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2 Title: A simple equation to estimate body fat percentage in ~~children~~ with overweight or
3 obesity: a retrospective study.

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20 ABSTRACT

21 **Background.** Dual-energy X-ray absorptiometry (DXA) provides separate measurements of
22 fat mass, fat-free mass and bone mass, and is a quick, accurate, **and safe technique, yet one**
23 that is not readily available in routine clinical practice. Consequently, we aimed to develop
24 statistical formulas to predict fat mass (%) and fat mass index (FMI) with simple parameters
25 (age, sex, weight and height).

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26 **Methods.** We conducted a retrospective observational cross-sectional study in 416
27 overweight or obese patients aged 4 to 18 years that involved assessing adiposity by DXA
28 (fat mass percentage and FMI), body mass index (BMI), sex and age. We randomly divided
29 the sample into two parts (construction and validation). In the construction sample, we
30 developed formulas to predict fat mass and FMI using linear multiple regression models. The
31 formulas were validated in the other sample, calculating the intraclass correlation coefficient
32 via bootstrapping.

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33 **Results.** The fat mass percentage formula had a coefficient of determination of 0.65. This
34 value was **0.86** for FMI. In the validation, the constructed formulas had an intraclass
35 correlation coefficient of 0.77 for fat mass percentage and 0.92 for FMI.

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36 **Conclusions.** Our predictive formulas accurately predicted fat mass and FMI with simple
37 parameters (BMI, sex and age) **in children with overweight and obesity**. The proposed
38 methodology could be applied in other fields. Further studies are needed to externally
39 validate these formulas.

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46 INTRODUCTION

47 During childhood and adolescence, there is a balanced growth of the different body
48 components: skeletal muscle, fat, bone and viscera. Obesity involves an increase in body
49 weight combined with an imbalance between these components, with a higher proportion of
50 body fat (Ballabriga & Carrascosa, 2006), and is defined as an excess of body fat relative to
51 total body mass (Himes & Dietz, 1994). There is nearly universal consensus in defining
52 overweight as a body mass index (BMI [kg/m^2]) between the 85th and 95th percentiles and
53 obesity as a BMI at the 95th percentile or greater (Power, Lake & Cole, 1997; Prentice, 1998;
54 Serra Majem et al., 2002; Cole & Lobstein, 2012). Determinants of body fat in children and
55 adolescents include socioeconomic factors, education of the mother, physical activity, and
56 physical fitness (Moliner-Urdiales et al., 2009; van Sluijs et al., 2010; Gómez-Martínez et al.,
57 2012).

58 ~~Age-~~ and sex-specific BMI percentile ~~values are~~ easy to calculate and is strongly
59 correlated with the body fat percentage, especially for high BMI values (Colomer, 2004;
60 Koplan, Liverman & Kraak, 2005; Krebs et al., 2007). But in clinical practice, it may be
61 more useful to combine age- and sex-specific BMI values with a body fat assessment
62 capable of detecting a high degree of adiposity to avoid classifying individuals whose
63 high BMI is attributable to a relatively greater fat-free mass or an athletic build as obese
64 (Serra Majem et al., 2002; Whitlock et al., 2005). Since BMI does not follow a normal
65 distribution in the pediatric age group, several indices have been proposed as alternatives.
66 Of these, the recently described inverted BMI (iBMI [cm^2/kg]) has been referred to as the
67 most useful and accurate proxy for body fat in adults (Nevill et al., 2011). A recent study
68 in the pediatric age group that used the fat mass determined by dual-energy X-ray
69 absorptiometry (DXA) as a reference found that the iBMI followed a normal distribution
70 and was a good predictor of body fat, as was BMI, with iBMI accounting for a greater

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75 amount of the variance (Duncan et al., 2014). Although various equations have been
76 proposed to calculate body fat based on skinfolds, they are not recommended for use in
77 the pediatric population (Almeida et al., 2016; Truesdale et al., 2016).

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78 DXA enables the independent assessment of fat mass, boneless fat-free mass, and
79 bone mass (Fields & Goran, 2000; Kehayias & Valtueña, 2001) and their distribution in each
80 region of the body. DXA is considered a fast, accurate, and safe method for assessment of
81 body fat (Ellis, 2001), as it is free of the drawbacks of computerized axial tomography and
82 magnetic resonance imaging (Goulding et al., 1996). However, since it is not widely
83 available, this technique is not suitable for large-scale and longitudinal studies. For this
84 reason, several indices (BMI, iBMI, conicity index, etc.) have been proposed to estimate the
85 value obtained by DXA. Other authors have constructed multivariable prediction models that
86 estimate body fat from different skinfolds. These methods have been validated by contrasting
87 the mathematical formula with DXA (reference standard) (Silva et al., 2013; Jensen,
88 Camargo & Bergamaschi, 2016). Nonetheless, they present great difficulty in routine clinical
89 practice because skinfolds are not as simple to measure or as reproducible as the weight and
90 height of a child. For all these reasons, we aimed to develop and internally validate [intraclass
91 correlation coefficient (ICC) and bootstrapping] a statistical model based on simple
92 parameters (BMI, iBMI, sex and age) to predict body fat. Our goal was a simple tool that
93 could be applied in clinical practice to assess adiposity in children and adolescents.

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Deleted: However, we must take into account that, as in any prediction study, the use of multivariate mathematical models improves the estimation of a single parameter to be studied (body fat in our case). Consequently, o

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95 MATERIALS & METHODS

96 *Study Population*

97 Patients referred for nutritional problems to the Nutrition, Growth and Metabolism Unit of
98 the Department of Pediatrics of San Juan de Alicante University Hospital. This hospital

108 covers an area of about 220,000 inhabitants in the province of Alicante, which is located in
109 the southeast of Spain and has a total of 1,843,589 inhabitants (National Statistics Institute,
110 2016). The health system is universal and free for both children and adults. The prevalence of
111 childhood obesity in the province of Alicante is approximately 13.5-18.8% (Ruiz Pérez et al.,
112 2008). The criteria for referral by the primary care pediatrician are the lack of correlation
113 between the height and weight of the child.

Comment [SK2]: That is an odd way to express this. Why not say that they were overweight or obese? Also, "criteria" is plural. Should you "criterion" since there is only one.

114 *Study design and participants*

115 We conducted a cross-sectional observational study in patients aged 4 to 18 years who met
116 the following inclusion criteria: having had an initial referred visit to the Nutrition, Growth
117 and Metabolism Unit of San Juan de Alicante University Hospital and a DXA assessment
118 prior to the implementation of dietary measures and lifestyle changes. The exclusion criteria
119 encompassed excess weight secondary to causes other than high caloric nutrition, such as
120 growth hormone deficiency with hormone replacement therapy, syndromic obesity, obesity
121 secondary to other diseases such as hypothyroidism, protracted treatment with corticosteroids
122 or other drugs that could influence energy intake or expenditure, precocious puberty, or
123 neurologic or neuromuscular disorders preventing the patient from walking or exercising
124 normally. The data were collected between July 2007 and July 2016, and all the study
125 children were Caucasian.

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126 *Variables and measurements*

127 Our main outcome variables were body fat (% total body fat) and fat mass index (FMI, in
128 kg/m²). These were measured with a General Electric Lunar DPXN PRO™ DXA
129 densitometer (GE Healthcare, Little Chalfont, Buckinghamshire, United Kingdom). The
130 software of this device is able to obtain measurements for the total weight and percentage of
131 body fat. These parameters were used as the reference standard measurements.

134 As secondary variables we used BMI (in kg/m²), sex (male or female) and age (in
135 years). To obtain the anthropometric measurements (weight and height), we followed a
136 standardized protocol with a stadiometer accurate to 0.1 cm and a SECA scale accurate to 0.1
137 kg. Each value was measured twice by a single individual, and the mean of the two
138 measurements was used in the analysis.

139 *Sample size calculation*

140 The sample collected during the study period was 416 children. This sample was randomly
141 divided into two equal parts (n=208). The first group was used to construct a predictive
142 model (multivariable linear regression) and the second group was used to validate it.

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143 Construction: To construct a multiple linear regression model we must look at the
144 relationship between the number of subjects and the number of predictors (subject-to-variable
145 ratio). As a heuristic rule, it was considered that this ratio should be at least 50, which
146 allowed the introduction of four explanatory variables in the predictive model.

147 Validation: The sample consisted of the other 208 subjects. This sample size was very
148 satisfactory in obtaining excellent predictions, since the constructed models had four
149 predictors and coefficients of determination of 0.65 and 0.86 for fat percentage and FMI
150 respectively (Knofczynski & Mundfrom, 2008). The coefficient of determination values were
151 obtained in the construction sample and were used to determine the sample size of the
152 validation.

153 *Statistical analysis*

154 Continuous variables (BMI, FMI, age and body fat) were summarized using means and
155 standard deviations. To describe the sex variable, we calculated absolute and relative
156 frequencies. To compare the homogeneity of the construction and validation samples, we

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163 performed the t-test and the Pearson's chi-squared test. We calculated the following
164 exponentiations: bases (BMI and age) and exponents (-2, -1, 1 and 2). All the interactions
165 between sex and the exponentiation variables were obtained. In the construction sample
166 (n=208) we aimed to construct a linear regression model to predict body fat. Taking into
167 account that we could only introduce 4 explanatory variables (subject-to-variable ratio: one
168 per each fifty subjects) and had 17, we applied the following algorithm in order to select
169 them: we obtained all the possible combinations of 1, 2, 3 and 4 elements from the total (17
170 variables): 3213 combinations. In each combination we estimated the linear regression model
171 with them in order to predict the body fat and calculated its coefficient of determination. The
172 combination/model with the maximum coefficient was then selected. The goodness-of-fit of
173 the model was assessed with the ANOVA test. The model was internally validated using
174 bootstrap methodology in the validation sample, calculating the intraclass correlation
175 distribution [two fixed judges (the predicted and observed value) with absolute agreement in
176 the ratings]. In addition, the scatter plot with the estimation and the real parameter was
177 obtained. Finally, we also ~~calculated~~ the Bland & Altman ~~limits of agreement~~ (Bland &
178 Altman, 1986). The same process was applied for FMI. We set the level of statistical
179 significance at 0.05. The statistical software used was IBM SPSS Statistics 19 and R 2.13.2.

180 *Ethical considerations*

181 This study adhered to the ethical principles of the Declaration of Helsinki, and only involved
182 the performance of procedures used in everyday clinical practice. The data were processed
183 safeguarding anonymity and confidentiality, and the study was approved by the
184 corresponding Ethics Committee (Comité Ético de Investigación Clínica del Hospital
185 Universitario de San Juan de Alicante, ref 16/305). Informed consent was not requested from
186 the parents for this study, since it was part of routine clinical practice without any type of
187 intervention. The Ethics Committee approved this procedure.

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191 RESULTS

192 We analyzed a total sample of 416 children divided into two parts: 208 children in each group
193 (construction and validation). Table 1 shows the descriptive analysis obtained for each group.
194 Of note were a mean body fat of 43% and 11.7 kg/m² for FMI. No differences were observed
195 in the groups, as all the p-values were greater than 0.05.

196 The optimal model for body fat had a coefficient of determination of 0.65 and the
197 following formulas for the body fat estimation (Table 2):

198 A) Boys: $62.627 - 11245.580 \cdot \text{BMI}^{-2} - 259.114 \cdot \text{BMI}^{-1} + 2.310 \cdot \text{Age} - 0.151 \cdot \text{Age}^2$.

199 B) Girls: $62.627 - 11245.580 \cdot \text{BMI}^{-2}$.

200 For FMI the optimal model had a coefficient of determination of 0.86, and the
201 formulas for the estimation of this parameter were (Table 2):

202 A) Boys: $18.655 + 0.007 \cdot \text{BMI}^2 - 293.601 \cdot \text{BMI}^{-1} + 0.112 \cdot \text{Age} - 0.018 \cdot \text{Age}^2$.

203 B) Girls: $18.655 + 0.007 \cdot \text{BMI}^2 - 293.601 \cdot \text{BMI}^{-1}$.

204 The intraclass correlation distribution is shown in Figure 1 (internal validation).
205 Regarding the adjustment between estimations and real values, Figure 2 illustrates that both
206 values were very similar. Finally, the Bland & Altman procedure was satisfactory (Fig. 3).
207 So that our equations may be easily applied, they have been included in Supplemental Table
208 S1.

209

210 DISCUSSION

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212 *Summary*

213 ~~We constructed and validated two~~ predictive models to determine body fat and FMI ~~in~~
214 ~~children with overweight and obesity, using the values obtained by DXA as the reference~~
215 ~~standard. Both models showed excellent accuracy (ICC>0.75) (Cicchetti, 1994).~~

216 *Strengths and limitations of the study*

217 The main strength of the study ~~is~~ the easy and cost-effective calculation of body fat
218 percentage and FMI based on the widely used standard anthropometric measurements (height
219 and weight), age and sex. Although more complex techniques, such as DXA, consume little
220 time and few resources and involve a very low radiation exposure, they are not widely
221 available in health care settings and are more complicated and costly to implement. We also
222 underscore the statistical methodology followed for its construction, which took into account
223 the subject-to-variable ratio of about 6500 models. For validation, the sample size was
224 adequate to obtain excellent predictions. Bootstrapping was applied (reference method to
225 validate predictive models) and the intraclass correlation coefficient was determined instead
226 of Pearson's, since the estimate and the value obtained by DXA referred to the same variable
227 (body fat or FMI) (Steyerberg et al., 2001).

228 Regarding limitations, the study was clearly lacking in normal-weight cases (selection
229 bias), but due to ethical and cost-of-care considerations, body fat measurement using DXA
230 was not justified in children ~~of normal weight~~ and was only performed for other clinical
231 purposes, such as in patients that required a bone mineral density assessment. On the other
232 hand, information bias was minimized through the use of fully validated and calibrated
233 devices, and confounding bias was minimized through the estimation of multivariable
234 models. Thus, ~~our~~ models can only be applied in children with overweight or obesity.
235 Furthermore, although DXA is not considered the gold standard for the assessment of body

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fat because a four-component model is better (Sopher et al., 2004; Sopher, Shen & Peitrobeilli, 2005; Williams et al., 2006), DXA is generally considered to provide the most valid estimates in clinical practice (Ellis, 2001). Finally, the models only included anthropometric parameters; that is they did not consider other factors associated with body fat (Moliner-Urdiales et al., 2009; van Sluijs et al., 2010; Gómez-Martínez et al., 2012). Nevertheless, even without these other factors our predictions were still precise.

Comparison with the existing literature

When comparing our predictive models with the existing literature, we find studies that evaluate a single anthropometric parameter and other authors who developed multivariable predictive models based on skinfolds (Silva et al., 2013; Jensen, Camargo & Bergamaschi, 2016). We must bear in mind that the studies evaluating a single anthropometric parameter (circumferences of the upper arm, waist, hip and others; ratios such as waist-to-height or waist-to-hip) (Freedman et al., 2004; Freedman et al., 2005; Freedman et al., 2012; Bergman et al., 2011; Goossens et al., 2012; Boeke et al., 2013; Weber et al., 2013; Craig et al., 2014) did not assess the power of this parameter, the interactions with other variables, or the use of a combination of factors to estimate body fat, which gives greater accuracy to the results obtained in our model. Multivariable models of using skinfolds have the clinical drawback of skinfolds being difficult to measure, and the methodological drawback that they did not follow the statistical techniques that yield the highest power in the construction and validation of a multiple linear regression predictive model (interactions, powers, bootstrapping, ICC and testing of approximately 6500 models) (Silva et al., 2013; Jensen, Camargo & Bergamaschi, 2016). In light of the above, our model clearly provides greater accuracy with respect to the others published in the scientific literature.

Implications for research and practice

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Deleted: This is the fundamental objective of elaborating an estimate for a certain parameter, such as body fat or FMI. Concerning the m

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284 The diagnosis, treatment and follow-up of obesity in the pediatric age group have become a
285 global health priority. Consequently, there is great interest in the healthcare field in the
286 development of quick and accurate tools that can be used in the follow-up of these patients.
287 In this study, we developed formulas for the calculation of body fat percentage and FMI
288 based on BMI, age and sex, which facilitate monitoring of adiposity in the management of
289 these patients, reserving the use of more accurate methods such as DXA for extreme cases.

290 Regarding possible future lines of research, we encourage other authors to externally
291 validate the equations developed in this paper. The methodology used in this work can be
292 applied to create new equations for body fat or for other types of parameters, both
293 anthropometric and non-anthropometric.

294

295 CONCLUSIONS

296 Body fat percentage and FMI measured by DXA can be accurately estimated in children,
297 and adolescents with overweight and obesity using our predictive models based on BMI,
298 age and sex. Our models enable quick calculation of body fat percentage and FMI,
299 thereby simplifying and reducing the use of resources in everyday clinical practice. We
300 also highlight our methodology, which could be applied to obtain similar equations for
301 the analyzed parameters.

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305 of this paper.

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