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# External validation of a prediction model for estimating fat mass in Arab children and adolescents

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## Abstract

**Background/Aims:** Current childhood fat mass (FM) assessment techniques are not suitable for clinical and population-level adiposity assessment. A prediction model, which accurately estimates childhood FM using predictor variables of weight, height, age, sex and ethnicity, requires validation in Arab populations. We evaluate the model's performance in Kuwaiti, Lebanese and Moroccan children/adolescents.

**Methods:** Data from three cross-sectional studies on 471 individuals, aged 6–15 years, were obtained with complete information on predictors and the outcome of log transformed fat-free mass assessed by reference standard deuterium dilution (lnFFM). Country-specific predictive performance statistics of $R^2$, calibration slope and calibration-in-the-large (measures the calibration/agreement between observed and predicted lnFFM with ideal values of 1 and 0, respectively) and root mean square error (RMSE) were quantified and pooled across countries via random-effects meta-analysis. FM estimates from bioimpedance were also available for Lebanese children and were compared to the reference standard.

**Results:** The model showed strong predictive ability in all populations. Pooled $R^2$ calibration slope and calibration-in-the-large values on the original lnFFM scale were 87.73% (95% CI: 77.20, 98.26%), 0.95 (95% CI: 0.83, 1.08) and −0.03 (95% CI: −0.16, 0.11), respectively. Model intercepts were recalibrated in each country to improve accuracy; updated country-specific equations are provided. After recalibration, RMSEs on the FM scale were 1.3, 1.6 and 2.8 kg in Kuwait, Lebanon and Morocco, respectively. The RMSE from the model was lower than bioimpedance (2.4 kg) amongst Lebanese children.

**Interpretation:** The model explained a large proportion of the variance in FM, produced well-calibrated predictions and relatively low RMSEs in Arab settings. It predicted FM more accurately than bioimpedance, indicating its potential for implementation in clinical- and population-level settings, particularly in low- and middle-income countries.

**KEYWORDS**
body composition, meta-analysis, observational study, real-world evidence

## 1 | INTRODUCTION

The global prevalence of paediatric overweight and obesity is increasing rapidly, becoming a major risk factor for numerous chronic diseases of public health importance.[1] Overweight and obesity are defined by the World Health Organization as abnormal or excessive fat accumulation that presents a risk to health.[2] Historically, in the absence of more direct techniques to assess (or estimate) body fat, overweight and obesity, proxy indirect markers of body fat were relied upon. The most widely used proxy marker of body fat is body mass index (BMI) which is calculated by dividing an individual's weight by the square of their height (weight/height$^2$), and thresholded to define overweight and obesity.[3,4] However, as BMI is a weight-based proxy marker of body fat, it is unable to discriminate between fat mass (FM) and fat-free mass (FFM), which can vary markedly in children and adolescents with a given BMI.[5] Several more direct in vivo techniques now exist to assess body fat, such as magnetic resonance imaging (MRI) scanning, dual energy X-ray absorptiometry (DXA), bioelectric impedance (BIA), the four-component model and the deuterium dilution technique.[3] However, these methods can be invasive (e.g. MRI), costly (e.g. MRI and deuterium dilution) and some have limited accuracy when used for individual-level assessment (e.g. DXA and BIA), which inhibits use for routine clinical and/or public health body fat assessment.[3,6–18] Thus, BMI has remained the preferred marker of body fat in children and adolescents.

An alternative approach for assessing FM in children and adolescents, an equation that relies solely on weight, height, age, sex and ethnicity to accurately estimate FFM (and thus FM) amongst individuals aged 4–15 years, has recently been proposed. The equation was initially developed and validated within UK children and adolescents,[12,19] and was found to produce highly accurate estimates of childhood FM. Crucially, when using reference-standard deuterium dilution as a benchmark, this model assessed FM more accurately than established techniques of BIA and DXA in UK children.[12] The UK-based model equation also underwent extensive external model validation in children and adolescents in 20 other settings outside the United Kingdom and demonstrated strong predictive performance in estimating FM across all settings.[20,21]

Recent evidence has suggested that childhood overweight and obesity rates are exceptionally high across the Middle East and North Africa (MENA) region,[22,23] highlighting the need for improved childhood adiposity assessment in order to aid efforts to tackle this public health crisis. Therefore, we performed an external validation of the UK-based FM prediction model to assess its predictive performance amongst children and adolescents from three countries in the MENA region: Kuwait, Lebanon and Morocco, and (where required) aimed to produce country-specific recalibrated model equations.

## 2 | METHODS

### 2.1 | Data sources and study population

To externally validate and potentially recalibrate the UK-based prediction equation for the MENA region, data were obtained from three observational studies conducted in Kuwait,[24] Lebanon[25] and Morocco,[26] which each utilised the deuterium dilution method to assess body composition in children. Each study contributed data on deuterium assessed fat-free mass and fat mass, weight, height, sex and age for children aged between 4 and 15 years and in total included 476 children. The Lebanese study also provided data on body composition ascertained by the BIA technique (assessed using the Imp DF50 tetrapolar single frequency [200 mA at 50 kHz] electrical bioimpedance analyser).[25,27] After removing implausible (negative) values of deuterium dilution assessed fat mass ($n = 5$), the analysis dataset was made up of 471 children (193 from Kuwait, 162 from Lebanon and 116 from Morocco).

### 2.2 | Outcome and predictor assessment

The outcome of the model being validated was natural log transformed FFM (lnFFM), ascertained using reference standard deuterium dilution.[8,28] This technique was used as the outcome for the initial development of the UK-based prediction model and the previous external validations of the model.[12,19,20] There were no missing data on the outcome (lnFFM) or the predictors (weight, height, sex, age or ethnicity).

### 2.3 | Statistical analysis

Statistical analyses were conducted in Stata (version 18.0). The Transparent Reporting of a multivariable model for Individual Prognosis Or Diagnosis (TRIPOD)[29] guideline for the reporting of studies validating a multivariable prediction model was followed.

### 2.4 | Evaluation of the performance of UK-based prediction model equation

The UK-based model equation[19] was applied to all individuals within this external validation dataset, and predictions of ln(FFM) were obtained using predictors of weight, height, sex, age and ethnicity. The country-specific predictive performance of the model equation was assessed by comparing lnFFM values from the deuterium dilution technique with the predicted values of lnFFM (obtained using the UK-based model). As recommended by the TRIPOD guidelines,[29] predictive performance was assessed using the following established predictive performance statistics:

1. $R^2$—The proportion of the variance in lnFFM that is explained by the model predicted lnFFM within these childhood settings. The variance and 95% confidence interval (95% CI) for $R^2$ was estimated using the Wald-type method by Tan.[30]
2. Calibration
   a. Calibration Slope—Provides a quantification of the accuracy of the predictions of lnFFM from the model across the range of lnFFM values from deuterium dilution. The ideal slope value is 1.
   b. Calibration-in-the-large (CITL)—Measurement of the overall agreement between average model predicted values of lnFFM and average deuterium dilution assessed values of lnFFM. The ideal value of CITL is 0.
   c. Calibration plot with flexible calibration curve—Graph of deuterium dilution assessed lnFFM plotted against model predicted values of lnFFM using a smoothed curve.
3. Root mean square error (RMSE)—The average difference between model predicted lnFFM values and the deuterium dilution assessed lnFFM.

While the primary results on the model performance are presented in terms of lnFFM, the outcome of the original UK-based model, we also present the performance in terms of FFM and FM.

To summarise the performance of the UK-based model across the MENA childhood settings and obtain estimates of the average performance and between-country heterogeneity, we pooled the country-specific predictive performance measures of $R^2$ Calibration Slope and CITL using a random effects meta-analysis fitted using restricted maximum likelihood estimation (REML)[31] with the Hartung–Knapp[32] approach used to derive confidence intervals. $Tau^2$, the estimate of between-study variance, was used to summarise heterogeneity for the three pooled performance measures.[33] Model performance was also assessed by sex.

### 2.5 | Country-specific recalibration of UK-based prediction model equation

Where systematic error in the prediction of lnFFM from the UK-based model was observed across countries, we recalibrated the model's intercept term and provided updated country-specific model equations.

### 2.6 | Comparisons of FM from the prediction equation and bioelectrical impedance with estimates from deuterium dilution from Lebanon

We also compared the accuracy of FM predictions from the Hudda et al. UK-based equation with FM predictions from BIA, using the deuterium dilution method as a reference standard in Lebanese children for whom FM estimates were available from all three techniques. To do so, FM estimates from BIA were compared with FM from deuterium dilution in terms of the $R^2$ calibration (slope and CITL) and RMSE values. We then compared these predictive performance statistics to those obtained when comparing the UK-based equation to deuterium dilution (before and after recalibration).

## 3 | RESULTS

The key characteristics of included participants are summarised by country in Table 1. Almost half of the participants from Kuwait and Lebanon were girls, while most of the Moroccan participants (73%) were girls. The median age of individuals from Kuwait (8.2 years) and Lebanon (9.2 years) was lower than those from Morocco (13.9 years). These age differences were reflected in the differences across countries in average levels of height and deuterium dilution assessed fat-free mass (Table 1). However, while the average age of Kuwaiti children was lower than that of their counterparts from Lebanon, their average weight and deuterium dilution assessed fat mass were higher. Median FM amongst children from the original UK development population (8.4 kg)[19] was similar to those from Lebanon (7.8 kg) but lower than that from Kuwait and Morocco in this external validation study.

### 3.1 | Assessment of UK-based model performance in MENA region countries

When applied to these external validation data, the UK-based model equation produced (in terms of lnFFM) high $R^2$ values of 91.44% (95% CI: 89.13%–93.75%), 87.35% (95% CI: 83.71%–90.99%) and 82.76% (95% CI: 77.05%–88.47%) from Kuwait, Lebanon and Morocco, respectively (Table 2). When the country-specific $R^2$ values were pooled via random-effects meta-analysis (Figure 1), the overall $R^2$ value was 87.73% (95% CI: 77.20%–98.26%) with some evidence of between-country heterogeneity in the $R^2$ values ($tau^2 = 13.59$). RMSE values were 0.10, 0.07 and 0.08 in terms of lnFFM (Table 2). For interprebility, in terms of FM, the RMSE values from the original UK-based model were 2.2, 1.7 and 2.9 kg from Kuwait, Lebanon and Morocco, respectively. These average errors represent approximately 16.5%, 21.7% and 18.4% of the average deuterium dilution assessed FM in each of the three countries.

The UK-based model demonstrated high levels of calibration between observed and predicted lnFFM in all three countries with calibration slopes of 1.01 (95% CI: 0.96–1.05), 0.91 (95% CI: 0.86–0.97) and 0.93 (95% CI:0.85–1.01) from Kuwait, Lebanon and Morocco,

**TABLE 1** Basic summary statistics of the analysis population, by country.

| Variable | Kuwait ($N = 193$) | Lebanon ($N = 162$) | Morocco ($N = 116$) |
|---|---|---|---|
| Age (years) | 8.2 (7.6, 8.7) | 9.2 (8.6, 9.8) | 13.9 (13.3, 14.4) |
| Height (m) | 1.29 (1.25, 1.35) | 1.34 (1.28, 1.40) | 1.58 (1.51, 1.62) |
| Weight (kg) | 32.83 (26.20, 41.60) | 30.90 (26.05, 37.60) | 54.00 (44.00, 63.25) |
| DD assessed fat mass (kg) | 13.37 (8.17, 18.30) | 7.82 (5.22, 11.87) | 15.72 (9.91, 21.80) |
| DD assessed fat-free mass (kg) | 20.49 (17.71, 23.43) | 23.20 (20.52, 26.38) | 36.11 (32.58, 41.58) |
| Boys (*n*, %) | 92 (47.7) | 77 (47.5) | 32 (27.6) |
| Ethnic Group (*n*, %) | | | |
| White | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Black | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| South Asian | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Other Asian | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Other | 193 (100.0) | 162 (100.0) | 116 (100.0) |

*Note*: Values are median (25th to 75th centile) unless stated otherwise.
Abbreviation: DD, deuterium dilution.

**TABLE 2** External validation predictive performance statistics based on natural log transformed fat-free mass before and after recalibration of the intercept term, by country.

| Variable | Kuwait ($N = 193$) | Lebanon ($N = 162$) | Morocco ($N = 116$) |
|---|---|---|---|
| Before recalibration | | | |
| $R^2$ (95% CI) | 91.44 (89.13 to 93.75) | 87.35 (83.71 to 90.99) | 82.76 (77.05 to 88.47) |
| Calibration Slope (95% CI) | 1.01 (0.96 to 1.05) | 0.91 (0.86 to 0.97) | 0.93 (0.85 to 1.01) |
| Calibration-in-the-large (95% CI) | −0.08 (−0.09 to −0.07) | 0.02 (0.01 to 0.03) | −0.02 (−0.03 to −0.01) |
| RMSE | 0.10 | 0.07 | 0.08 |
| After recalibration | | | |
| $R^2$ (95% CI) | 91.44 (89.13 to 93.75) | 87.35 (83.71 to 90.99) | 82.76 (77.05 to 88.47) |
| Calibration Slope (95% CI) | 1.01 (0.96 to 1.05) | 0.91 (0.86 to 0.97) | 0.93 (0.85 to 1.01) |
| Calibration-in-the-large (95% CI) | 0.00 (−0.01 to 0.01) | 0.00 (−0.01 to 0.01) | 0.00 (−0.01 to 0.01) |
| RMSE | 0.06 | 0.07 | 0.07 |

*Note*: Hudda et al. is the fat-free mass prediction equation proposed in Hudda et al. BMJ 2019 doi: 10.1136/bmj.l4293, recalibration refers to recalibration of the intercept term.
Abbreviations: BIA, bioelectrical impedance analysis; CI, confidence interval; DD, deuterium dilution; RMSE, root mean square error of lnFFM.

respectively (Table 2). The pooled calibration slope (Figure 1) was 0.95 (95% CI: 0.83–1.08) with no evidence of between-country heterogeneity in the calibration slopes ($tau^2 = 0$). While country-specific CITL values were close to the ideal value of 0, the associated 95% confidence intervals failed to contain the ideal value of 0 in any of the settings (Table 2). When pooled, the overall pooled CITL value was close to the ideal value of zero (pooled CITL = −0.03) (Figure 1) and there was no evidence of heterogeneity in the CITL values ($tau^2 = 0$). The calibration plots demonstrated the good levels of calibration across the range of lnFFM (Figure 2) and FM values (Figure S1) within each of the three countries, including at the lower- and upper-ends of the distribution, with the flexible calibration curve close to the ideal 45 degree line of perfect calibration. However, as observed from the CITL results, the graphs demonstrated some systematic error in the prediction of lnFFM and FM within each of the settings, particularly amongst Kuwaiti children (Figure 2, Figure S1). As a result of this observed systematic error in the UK-based model's prediction of lnFFM, the model intercept was recalibrated to provide updated country-specific equations (Box 1).

After recalibration, the CITL and RMSE values on the lnFFM scale were closer to the ideal values of 0 in all three settings, with all of the country-specific 95% CIs for the CITL now containing the ideal value (Table 2). Updated calibration plots after recalibration on the lnFFM scale are provided in Figure S2. We also provide the country-specific predictive performance statistics after recalibration of the interecept on the FM scale overall (Table 3, Figure S3) and by sex (Figure S4). The RMSE values from the recalibrated model equation in terms of FM were 1.28, 1.60 and 2.76 kg from Kuwait, Lebanon and Morocco, respectively (Table 3). On the FM scale, these average errors from the recalibrated prediction model represent 9.6%, 20.5% and 17.6% of average deuterium dilution assessed FM in Kuwait, Lebanon and Morocco, respectively.

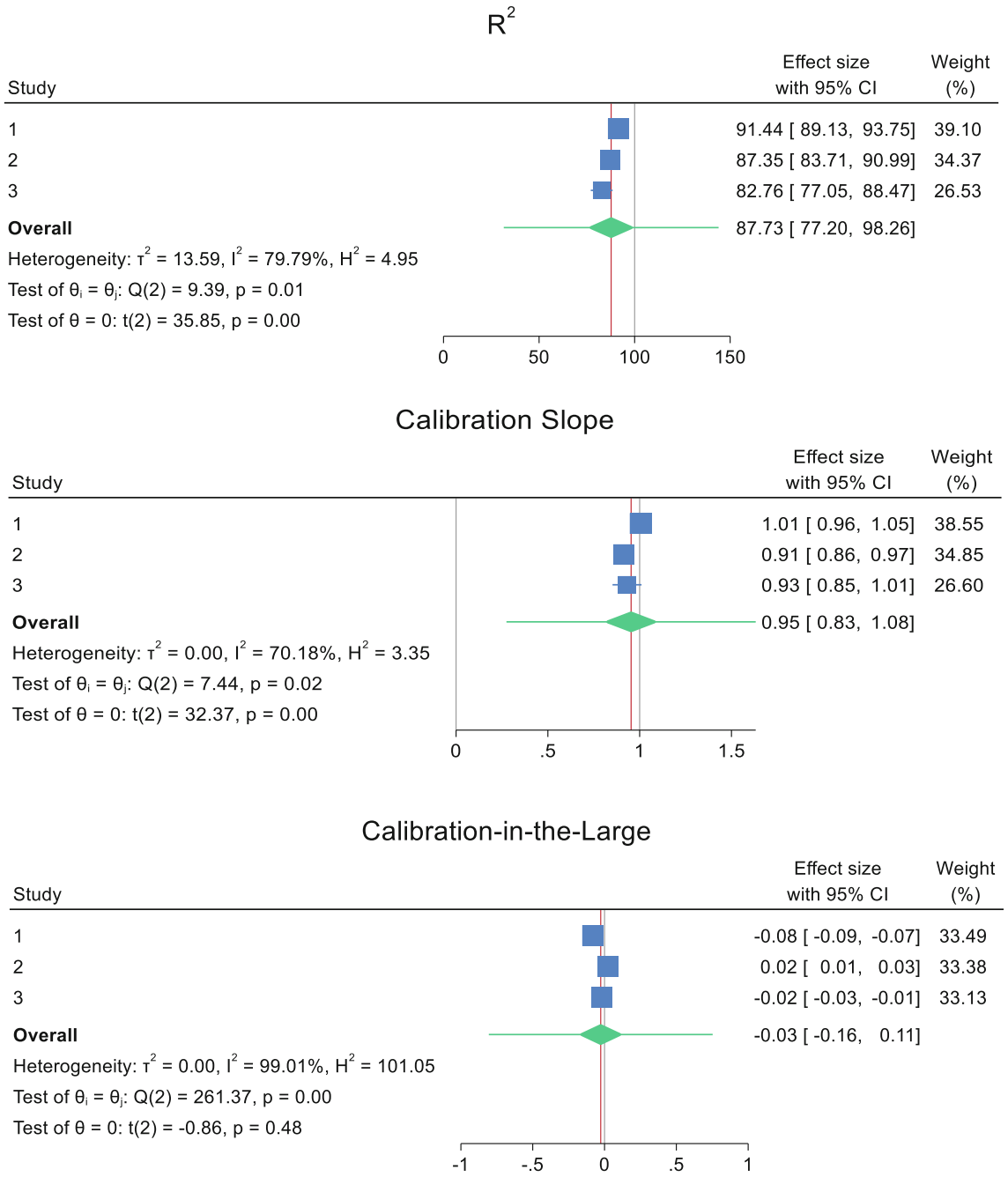


**FIGURE 1** Forest plot of $R^2$ values, calibration slope and calibration-in-the-large based on natural log transformed fat-free mass before recalibration of the intercept term, by country and overall. Study labels: 1 = Kuwait, 2 = Lebanon, 3 = Morocco. Overall estimates are from the random effect restricted maximum likelihood model with Hartung–Knapp standard errors.

### 3.2 | Comparisons of FM from the UK-based equation and bioelectrical impedance with estimates from deuterium dilution from Lebanon

Table 4 contains a comparison of the predictive performance statistics from BIA and the UK-based equation with estimates from the deuterium dilution reference standard for children from Lebanon. Figure S5 contains a calibration plot comparing FM estimates from BIA with those of deuterium dilution observed FM. When using deuterium dilution assessed FM as the reference, FM predictions obtained from BIA were not as accurate as the predictions from the UK-based equation even before local recalibration. The $R^2$ value from BIA was lower than that of the UK-based equation (87.7% vs. 91.9%), and BIA produced higher values of the CITL (1.29 kg vs. −0.52 kg) and a higher RMSE (2.36 kg vs. 1.66 kg) (Table 4). This RMSE from BIA of 2.36 kg represents 30.2% of the average deuterium dilution assessed FM (7.82 kg) in Lebanese children. These differences in accuracy were more marked after the recalibration of the UK-based equation.

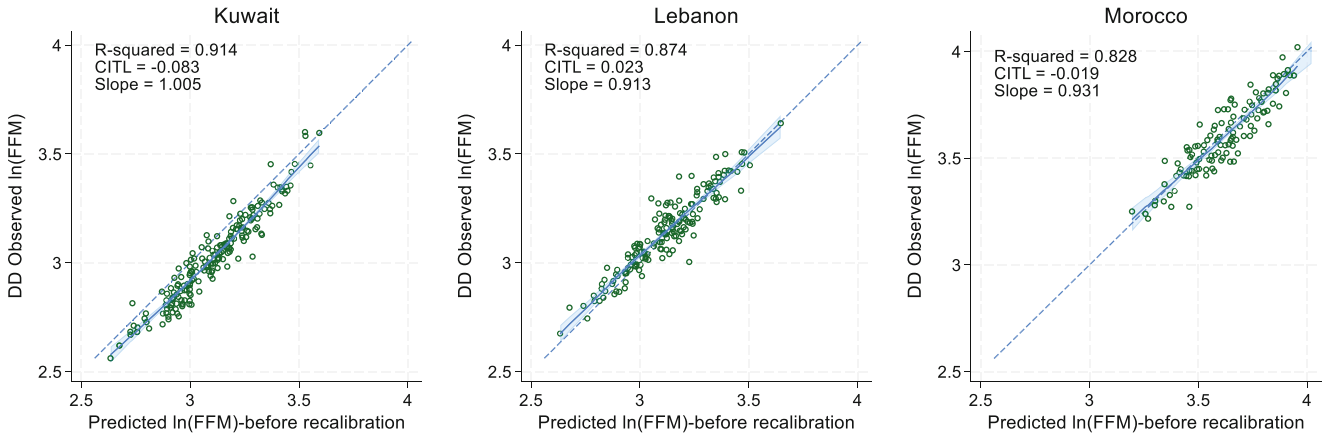


**FIGURE 2** Calibration assessment of the model based on natural log transformed fat-free mass (lnFFM) before recalibration of the intercept term, by country. Each plot shows the agreement between individuals' predicted values of lnFFM from the model (x-axis) against the individuals' observed lnFFM values (y-axis). The dashed line represents the line of equality. The solid line is the calibration curve, which is a smooth fit through the individual data points, showing the average calibration across individuals (with lighter shading the 95% CI of the curve). Slope = calibration slope (ideal value 1); CITL = calibration-in-the-large (ideal value 0).

**BOX 1 Recalibrated country-specific constant terms for the prediction of natural log transformed fat-free mass in children and adolescents.**

| Country | Constant term |
|---|---|
| Kuwait | 2.7227667 |
| Lebanon | 2.8283926 |
| Morocco | 2.7863799 |

$$\begin{aligned} Fat\ Mass = Weight - \exp\Big(&0.3073 * height^2 - 10.0155 * weight^{-1} \\ &+0.004571 * weight + 0.01408 * BA - 0.06509 * SA \\ &-0.02624 * AO - 0.01745 * Other - 0.9180 * \ln(age) \\ &+0.6488 * age^{0.5} + 0.04723 * male \\ &+Country\ specific\ Constant\ Term\ from\ above\ table\Big). \end{aligned}$$

Ln = natural logarithmic transformation, FFM = fat-free mass. BA, SA, AO and Other = 1 if child is of Black, South Asian, Other Asian or Other ethnic origins respectively and = 0 if not. If child is of unknown ethnic group, treat as of White ethnic origins. Height is measured in metres, weight in kilograms and age in years.

## 4 | DISCUSSION

### 4.1 | Principal findings

We externally validated, within three MENA countries, the predictive performance of an earlier proposed UK-based model which uses weight, height, sex, age and ethnicity to estimate childhood FM levels. The UK-based model equation showed very strong predictive ability in all the three new settings, with large percentage of variation explained, and good overall calibration of observed (deuterium dilution) and model predicted FM values. The RMSE values (in terms of FM for interprebility) were 2.19 kg in Kuwaiti children, 1.66 kg in Lebanese children and 2.86 kg in Moroccan children. This demonstrates the generalisability of the model within the MENA region, where it had not previously been extensively externally validated. While the calibration slopes were close to the ideal of 1 for all three countries, there was evidence of a small systematic error in the predictions from the UK-based model. Therefore, the model intercept was recalibrated and updated country-specific prediction equations were provided to further improve country-specific accuracy. Following recalibration, and as expected, the model performance showed improvement in the CITL and RMSE values in all three settings. Finally, amongst Lebanese children for whom BIA-assessed FM was also available, the UK-based prediction model validated in this study, both before and after local recalibration of the intercept term, produced more accurate predictions of FM than BIA, from which the CITL was 1.29 kg and the RMSE was 2.36 kg.

### 4.2 | Comparison with other studies

The UK-based prediction model[19] has previously been extensively externally validated in 19 settings outside the United Kingdom,[20,21] and has shown to produce accurate predictions of FM in children aged 4–15 years across all settings. However, it was noted that further validation within settings from the MENA region was required, as Tunisia was the only country included in the external validation.[20] Amongst Tunisian children, the predictive performance of the UK-based equation prior to recalibration of the intercept was observed to be strong with good calibration of observed and model predicted values of

**TABLE 3** External validation predictive performance statistics based on fat-free mass and fat mass after recalibration of the intercept term, by country.

| Variable | Kuwait ($N = 193$) | Lebanon ($N = 162$) | Morocco ($N = 116$) |
|---|---|---|---|
| Fat-free Mass | | | |
| $R^2$ (95% CI) | 91.16 (88.78 to 93.54) | 86.50 (82.64 to 90.37) | 82.96 (77.31 to 88.61) |
| Calibration Slope (95% CI) | 1.03 (0.99 to 1.08) | 0.91 (0.85 to 0.96) | 0.94 (0.87 to 1.02) |
| Calibration-in-the-large (95% CI) | 0.04 (−0.14 to 0.23) | −0.02 (−0.27 to 0.23) | 0.03 (−0.48 to 0.54) |
| RMSE | 1.28 | 1.60 | 2.76 |
| Fat Mass | | | |
| $R^2$ (95% CI) | 96.83 (95.96 to 97.71) | 91.94 (89.56 to 94.32) | 89.99 (86.53 to 93.44) |
| Calibration Slope (95% CI) | 0.98 (0.95 to 1.00) | 1.10 (1.05 to 1.15) | 1.08 (1.01 to 1.15) |
| Calibration-in-the-large (95% CI) | −0.04 (−0.23 to 0.14) | 0.02 (−0.23 to 0.27) | −0.03 (−0.54 to 0.48) |
| RMSE | 1.28 | 1.60 | 2.76 |

*Note*: Recalibration refers to recalibration of the intercept term.
Abbreviation: RMSE, root mean square error.

**TABLE 4** Comparison of the performance of fat mass estimates from bioelectrical impedance and the Hudda et al. equation with estimates from the deuterium dilution reference standard for children from Lebanon.

| Variable | BIA versus DD | Hudda et al. versus DD (before recalibration) | Hudda et al. versus DD (after recalibration) |
|---|---|---|---|
| Fat Mass | | | |
| $R^2$ (95% CI) | 87.66 (84.09 to 91.23) | 91.92 (89.54 to 94.31) | 91.94 (89.56 to 94.32) |
| Calibration Slope (95% CI) | 0.90 (0.85 to 0.95) | 1.08 (1.03 to 1.13) | 1.10 (1.05 to 1.15) |
| Calibration-in-the-large (95% CI) | 1.29 (0.99 to 1.60) | −0.52 (−0.76 to −0.27) | 0.02 (−0.23 to 0.27) |
| RMSE | 2.36 | 1.66 | 1.60 |

*Note*: Hudda et al. is the fat-free mass prediction equation proposed in Hudda et al. BMJ 2019 doi: 10.1136/bmj.l4293, recalibration refers to recalibration of the intercept term.
Abbreviations: BIA, bioelectrical impedance analysis; CI, confidence interval; DD, deuterium dilution; RMSE, root mean square error of FM.

lnFFM, a high $R^2$ value of 81.0% and an RMSE value of 0.08.[20] These performance statistics from Tunisia are very similar to those observed when assessing the performance of the UK-based equation in Lebanese and Moroccan children in the current study. Moreover, the updated constant term for Tunisian children of 2.7858[20] is remarkably similar to that of Moroccan children found in this study of 2.7864.

While several other studies have developed prediction models to estimate FM in childhood populations outside of the United Kingdom,[21,26,34–39] as discussed previously,[20] direct comparisons of the performance of those models with the model being validated in this study are difficult for several reasons such as models adopting different outcome variables (e.g., FM%), most models contain additional measurements (e.g., skinfold thickness, waist circumference, bioimpedance) as predictors rather than being based on readily available anthropometric and demographic predictors, studies not reporting the calibration and/or the RMSE statistics of their models. To our knowledge, just one published equation exists from the MENA region which uses only readily available information on weight, height, sex and age.[26] This study developed a model equation in Moroccan children and adults to estimate FM (via total body water estimation) and validated the developed equation in adults from Tunisia. This previous study did not report the performance of the developed equation in children separately from adults and therefore is not suitable for comparison with the UK-based childhood equation being validated in this study.

Furthermore, results presented in this study demonstrate the superior performance of the UK-based equation compared with BIA at predicting FM amongst Lebanese children (using deuterium dilution as the reference standard) were consistent with those of earlier studies which made the same comparisons amongst UK children.[7,12] Just as we found in this study, we previously also observed that when using BIA to assess FM, while $R^2$ values were high, there was evidence of miscalibration between BIA-produced FM predictions and deuterium assessed FM. Crucially, we demonstrated in our earlier study that RMSE values were lower from the UK-based model (2.6 kg) than from BIA (3.1 kg) and DXA (3.4 kg) when deuterium dilution was used as the reference standard.[12]

## 4.3 | Strengths and limitations

The current study has several strengths in validating the previously developed UK-based model equation.[19] Most importantly, the same reference standard technique which was used to assess body fat in

the UK model development study, deuterium dilution, was used as the reference standard in each of the three countries being used in this validation study. This technique is known to provide accurate, safe and minimally invasive measurements of TBW (and FFM) with very low error.[8,28] Furthermore, the sample size of each of the country-specific databases was reasonable to assess the generalisability of the UK-based model in each of the settings. There were also a few limitations. Firstly, while there were a reasonable number of individuals from each of the three settings, there was a fairly narrow age range available, with the youngest children being 8 years of age, and thus, the generalisability of the model to younger children from these settings could not be ascertained. However, as the model performed very well across the range of FM values included, it is likely the model will also provide accurate predictions of FM for children aged 5–7 years of age for whom FM values will on average be lower than their older counterparts included here. Finally, BIA assessments were only available from the Lebanese study, and therefore we could not make comparisons between the UK-based model equation and BIA across all three settings.

### 4.4 | Implications for clinicians and policymakers

The World Health Organization defines obesity by 'excessive fat deposits that can impair health', which can influence an individual's quality of life,[40] and therefore the availability of simple, accurate methods for FM assessment would represent an important advance in the field of adiposity. All available techniques to assess fat mass (and thus excessive or insufficient levels) in vivo are based upon a predictive model equation which in most cases is embedded within apparatus (such as DXA, MRI or BIA). While some of these techniques are being utilised in research settings, they are not being utilised at the clinical- or population-level largely due to either their accuracy, the time and/or cost associated with implementing these procedures in practice. However, a new predictive model was recently developed and extensively validated which, as it only requires information on childhood age, sex, weight, height and ethnicity, can easily be integrated into clinical- and population-level practice with no additional monetary or time burdens. In MENA region settings where electronic medical systems are in routine use at the clinical- and population-level, the validated model equation can be programmed into existing electronic software to automatically generate the estimated FM values for children where information on weight, height, sex and age are available. In settings where electronic medical systems are still not routinely utilised, then a Microsoft Excel based calculator has been developed (Data S2) to quickly and easily estimate FM based on the inserted values of weight, height, sex and age. The findings of this external validation study emphasise the strong predictive ability of the developed UK-based model in three new childhood settings from the MENA region across a range of FM values and ages. While the country-specific RMSE values from the model, particularly when presented as a proportion of the average deuterium dilution assessed FM levels, appear to be considerable, this magnitude of error is considerable lower than that produced from other widely accepted and utilised body composition assessment methods of BIA (as shown amongst Lebanese children in this study and UK children in our earlier study[12]) and DXA (in our earlier study[12]). Therefore, the consistently high performance of the model at predicting FM across more than 20 settings further strengthens conclusions that, particularly after local-level recalibration, the model can be used to accurately assess body composition at the individual-level, where it outperforms established current methods of BIA and DXA. At the population-level, where given the extremely high reported prevalence of obesity, its related complications and consequences within the MENA region, this model can play a valuable role in providing improved FM assessment for epidemiological and public health obesity research and policy. For example, the model can provide accurate childhood FM assessment in order to (i) quantify associations between childhood body composition and short- and long-term disease risk, (ii) assess geographical, ethnic, socio-economic and temporal variations in FM within surveillance and monitoring initiatives from MENA region settings and (iii) assess the efficacy and effectiveness of novel interventions for the prevention of childhood obesity using FM (predicted from the model) as the outcome measure of interest as opposed to weight-based proxy measures.

### 4.5 | Further research

Further external validation in other MENA region settings would add to the model's generalisability, particularly including Arab children under the age of 8 years where deuterium dilution reference data are currently lacking and settings within the region of different socio-economic groups and/or those with different dietary patterns. Furthermore, to reduce RMSE further and thus improve the precision of individual-level predictions, additional predictors could be identified that add predictive value over those included in our models; ideally, these should also be readily available or easily measured variables to ensure the model retains easy implementation. Comparisons between DD, BIA and the prediction model in other MENA settings in the future would also be of value to further demonstrate the superiority of the model over BIA for total body FM assessment. Additionally, the development of sex- and age-specific FM reference values, based upon prospectively associated disease risks, would allow individuals to be classified into groups based on future disease risk attributable to their current FM levels, as opposed to current centile-based approaches to classify FM.[41]

#### AUTHOR CONTRIBUTIONS

Study design—Hudda MT, Al-Ati T. Data contributors—Al-Ati T, El Kari K, Nasreddine L. Data analysis—Hudda MT. Data interpretation—All authors. Drafting manuscript—Hudda MT. Critical evaluation and revision of manuscript—All authors.

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## CONFLICT OF INTEREST STATEMENT

The authors confirm we have no competing interests.

## PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.16281.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are from three independent research studies, each with their own ethical approvals and data sharing legislations. The PIs of each of the three studies [Kuwait: T Al-Ati, Morocco: K El Kari, Lebanon: L Nasreddine] should be contacted for data requests via the corresponding author.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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