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Development and validation of a novel paediatric weight estimation equation in multinational cohorts of sick children

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Short Title: International paediatric weight prediction equation

Abbreviations: Advanced Paediatric Life Support (APLS), European Resuscitation Council (ERC), Children's European Estimator of Weight (CEEW), mid-upper arm circumference (MUAC)

Key Words: Weight estimation equations, Paediatrics

Abstract

Aim: In sick children who are unable to be weighed estimation of weight is often required, but the routinely used equations lack accuracy and precision. This study aimed to develop a novel equation (Children's European Estimator of Weight-CEEW) using measurements of mid-upper arm circumference (MUAC) and other predictors in multinational groups of sick children in Europe.

Methods: Weight estimation equations were developed in 2,086 children from the UK, Greece and the Netherlands, using a combination of demographics, MUAC and height measurements. The final CEEW equations were compared against the performance of the European Resuscitation Council (ERC), Advanced Paediatric Life Support (APLS) and the Cattermole equations.

Results: Two final CEEW equations were developed, incorporating measurements of age, gender and MUAC, with (CEEW1) or without (CEEW2) the inclusion of height. Both equations presented very high coefficients of determination (R^2>96.5%), minimal mean prediction error and narrower limits of agreement than the comparator equations. 88% (CEEW1) and 77% (CEEW2) of weight estimates fell within 15% of measured body weight. These figures compared with less than 57%, 57% and 37% for the ERC, APLS and Cattermole equations respectively.

Conclusion: The CEEW equations performed substantially better than other routinely used equations for weight estimation. An electronic application for mobile use is presented.

Introduction

Measurement of body weight in sick children is essential for calculation of resuscitation fluid volumes, defibrillation energy settings and emergency drug dosages; particularly in those drugs with a narrow therapeutic window. Measuring weight with scales is undoubtedly the 'gold standard' and should be applied where possible. However, there are clinical situations where measuring the weight of a sick child might not be possible, such as in critical care or during their initial resuscitation and stabilisation in emergency medicine.

A European survey in paediatric critical care departments showed that while 97% of units used body weight, a weighing protocol was present in only 12% of these, and weight was often predicted rather than measured [1]. Prediction models have gained wide acceptance with several equations available to quickly estimate weight. Those most commonly used are endorsed by the European Resuscitation Council (ERC) and the Advanced Paediatric Life Support (APLS) course and are based solely on the age of the child [2-4]. While these are easy to compute, substantial evidence suggests these are frequently inaccurate, particularly when used for individual patient estimates [2-4]. The advent of mobile applications enables use of accurate, complex mathematical algorithms to predict weight, while minimising computation errors.

This study aimed to develop a set of equations (Children's European Estimator of Weight-CEEW) to predict weight using a combination of demographics, height and mid-upper arm circumference (MUAC), a dynamic proxy for body size which is convenient to measure in the emergency setting. The performance of the CEEW equations was compared against other popular methods in multinational cohorts of sick children. We also developed and present an electronic application for free mobile use of the CEEW equation.

Methods

Subjects

To develop the CEEW equations, sick children (0.1 to 18 years) were recruited from the Emergency Department of the Royal Hospital for Sick Children, Glasgow. Data were merged with datasets from independent studies in sick children in the United Kingdom (Royal Hospital for Sick Children, Glasgow), Greece (Hippokration Hospital, Thessaloniki) and the Netherlands (Erasmus MC-Sophia Children's Hospital, Rotterdam) [5, 6].

For all patients, demographics and disease information were collected from medical notes and via face-to-face interview. Presence of chronic conditions likely to affect nutritional status (e.g. Crohn's disease) was recorded as binary response. Body weight and length/height were measured according to the World Health Organisation standards and as described previously [7]. MUAC was measured, to the nearest 0.1 cm, at the mid-point between the acromion process and the olecranon [8].

Development of the CEEW equation

Stepwise linear regression analysis was used to construct predictive models for weight using age, gender, presence of chronic illness likely to affect nutritional status and MUAC. Height was also considered as a predictor of weight, but as this might be difficult to measure in acutely unwell children, separate models were produced with (CEEW1) and without (CEEW2) inclusion of height. Data were transformed on the logarithmic scale and polynomials were used to improve model fit, as measured by the coefficient of determination and distribution of residuals.

The predictive ability of the models and β-coefficients of each predictor were tested using bootstrapping in the R statistical package. Five hundred bootstrap datasets were constructed using a random sample of half of the data to fit the regression model and the other half of the sample to test the predictive ability. Results were averaged over the 500 bootstraps. Agreement between predicted and measured weights was calculated using 95% limits of agreement.

Performance of other existing weight prediction equations

The predictive ability of the ERC and the APLS weight prediction equations, commonly used in clinical practice [9], and an equation based on measurements of MUAC (developed by Cattermole, in healthy Hong Kong Chinese children) [10] were tested in the same cohort of patients. The mean prediction error (accuracy) and 95% limits of agreement between measured and predicted weight (precision), were calculated for the ERC, APLS and the Cattermole equations and displayed graphically on Bland-Altman plots. Prediction error was expressed in mass of weight (kg) and as a percentage (%) of measured weight. The percentages of patients with predicted values falling within 10%, 15% and 20% of the measured weight (error bands) were calculated.

Ethical considerations

Approval to carry out the study was obtained by the local research ethics committee (12/WS/0154). In all cases, carers and children (when age appropriate) provided signed informed consent according to Good Clinical Practice for research.

Results

Subject characteristics

Data from 2,086 UK, Dutch and Greek participants (males: 1,200, 58%) were used in the development of the CEEW equation. Four hundred and twenty four participants

(20.3%) were infants (< 1 y). Eight percent were obese and six percent had short stature or were underweight (Table 1).

Development and performance of the CEEW equations

Age, gender, height and MUAC were all significant predictors of weight and were included in the multivariate model. Presence of a chronic illness likely to affect nutritional status was not a significant predictor of weight. Multiple multivariate models were tested with stepwise inclusion of predictors. Height explained the gender effect on prediction of weight; hence this became non-significant in multivariate analysis. Two final CEEW equations were produced: CEEW1, which includes height/length measurements; and CEEW2, where height was replaced by gender.

CEEW1: $\text{Ln(weight)} = 0.0151222388 \times \text{Age} - 0.0011458885 \times \text{Age}^2 + 0.2967431897 \times \text{MUAC} - 0.0104572693 \times \text{MUAC}^2 + 0.0001381567 \times \text{MUAC}^3 + 0.0149652312 \times \text{Height} - 1.4955305740$

CEEW2: $\text{Ln(weight)} = 0.1443608977 \times \text{Age} - 0.0040395021 \times \text{Age}^2 + 0.4223311859 \times \text{MUAC} - 0.0148641297 \times \text{MUAC}^2 + 0.0001923541 \times \text{MUAC}^3 + 0.0258703205 \times \text{Gender} - 1.6251030158$

Both of the CEEW equations presented very high (>96.5%) coefficients of determination (Table 2). The CEEW equations performed better than the comparator equations, presenting the lowest mean bias and the narrowest limits of agreement; hence the greatest precision on per subject estimations (Table 2 and Supplementary Figure 1). The proportions of estimated body weights falling within 10%, 15% and 20% of actual measurements were superior for the CEEW equations than the comparator equations, particularly for CEEW1 (Table 2). The proportion of subjects with weight estimation within 15% of the true value was 77% for CEEW2, 88% for CEEW1, 57% for ERC, 57% for APLS, and 37% for Cattermole (Table 2). The performance of the ERC, APLS and the Cattermole equations was similar in each of the international cohorts (Supplementary Table 1).

Discussion

In this study, we have proven that the CEEW equations, which incorporate a dynamic, indirect measurement of body size, perform better than the current equations used in clinical practice and an alternative equation using MUAC.

This was demonstrated by the tighter limits of agreement and a higher percentage of estimated weights falling within each of the error bands. Collectively, these findings suggest the accuracy of the CEEW method is superior, particularly in terms of individual estimates, which are clinically more important than group means. The inclusion of multinational European cohorts also offers confidence that the CEEW equation is likely to be equally valid in other ethnicities of the European continent.

In this study two CEEW equations were presented; with (CEEW1) and without (CEEW2) inclusion of height, with the former presenting the best performance. Paediatric resuscitation is a busy and often stressful environment, where simple methods are required for quick results, particularly those involving calculations. We suggest that CEEW2 is more appropriate for this setting, as measuring height/length may be time consuming in very unwell children unable to bear weight. Instead, CEEW1 may be more useful in the paediatric critical care unit, where appropriate equipment for measuring height/length is likely to be available.

The level of accuracy required from a weight estimation equation remains the subject of debate, particularly when some of our current knowledge on drug dosages in paediatric medicine is extrapolated from adult pharmacokinetic studies. In current practice, we routinely weigh children where possible, and calculate drug dosages based on a precise measurement of body weight. Therefore, a weight estimate close to the actual measurement of the patient should be considered the best. Furthermore, the implications of an “inaccurate” estimate of weight are likely to extend beyond the direct effects of individual drug dosages in the Emergency Department (related to efficacy or toxicity in drugs with a narrow therapeutic window), to cumulative effects on fluid balance, sedation and nutritional support in the critical care unit. Hence, a 'reasonable' estimate of weight is becoming less acceptable, particularly given that polypharmacy is now common and pharmacokinetic data are sometimes incomplete. We should, where possible, strive for improved accuracy. This may affect long-term outcomes and healthcare expenditure in patients with lengthy hospital admissions in critical care and other specialties. Such aspects should be explored formally in future research.

The CEEW equations are complex and are therefore impractical for quick mental calculations. New technology and electronic applications overcome these limitations and allow an easy, quick and accurate approach which also aligns with recent initiatives for "paperlite" healthcare services. In this study, a free application for mobile telephone and computer use was developed to enable rapid and error free computation of the CEEW equations in the clinical setting. The algorithms of the CEEW equations could also be incorporated in other electronic applications or into patient's electronic records (Supplementary Figure 2). https://itunes.apple.com/us/app/CEEW-paed-calculator/id964966580?ls=1&mt=8

Conclusions

Compared with the current equations in routine use, the CEEW equations provide the most precise method of weight estimation, and are also applicable to the entire paediatric age range. Future research should aim to assess the performance of the CEEW equation in routine clinical practice, and its impact on patient care and clinical outcomes.

Conflicts of Interest: None of the authors have conflicts of interest to disclose

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Figure Legends

Figure 1: Bland-Altman plots displaying mean agreement and 95% limits of agreement between estimated and actual measurements of weight

Panel A): Mean absolute (kg) prediction error and B) percentage (% of measured weight) weight prediction error

Supplementary Figure Legends

Supplementary Figure 1: Linear regression analysis between measured and predicted weight for each equation

Supplementary Figure 2: The interface of the CEEW application

Table 1

Table 1: Demographics and anthropometry of the international cohorts of sick children

	UK *(n=1212)*		**Dutch** *(n=363)*		**Greek** *(n=511)*		**Total** *(n=2086)*	
	#	%	#	%	#	%	#	%
Gender (M)	682	56.3	233	64.2	285	55.8	1200	57.5
Age, year (mean, SD)	6.3	4.8	5.6	5.3	5.3	4.6	5.9	4.9
ERC								
< 1 year	218	18.0	111	30.6	93	18.2	422	20.2
1 to 10 years	729	60.2	176	48.5	335	65.6	1240	59.4
>10 years	265	21.9	76	20.9	83	16.2	424	20.3
APLS								
< 1 month	18	1.5	1	0.3	0	0.0	19	0.9
1 to 12 months	200	16.5	110	30.3	93	18.4	403	19.3
1 to 5 years	418	34.5	106	29.2	231	45.0	755	36.2
6 to 12 years	439	36.2	97	26.7	137	26.8	673	32.3
>12 years	137	11.3	49	13.5	50	9.8	236	11.3
Cattermole								
< 1 year	218	18.0	111	30.6	93	18.2	422	20.2
1 to 11 years	804	66.3	192	52.9	351	68.7	1347	64.6
> 11 years	190	15.7	60	16.5	67	13.1	317	15.2

BMI SDS	0.25	1.3	-0.23	1.5	0.12	1.3	0.13	1.3
Underweight (n, %)	62	5.1	38	10.5	26	5.1	126	6.0
Obese (n, %)	116	9.6	21	5.8	37	7.2	174	8.3
Short stature (n, %)	83	6.8	18	5.0	30	5.9	131	6.3

ERC: European Resuscitation Council; APLS: Advanced Paediatric Life Support; Cattermole; IQR: interquartile range; SDS: Standard deviation score; Short stature and underweight were defined as height and BMI z-scores below - 2 SD respectively; Obese status was defined as a BMI zscore higher than 2 SD.

Table 2

Table 2: Performance of the CEEW and other popular weight prediction equations in multinational cohorts of hospitalised children in Europe

	CEEW1	**CEEW2**	**ERC**	**A**
Mean prediction error (kg)	0.05	0.16	-3.1	-
Limits of agreement (kg)	-7.0: 7.1	-8.4 : 8.7	-14.1 : 8.0	-11.0
Mean prediction error (%)	-0.52	-0.95	-9.8	-
Limits of agreement (%)	-20.5 : 19.4	-28.6 : 26.7	-43.4 : 23.8	-40.7
Predicted weight error bands				
10% of true weight	74.7	57.2	40.0	3
15% of true weight	88.4	77.0	56.5	5
20% of true weight	94.2	87.2	71.3	7

CEEW: Children's European Estimator of Weight; ERC: European Resuscitation Council; APLS: Advanced Paediatric Life Support

CEEW1: $\mathrm{Ln(weight)} = 0.0151222388 \times \mathrm{Age} - 0.0011458885 \times \mathrm{Age}^2 + 0.2967431897 \times \mathrm{MUAC} - 0.0104572693 \times \mathrm{MUAC}^2 + 0.0001381567 \times \mathrm{MUAC}^3 + 0.0149652312 \times \mathrm{Height} - 1.4955305740$

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Supplementary Table 1

Supplementary Fig 1

Supplementary Fig 2

***Conflict of Interest Statement**

Development and validation of a novel paediatric weight estimation equation in multinational cohorts of sick children

Conflicts of Interest: None of the authors have conflicts of interest to disclose