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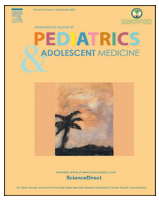

Full length article

Estimation of body surface area in neonates, infants, and children using body weight alone

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ABSTRACT

Background: The aim of this study was to use Body Surface Area (BSA) data calculated with the Mosteller equation to test potential new equations that estimate BSA using Body Weight (BW) alone in children aged 0–18 years.
Mosteller's equation, the golden standard at our hospital, was used to calculate the BSA in infants and children aged 0–18 years using BW and height data from 27,440 hospital visits by 20,635 patients over one year.
Methods: The best fit of three nonlinear regression equations (third-order polynomial, Meeh-type, and modified Boyd self-adjusting-type) to a plot of the calculated Mosteller BSA values versus BW was then investigated. The correlation between the BSA values estimated by these equations and the Mosteller BSA values was established by the Spearman rank correlation test. Bias and precision were evaluated as outlined by Sheiner and Beal. Measured and estimated BSA values were compared using the Eksborg plot.
Results: The estimated BSA values from all three equations and the BSA values from the Mosteller equation were closely correlated ($P < .0001$). The third-order polynomial and Meeh-type equations overestimated BSA by 0.13% and 0.40%, respectively, while the Boyd self-adjusted-type equation underestimated BSA by 0.060%. For the entire pediatric population, the best fit was obtained with the Meeh-type equation: 99.2% of the Meeh/Mosteller BSA ratios were within the range of 0.9–1.1 when compared with 98.3% and 97.2% for the polynomial and Boyd-type equations, respectively.
Conclusion: A single Meeh-type equation can be used to predict the results of Mosteller equation when H is not available with high precision and accuracy in children aged 0–18 years, including term neonates. We now plan to include the results of this study in CPOE systems in Sweden to improve drug dosage in all children.

1. Introduction

It has been established that many physiological processes, such as oxygen consumption [1], cardiac index [2,3], basal metabolic rate [4–6], and blood volume [7], are correlated with body surface area (BSA). Schwartz et al. and Blake et al. [8,9] also found a correlation between BSA and glomerular filtration rate, but this has been questioned by Dooley et al. [10] The BSA is also used as a prognostic indicator for adverse outcomes in chronic heart failure patients [11]. For burn injuries, accurate estimation of BSA, in combination with the segmentation of the body to estimate the percentage affected (the Wallace Rule of Nines), is essential for determining the initial management of the patient, e.g., for estimating fluid requirements and nutritional needs [12–14].

Pharmacokinetic parameters in pediatric patients, e.g., clearance, are usually more closely correlated with BSA than with body weight (BW) or height (H) [15–18]. The use of BSA makes a considerable contribution to optimizing pediatric drug dosage, but

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every substance is unique and the impact of BSA can vary. Bartelink et al. have presented guidelines for adjusting pediatric dosages on the basis of developmental physiology and pharmacokinetic considerations [19]. BSA can be measured with high precision and accuracy by using a three-dimensional (3D) scan, but this technique is only rarely used in the clinic [20–22].

The interest in calculating BSA dates back to 1879, when Meeh constructed the first available BSA formula using only BW [23]. Later, Boyd obtained direct measurements of BSA and constructed an equation to calculate BSA based on BW alone [24]. A number of equations have also been derived for estimating BSA from both BW and H [25]. DuBois and DuBois were the first to construct a BSA equation, by including H as an additional variable to BW [26]. In clinical practice, the DuBois equation has often been replaced by a simplified equation developed by Mosteller [27], but computer-based systems are now able to estimate BSA from many different equations. We validated the Mosteller equation in children of various ages and found that it underestimates BSA by 4% versus measured BSA values [28]. Astrid Lindgrens Children's Hospital provides highly advanced specialized care for young patients. The hospital is specialized, e.g., in pediatric emergency, neonatal and pediatric intensive care, pediatric surgery, and oncology.

Recording the BW of pediatric patients is mandatory in the Computerized Physician Order Entry (CPOE) form at the Astrid Lindgren Children's Hospital at Karolinska University Hospital, Stockholm, while the measurement of H is neither mandatory nor routinely recorded in the CPOE.

The Mosteller equation [27] is used at the Karolinska University Hospital to calculate the BSA from the BW and H, but it would be advantageous to estimate the BSA from the BW alone if the H of the patient cannot be measured, e.g., in emergency situations.

The body constitution has changed over the years. Thus, there might be a need to modify existing equations to suit pediatric patients of different ethnic/racial backgrounds living in Sweden.

The aim of this study was to calculate BSA for children belonging to a particular age range by using the Mosteller equation (BW + H) as currently used in the clinical setting, and to test three equations by using the nonlinear regression [29] that uses BW alone. A modified Boyd self-adjusting equation, a modified Meeh type equation, and a polynomial equation are potential alternatives for implementation of the CPOE system.

2. Materials and methods

The study was approved by the local ethics committee (Dnr: 2015/2136-31/1).

Registration data, including BW, H, gender, and birth date, for all children aged 0–18 years admitted to Karolinska Hospital from January 1, 2013 to December 31, 2013 were extracted from the electronic health record (EHR) of the Karolinska data warehouse (KARDA) on the day of registration or up to seven days after registration and included in an excel file**.** Patients older than one year of age were included in the study only for their first admission, with both BW and H recorded. Data from pediatric patients younger than one year of age were included for all hospital admissions with both BW and H recorded. Patients with missing information concerning gender in the EHR and with body mass index (BMI) above 70 were excluded from the study on the recommendation of the senior consultant for pediatric endocrinology. We did not manually correct any patient data in the excel file. BSA was calculated using the Mosteller equation:

$$\mathrm{BSA}\left(\mathrm{m}^2\right) \cdot = \cdot(\mathrm{BW} \cdot (\mathrm{kg}) \cdot * \cdot \mathrm{H} \cdot (\mathrm{cm})/3600)^{0.5}$$

The calculated BSA values were plotted versus BW. BSA was then estimated from the BW by nonlinear regression (weighted by 1/Y) in accordance with recommendations by Motulsky et al. [29], using three equations:

Third order polynomial equation: BSA=B0+ B1*BW + B2*BW [**2**]+ B3*BW [**3**].

Meeh-type equation: $\mathrm{BSA} = \mathrm{A}*\mathrm{BW}^{\mathbf{B}}$

Boyd self-adjusting-type equation: $\mathrm{BSA} = \mathrm{A}*\mathrm{BW}^{(\mathbf{B}\_\mathbf{C}*\mathbf{logBW})}$.

where A, B, and C are regression coefficients. The equations of Meeh and Boyd were, thus, modified with new regression coefficients optimized for our patient population.

For closer examination of the results, the patients were divided into four age groups: neonates (0 – 28 days), infants (>28 days – 2 years), children (>2 – 12 years), and adolescents (>12 – 18) years as suggested by the European Medicines Agency [30]. The BSA estimates from all three equations were compared with BSA values calculated by the Mosteller equation. The equation presenting BSA values closest to the formula of Mosteller in all age groups, particularly in newborns and younger children, will be chosen as the golden standard equation in our hospital.

3. Statistics

The data were handled by Microsoft Office Excel 2016 (Microsoft Corporation, Redmond, Washington, USA). The nonlinear regression procedure (weighted by 1/Y) was carried out using the GraphPad Prism version 5.04 (GraphPad Software, Inc. La Jolla, CA, USA).

The Friedman test with Dunn's multiple comparison test was used for the comparison of several related observations and the Mann-Whitney U test was used for the comparison of data from two independent populations. Correlation was established by the Spearman rank correlation test. Results from the nonlinear regression procedure were evaluated as outlined by Sheiner and Biel and by using the Eksborg plot [31,32]. All statistical tests were two-sided and p-values less than 0.05 were considered to be statistically significant.

4. Results

Information from 95,593 hospital admissions (43,401 patients; 18,271 females and 25,114 males; 16 patients without information concerning gender) were extracted from KARDA from January 1, 2013 to December 31, 2013. Ninety-five and eighty-nine percent of the files contained information concerning BW in the age groups 0–1 year and >1–18 years, respectively, while about 55% did not have information concerning H. In the age group 0–1 years, information concerning BW or H was missing for 300 and 4,639 patients, respectively, for their first hospital visit in 2013. The inclusion criteria (information concerning BW, H, and gender) were fulfilled for 10,327 hospital admissions (44%; 4,526 female and 5,801 male patients) of 3,522 patients (49%; 1,481 female and 2,041 male patients). In the age group >1–18 years, 17,113 patients (47%; 7,290 female and 9,823 male patients) were included at the first hospital admission when information concerning BW, H, and gender were recorded.

The total number of extracted recordings and the number of excluded and included hospital admissions for pediatric patients in the two study groups (0–1 years and 1–18 years) are shown in Fig. 1.

Demographic data for the included patients are presented in Table 1.

BSA was estimated from the BW using three nonlinear regression equations: a third-order polynomial equation, a Meeh-type equation [23], and a Boyd self-adjusting-type equation [24]. The results of the curve-fitting procedures are presented in Table 2 and

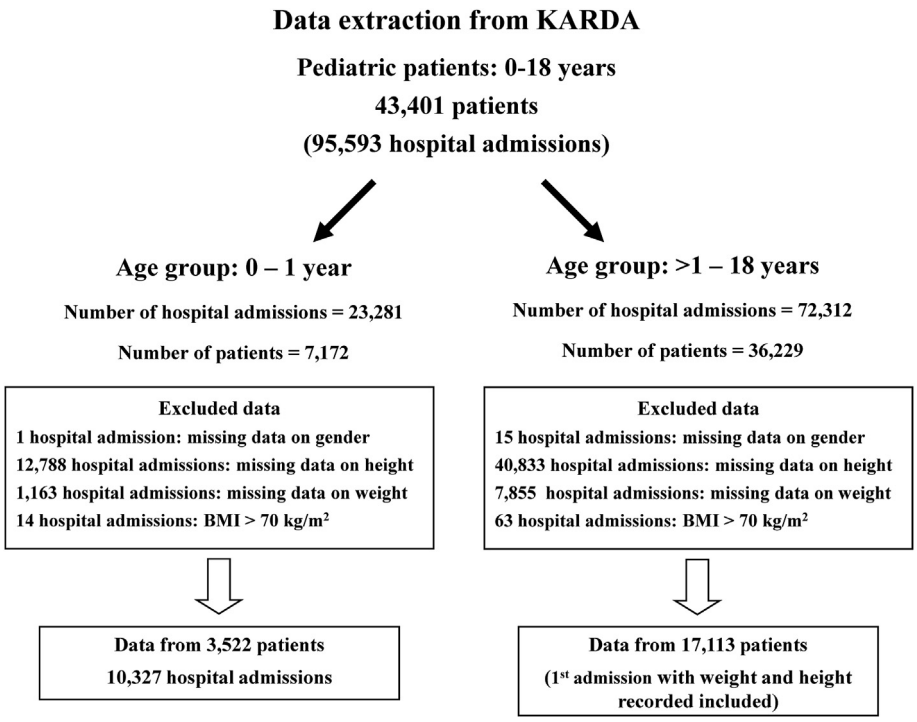

Fig. 1. Consort flow diagram.

Table 1
Demographic data for included patients.

Patients 0–1 years (1st admission)		
Males, n	2,041	
Females, n	1,481	
Body surface area (m^2)	0.27	(from 0.21 to 0.37)
Body weight (kg)	4.55	(from 3.26 to 7.35)
Height (cm)	55	(from 50 to 66)
Body mass index ($kg*m^{-2}$)	14.9	(from 13.0 to 16.7)
Age (years)	0.12	(from 0.016 to 0.50)
Patients > 1–18 years		
Males, n	9,823	
Females, n	7,290	
Body surface area (m^2)	0.93	(from 0.65 to 1.35)
Body weight (kg)	25	(from 15.5 to 43.3)
Height (cm)	124	(from 98.5 to 151)
Body mass index ($kg*m^{-2}$)	16.9	(from 15.5 to 19.3)
Age (years)	7.25	(from 3.45 to 11.9)

Data are expressed as median values (IQR)

Fig. 2.

The BSA values estimated with the three equations using BW alone and the BSA values estimated with the Mosteller equation using BW and H were closely correlated. The BSA values estimated from BW using the three equations were similar for patients weighing up to 120 kg, Fig. 2A. For patients weighing more than 120 kg, all three equations appeared to overestimate the BSA; this was particularly noticeable with the Meeh-type equation. Detailed information from patients with BW below 10 kg is presented in Fig. 2B. The three equations resulted in similar estimates of BSA for patients weighing from >2 kg to 10 kg. The Meeh- and Boyd-type equations also appeared to give satisfactory estimations of BSA from the BW of patients in the range of 1.4–2 kg.

Data analysis according to the principles given by Sheiner and Beil showed that the third order polynomial and Meeh-type equations overestimated BSA (Mean Prediction Error (MPE %) = 0.13% and 0.40%, respectively), while the Boyd self-adjusted-type equation underestimated BSA (MPE% = −0.060%). The precision, expressed as Root Mean Square Prediction Error (RMSE%), for the third order polynomial, Meeh-type, and Boyd self-adjusted-type equations was 3.77%, 3.78%, and 4.30%, respectively.

The evaluation of BSA values estimated from BW + H (Mosteller equation) and from BW alone by using the Eksborg plot showed that all three tested equations reliably estimated BSA from BW alone, Table 3.

The Boyd self-adjusting-type equation seems to be slightly less suitable for estimating BSA in infants. In the total pediatric population, the quotients of BW alone/BW + H showed that the Meeh-type equation had the best fit, with 99.2% of the quotients within the generally accepted range of 0.90–1.10 when compared with 98.3% and 97.2% for the polynomial and Boyd-type equations, respectively. The Meeh-type equation is therefore recommended

Table 2
Results from nonlinear regression.

Equation		Best fit values	95% Confidenceintervals
Third order polynomial equation			
BSA=B0+ B1*BW + B2*BW [2]+ B3*BW [3]	**B0**	0.07758	0.07717 to 0.07800
	B1	0.04165	0.04159 to 0.04172
	B2	−0.0003307	- 0.0003327 to - 0.0003287
	B3	1.25E-06	1.236E-006 to 1.268E-006
	R square (weighted)	0.9979	
	n	27400	
Meeh type equation			
$BSA = A*BW^{B}$	**A**	0.09395	0.9378 to 0.09412
	B	0.7032	0.7027 to 0.7038
	R square (weighted)	0.9966	
	n	27440	
Boyd self-adjusting type equation			
$BSA = A*BW^{(B\_C*logBW)}$	**A**	0.08319	0.08286 to 0.08352
	B	0.7955	0.7927 to 0.7983
	C	0.03625	0.03518 to 0.03732
	R square (weighted)	0.9971	
	n	27440	

A, B, and C are regression coefficients; BW = independent variable (body weight) and BSA = dependent variable (body surface area).

for use in children, even for children younger than 2 years of age. The ratio of Meeh BSA/Mosteller BSA as a function of age is presented for the four age groups in Fig. 3.

The ratio of Meeh BSA/Mosteller BSA increased with increasing BMI (rs = 0.4376 and $P < .0001$), Fig. 4.

There were no statistical differences in the ratios of Meeh-type BSA/Mosteller BSA between female and male subjects ($P = .6386$).

BW and H values from the participating patients were compared with the Swedish population-based reference values [33]. Eighty-eight percent and 89.4% of the H values and 87.6% and 87.3% of the BW values were within ± 3*SD of age-matched reference data for female and male subjects, respectively. Plots of the percentages of H and BW values that were outside ± 3*SD in the various age groups are presented in Table 4. The H and BW values were almost 30% and 20%, respectively, below 3*SD of the reference values in neonates and infants.

In the neonatal group, H and BW values were about 11% and 5%, respectively, below 5* SD of the reference data from age-matched subjects (data not shown).

The estimation of BSA using the original coefficients of the Boyd self-adjusting equation showed that 96% of the original Boyd/Mosteller BSA ratios were within the range from 0.90 to 1.10. The original Boyd/Mosteller BSA ratio increased with increasing BMI (rs = 0.1688; $P < .0001$) (data not shown). Analysis according to Sheiner and Beil showed MPE% = 2.96% and RMSE% = 3.47%.

5. Discussion

BSA is an important measurement for decisions regarding many physiological processes including the determination of the correct drug dosages for adults and children. At Astrid Lindgren Children's Hospital, BSA is estimated from BW and H using the Mosteller equation for all age groups, even though it has been claimed that the Meban equation might be more accurate in newborns [34].

BSA was estimated in children 0–18 years by using only BW.

The main finding of this study is that any of the three equations can be substituted for the Mosteller equation (BSA from BW + H); i.e., BSA can be estimated from BW alone for children aged from 0 to 18 years (BW: 0.38 kg–158 kg) with high precision and accuracy, Fig. 2. Overall, the data indicate that the Meeh-type equation is the most suitable for estimating BSA from BW in the entire pediatric population. It is, thus, possible to also estimate the BSA of neonates and infants, Fig. 2.

In two studies, it is suggested that BSA can be estimated using a linear equation in children and infants [35,36]. On a closer examination of our results, it was found that Fig. 2 contradicts this assumption of a linear relationship between BSA and BW in these age groups.

It has always been important to document both BW and H when monitoring the growth of children. In children younger than two years of age, H should be measured using standardized procedures with a recumbent length board [37]. Height measurements in newborns are hard to take and are generally associated with low precision and accuracy [16,37–39]. It has been claimed that routinely collected child health record's height/length and weight data are compatible with no systematic bias, which supports their use in clinical practice and research, albeit with somewhat lower precision for younger infants [40].

Data in Table 4 show that many patients in the various age groups, particularly neonates presented H and BW values outside ± 3* SD as compared to reference values. It is, however, not surprising because a lot of premature infants are treated at Astrid Lindgrens Children's Hospital.

We evaluated the impact of inaccurate BW and H values on the estimation of BSA using the Mosteller equation. A 500 g deviation from the correct BW in a child with H = 50 cm and BW exceeding 2 kg will influence the accuracy of BSA by less than 11%. A 5-cm deviation from the correct H in a child with BW = 2 kg and H exceeding 30 cm will influence the accuracy of BSA by less than 9%. For children weighing 70 kg, the BSA will vary by 3.5% with every 5 kg deviation from the correct BW and by 1.46% with every 5 cm deviation from the correct H. We, therefore, concluded that it was not necessary to exclude neonates and infants from the study. This is in contrast to the suggestion by Sharkey et al. that the accurate measurement of BSA in neonates and infants is unreliable because the extremities are elastic and soft and consequently reliable measurement of H is not possible in patients with BW < 10 kg [16].

The modified Meeh-type equation gave the best estimates of BSA in our entire patient population, while the modified Boyd-type equation gave the best estimates of BSA for children aged 12–18 years. The difference was, however, only minor as compared to the Meeh-type equation, which was indicated by the Eksborg plot, Table 3. In our opinion, it is more important to correctly estimate BSA in neonates and infants than in older children, because the BSA might be included in drug dosage optimization strategies for these patient groups and older children might be less vulnerable to the

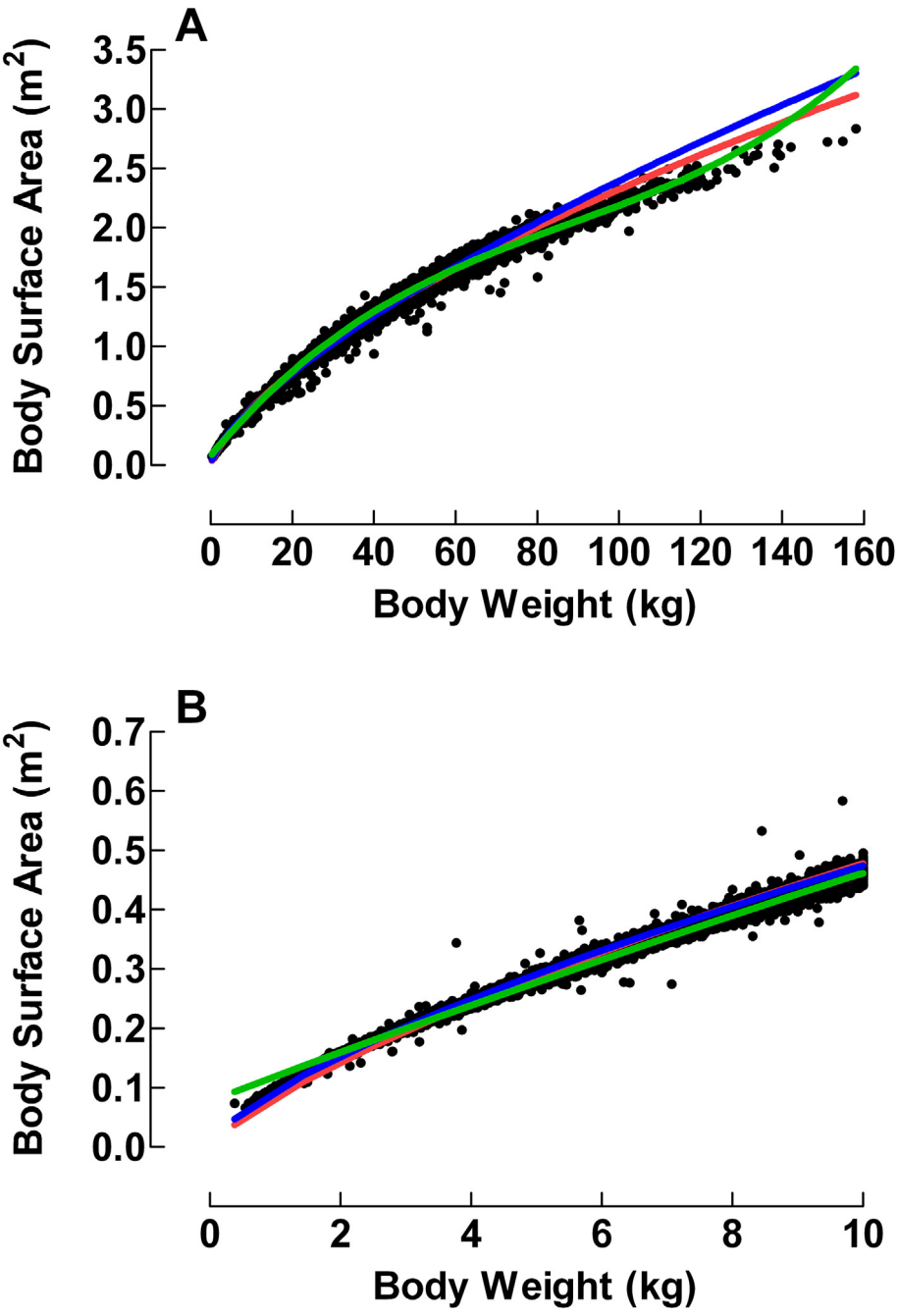

Fig. 2. Results from nonlinear regression analysis.
Green line: results from the third-order polynomial equation; blue line: results from the Meeh-type equation; and red line: results from the Boyd self-adjusting-type equation. Filled symbols: body surface area values calculated from the Mosteller formula using BW and height.
Fig. 2A. Weight span: 0–160 kg.
Fig. 2B. Weight span: 1.4–10 kg.

effects of inaccurate drug dosages [16,19].

The Meeh-type/Mosteller BSA ratio as a function of age in the four age groups, Fig. 3, shows evenly distributed data both above and below 0.9–1.1, indicating a lack of systematic errors; 99.2% of the ratios were within the range of 0.9–1.1. It is important to note, for the clinical implications of these findings, that the Meeh-type/Mosteller BSA ratios did not differ between female and male subjects, i.e., the same equation for estimating BSA from BW can be used independently of gender and age group.

Fig. 4 shows an increase in the Meeh-type/Mosteller BSA ratio with increasing BMI. BSA values that have been estimated with the Meeh-type equation should be used with caution in patients with very low or very high BMI values (<5 or >45). It should be noted that decisions on the dosage of drugs that are based on BSA in cachectic or obese patients has been questioned [40–43].

5.1. Modification of existing formulas

Estimation of BSA in patients from different races/ethnicities might require the modification of equations to cater to differences

Table 3
Results from Eksborg's plot for BSA ratios.

	Polynom/Mosteller	Meeh type/Mosteller	Boyd type/Mosteller
Age group: 0–28 days (n = 2,648)			
Percentage within 0.90–1.10	90.9	99.47	81.0
Percentage above 1.10	9.1	0.19	0.11
Percentage below 0.90	0	0.34	18.88
Age group: > 28 days - 2 years (n = 9,796)			
Percentage within 0.90–1.10	98.57	99.47	98.03
Percentage above 1.10	1.31	0.45	0.52
Percentage below 0.90	0.12	0.12	1.45
Age group: > 2–12 years (n = 10,808)			
Percentage within 0.90–1.10	99.3	99.48	99.55
Percentage above 1.10	0.61	0.43	0.41
Percentage below 0.90	0.09	0.08	0.05
Age group: > 12–18 years (n = 4,188)			
Percentage within 0.90–1.10	99.64	97.66	99.21
Percentage above 1.10	0.31	2.2	0.69
Percentage below 0.90	0.05	0.14	0.10

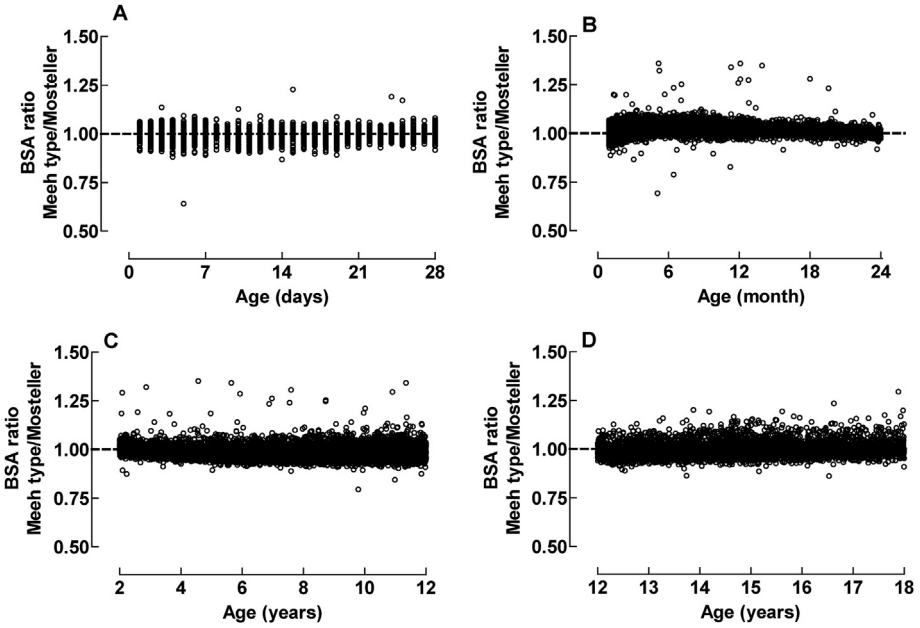

Fig. 3. Ratio of Meeh/Mosteller equation body surface area (BSA) values.
Fig. 3A. Data from neonates (aged 0–28 days); Fig. 3B: data from infants (aged >28 days - 2 years); Fig. 3C: data from children (aged >2–12 years); and Fig. 3D: data from adolescents (aged >12–18 years).

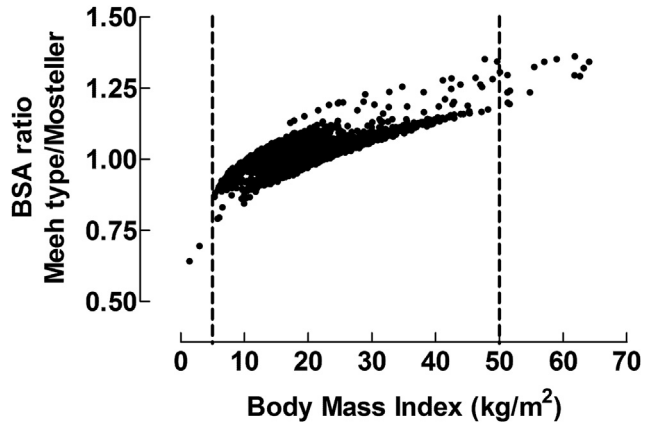

Fig. 4. Effect of body mass index on the Meeh/Mosteller body surface area (BSA) ratio. The increase of the BSA ratio of Meeh type/Mosteller with increasing BMI was statistically significant (rs = 0.4376 and P < .0001).

in body shape and build [15,44–47]. Of several tested equations, the Mosteller equation gave the most accurate prediction of BSA in Saudi Arabian neonates according to Nwoye et al. [48].

The regression coefficients given in this paper differ significantly from those in Boyd's paper. Boyd used linear regression analysis after logarithmic transformation and used units of cm^2 and grams in her calculations [24]. Our modified Boyd self-adjusting equation had significantly higher precision and accuracy for the BSA estimates than obtained with the original regression coefficients. The reasons for this discrepancy include different study populations and differences in regression techniques, but the fact that Boyd used measured BSA values instead of estimates using the Mosteller equation is also relevant. Nonetheless, the precision and accuracy estimates for BSA using the original Boyd equation are remarkably high, and the original Boyd equation is less likely to overestimate BSA than the original Meeh equation.

Table 4
Body weight and height of included patients as compared to population-based reference values.

Patient group	Percentage outside reference values			
	H (>3 SD)	H (<3 SD)	BW (>3 SD)	BW (<3 SD)
Neonates (0–28 days)	0.7	27	0.52	28.68
Infants (> 28 days - 2 years)	1.49	18.16	1.8	16.71
Children (> 2–12 years)	0.81	3.39	4.28	0.39
Adolescents (> 12–18 years)	0.44	3.42	6.24	0.66

5.2. Strengths and drawbacks in the study

The main strength of our study is the large number of patients included. It is particularly notable that we had many low weight and/or under H values because we included neonates.

One possible drawback of our study is that we included patients only if both BW and H were recorded. There is a possibility for a selection bias, patients with recorded H could present different attributes, e.g., H was only recorded when it was of clinical interest (e.g., patients with growth disorder).

The use of the Mosteller equation as the gold standard against which to test our data could be considered as another drawback because it has been shown to underestimate BSA in children [28]. The Mosteller equation is, however, used as a gold standard by our hospital, which is based on good clinical experience.

6. Conclusion

All three equations can be used to predict the results of Mosteller equation, when H is not available with high precision and accuracy in all children, including term neonates with the best fit using the Meeh-type equation. We plan to include the results of this study in CPOE systems in Sweden to improve drug dosage in all children.

Declaration of competing interest

None.

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Visual abstract

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