.01
BMI (kg/m <sup>2</sup> )	59	31.4 ± 5.2	32.7 ± 5.9	0.6 ± 1.4	0.002
BMI z-score <sup>2</sup>	59	2.98 ± 0.42	2.96 ± 0.69	-0.01 ± 0.22	0.7
%IOTF-25 <sup>3</sup>	59	148.7 ± 14.8	145.5 ± 18.3	-1.6 ± 6.5	0.07
<b>Body composition determined by DXA</b>					
%BF	59	47.4 ± 4.9	46.4 ± 6.3	-0.4 ± 2.6	0.2
Fat mass (kg)	59	35.2 ± 13.1	37.6 ± 12.7	1.2 ± 3.6	0.02
Lean mass (kg)	59	38.1 ± 12.5	43.0 ± 13.1	2.3 ± 2.0	<0.001

\*p-value obtained from paired samples t-test

<sup>1</sup> (follow-up - baseline)/(time interval)

<sup>2</sup>Based on the Norwegian Growth Chart

<sup>3</sup>Calculated using the International Obesity Task Force's overweight criterion for children and adolescents.

Abbreviations: BMI, body mass index; DXA, dual-energy x-ray absorptiometry; SD, standard deviation; %BF, percentage body fat; %IOTF-25, percentage above the International Obesity Task Force's overweight criterion

## Figure legends

**Figure 1.** Annual change in %IOTF25, BMI, and BMI z-score according to the annual change in percentage body fat measured with DXA (%BF). The dashed lines indicate the boundary of an increase or decrease for each parameter. The percentages above and below the horizontal zero line are calculated on the total number of participants in whom the %BF increases (right) or decreases (left). The percentages left and right of the vertical axis are calculated on the total number of participants with an increase (numbers at the top) or decrease (numbers at the bottom) of the other variable. These numbers correspond to respectively the true positive rate (TP), false positive rate (FP), True Negative rate (TN), False negative rate (FN), sensitivity (SENS) and specificity (SPEC) of the test to detect a decrease in %BF.

