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WEIGHT LOSS AND WEIGHT MAINTENANCE

A systematic review and quantitative analysis of resting energy expenditure prediction equations in healthy overweight and obese children and adolescents

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Abstract

Background: Resting energy expenditure (REE) estimates are often needed in young people and can be predicted using prediction equations based on body weight. However, these equations may perform poorly in those who are obese and overweight. The aim of this systematic review was to identify equations based on simple anthropometric and demographic variables that provide the most accurate and precise estimates of REE in healthy obese and overweight young people.
Methods: Systematic searches for relevant studies in healthy obese and overweight young people aged ≤18 years were undertaken using PubMed, Scopus, Cinahl, OpenGrey and Cochrane Library (completed January 2018). Search terms included metabolism, calorimetry, obesity and prediction equation. Data extraction, study appraisal and synthesis followed PRISMA guidelines.
Results: From 390 screened titles, 13 studies met inclusion criteria. The most accurate REE predictions (least biased) were provided by Schofield equations [+0.8% (3–18 years); 0% (11–18 years); +1.1% (3–10 years)]. The most precise REE estimations (percentage of predictions ± 10% of measured) for 11–18 years were provided by Mifflin equations (62%) and, for 7–18 years, by the equations of Schmelzle (57%), Henry (56%) and Harris Benedict (54%). Precision of Schofield predictions was 43% in both age groups. No accuracy data were available for those <3 years or for precision for those <7 years.
Conclusions: No single equation provided accurate and precise REE estimations in this population. Schofield equations provided the most accurate REE predictions so are useful for groups. Mifflin equations provided the most precise estimates for individuals aged 11–18 years but tended to underestimate REE.

Introduction

Excess weight in children continues to be a major public health problem globally (1) and in the UK. According to the latest National Child Measurement Programme, which measures weight and height of children at school, 12.8% of 4–5 year olds and 14.2% of 10–11 year olds in England are overweight and 9.5% and 20.1%, respectively, are obese (2). Excess weight is not evenly distributed among children; obesity prevalence is higher in boys than girls in both age groups and is also highest in black children compared to other ethnicities. It is also socially patterned, with prevalence rates double in the most deprived compared with the least deprived children [2,3]. This is of concern because excess weight in children is highly visible and with implications for poorer physical and mental health [4] and reduced educational attainment [5–7]. Additionally, childhood and especially adolescent obesity tracks strongly into adulthood [7–11]. The negative health impacts of excess weight in adulthood have been well documented, including an increased risk of type 2 diabetes, some cancers, non-alcoholic fatty liver disease, musculoskeletal disorders and cardiovascular disease, as well as poorer mental health [9,12]. It therefore follows that tackling excess weight in children is beneficial for their long-term health prospects [7].

Current guidance on weight management in childhood recommends that children should reduce weight gain if they are still gaining height [13,14]. For those who have achieved their full height, weight loss will be required to achieve healthy weight status [13,14]. This depends on the child and family's ability to support the long-term changes to behaviour required to achieve and maintain weight loss [9,11,13,14]. Quantity and rate of target weight loss are clinical decisions [9]; dependent on those decisions and the child's current energy intake and expenditure, personalised weight loss plans should be developed, tailored to the individual [13]. To achieve weight loss, an energy deficit will be required [15]. A starting point for determining the deficit is estimating total energy expenditure (TEE).

TEE is the amount of energy used daily by individuals [16], of which approximately 60–70% is basal metabolic rate (BMR)[17,18]. TEE is difficult and expensive to measure and may be estimated from BMR using the factorial method to include contributions from dietary induced thermogenesis and activity [19]. Because measurement of true BMR is unfeasible [20], the term resting energy expenditure (REE) is used throughout this review and refers to estimated BMR. The 'gold standard' for REE measurement is indirect calorimetry (IC), in which oxygen consumption (VO_2) and carbon dioxide production (VCO_2) are measured with appropriately calibrated and validated equipment (e.g. metabolic cart) under controlled conditions [20] and used to calculate REE [21]. Requisite equipment is bulky, costly, and requires external calibration and training for proper use. Inexpensive, lightweight, uncalibrated devices (e.g. handheld indirect calorimeters) usually rely on measurement of VO_2 only, make assumptions regarding substrate metabolism and lack consistent validation [22]. To estimate REE without the need for IC, a number of predictive energy expenditure equations have been developed and are used widely [23]. Many are complex, requiring access to measurements not usually available in standard clinical settings (e.g. fat-free mass, organ weights). Single equations have been proposed [23,24] or, more commonly, multiple age or sex specific variants [25,26]. At a given weight, individual REE depends largely on body composition with fat-free mass (FFM) exhibiting greater metabolic activity than fat mass (FM)[27]. In obesity, FM increases more than FFM [28], and so an increase in REE is not directly proportional to weight gain. Additionally, body composition at any weight has altered over two generations to favour a higher proportion of FM [29]. Historic prediction equations derived from populations with lower prevalence of overweight and obesity, or in lean subjects who are not overweight or obese may lead to inaccurate estimation of TEE [30–32] in this population. In different scenarios, overestimation of REE may fail to impose the level of caloric restriction required to achieve negative energy balance. Underestimation may frustrate weight management by imposing inappropriate and unsustainable dietary restrictions. Importantly, over restriction in children may also adversely affect their growth and nutritional status [33].

In current clinical practice, simple weight-based equations or estimated average requirements are used to estimate energy requirements regardless of adiposity [34,35]. Many different equations have been published, although selection of the most appropriate predictive equation will help to avoid either over or underestimation of energy requirements when developing a tailored plan [36]. Although a previous systematic review examined the accuracy and precision of REE prediction equations in overweight and obese adults [37], there is no consensus about which equation(s) are most appropriate for accurate estimation of REE in children [38,39]. Therefore, the aim of this systematic review was to determine which prediction equations based on simple anthropometric and demographic variables provide the most accurate (closeness to measured energy expenditure) and precise (proportion of participants with predicted values within 10% of measured) estimates of REE in healthy overweight and obese young people aged 1–18 years.

Materials and methods

A systematic review of the published literature was undertaken in accordance with the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) guidance [40]. Details of the protocol were registered with the PROSPERO International Prospective Register of Systematic Reviews [41].

Search strategy

Boolean searches for published studies were undertaken by two researchers within the electronic databases PubMed, Scopus, Cinahl, OpenGrey and the Cochrane

Library using the key words (basal metabolism OR calorimetry) AND (obesity OR overweight) AND (prediction equation OR predictive equation). MESH terms were used within PubMed for all key words except prediction equation and predictive equation. To prevent exclusion of relevant studies, no further search limits were applied. No studies were excluded on the basis of language; all studies were published in English or reliable translations were available. Publications for all dates until 15 January 2018 were searched. All types of study design were included. Additional primary studies were identified by manually searching the reference lists of review articles.

Screening, inclusion and exclusion criteria

Published studies identified in the search were evaluated independently by two researchers initially using titles and abstracts. On the basis of the screening, studies were identified as either 'excluded' or 'full text assessed for eligibility'. Papers which provided original research data comparing predicted energy expenditure (pREE) calculated using a prediction equation with energy expenditure measured using IC (mREE) were extracted. Studies were included if they utilised prediction equations which were based on variables easily measured in clinical or public health practice (e.g. height, weight, waist circumference, age, sex); equations based on more complex variables not generally available in clinical practice (e.g. fat-free mass, organ weight) were excluded. Studies which used recognised diagnostic criteria for identifying overweight and obesity in children (e.g. using appropriate centiles) were included, and excluded if they did not. Studies were excluded if study populations did not include overweight or obese participants, or if overweight or obese participants were included but not reported separately. Studies were excluded if study participants were not aged 1–18 years.

Studies were included if participants were stated to be in good health or free from illness and disease but excluded if they were described as being acutely ill, having a chronic condition that might influence metabolic rate, taking medication that might have this effect, or if this was not clear from the methods described. The validity of the method of measuring energy expenditure was also considered. Studies were included if an externally calibrated indirect calorimeter measuring VO_2 and VCO_2 was used. Studies using uncalibrated devices were excluded. Studies were excluded if participants were asleep or active during REE measurement, or if they had not fasted for a minimum of 6 h beforehand. The reference lists of papers identified as reviews or meta-analysis studies were examined for additional sources, which were then screened using the approach described above.

Extraction of data

Papers which met the inclusion criteria were examined by two researchers. Data were extracted into a specifically prepared form and included study population, context of study and method of REE measurement. A table of equations based on simple variables evaluated by included studies was compiled from the original publications. Papers were critically evaluated using primary summary measures for each of the prediction equations reported: (i) accuracy (i.e. predicted energy expenditure expressed as a percentage of the measured energy expenditure or in a format where this could be calculated) and (ii) precision (i.e. percentage of participants with predicted energy expenditure within 10% of measured values). To facilitate calculation of these data, equations were excluded from the analysis if they were evaluated by fewer than two studies. Studies reported data for whole populations, age-based subgroups, male/female subgroups, or a combination of these. Where reporting for multiple subgroups led to duplicate reporting of participant data, age-based subgroups were prioritised for analysis and data for alternative subgroup divisions were removed. Most studies applied age specific variants of equations as appropriate to the individual participant. The intention was to include data for 1–18 years. Because none of the papers that met the criteria for this review included data for 1–2 years, data were analysed for the whole population of 3–18 year and separately for 11–18 years and 3–10 years subgroups with the age ranges determined pragmatically from the data in the included studies and with regard to puberty, which impacts on body composition and thus energy expenditure. In each group, data were analysed by study subgroup and by participant to give mean precision and accuracy for each equation. Data from all categories of overweight and obesity were considered together in the analyses because there were insufficient to separate into meaningful subgroups of excess body weight. The data were extracted and the findings synthesised manually to allow for analysis by participant as well as by study. Data from 50% of participants in the accuracy analysis and 68% of those in the precision analysis came from one study centre in Northern Italy [23,42,43]. Analyses were repeated with and without these data to investigate their potential influence on the overall results. Where any clarification was needed to determine inclusion of data, the authors of original papers that met the inclusion criteria were contacted. Stages 2 and 3 of the ROBIS tool [44] were used to assess risk of bias in the present systematic review; the optional stage 1 was omitted because evaluating prediction equations falls outside the four PICO questions included in this tool.

Results

The searches identified 390 possible studies; after exclusion of duplicates, 246 papers were initially screened of which 166 were excluded. Eighty full-text papers were assessed for eligibility, of which 67 were excluded. Thirteen studies [23,39,42,43,45–53] met the criteria for inclusion in the systematic review (Fig. 1). Characteristics of studies included are shown in Table 1. Studies included evaluated a total of 14 individual or groups of REE prediction equations in populations from seven countries in Europe and North America (Table 2).

The accuracy of predictions was reported by studies comprising between 121 and 2636 participants with smaller study populations in younger children (3–10 years). Accuracy in all age groups varied with mean bias ranging from an underestimation of 14.0% to an overestimation of 11.6% compared to measured values (Table 3). Considering analysis by individual participants, the least mean bias was observed in the predictions derived using the equations of Schofield [25] in all age groups: +0.8% (3–18 years); 0% (11–18 years); +1.1% (3–10 years). The predictions from the World Health Ogranization (WHO) [26] equations based on weight and height also provided values with low mean bias but these have not been evaluated in younger children: +0.8% (3–18 years); +1.1% (11–18 years). When results were examined by studies, the same equations provided least mean bias: Schofield + 0.4% (3–18 years); +0.5% (11–18 years); 0% (3–10 years) and WHO weight and height +1.3% (3–18 years); −0.3% (11–18 years). The WHO [26] equations based solely on weight provided less accurate mean predicted REE values with a tendency to overestimate by >8%.

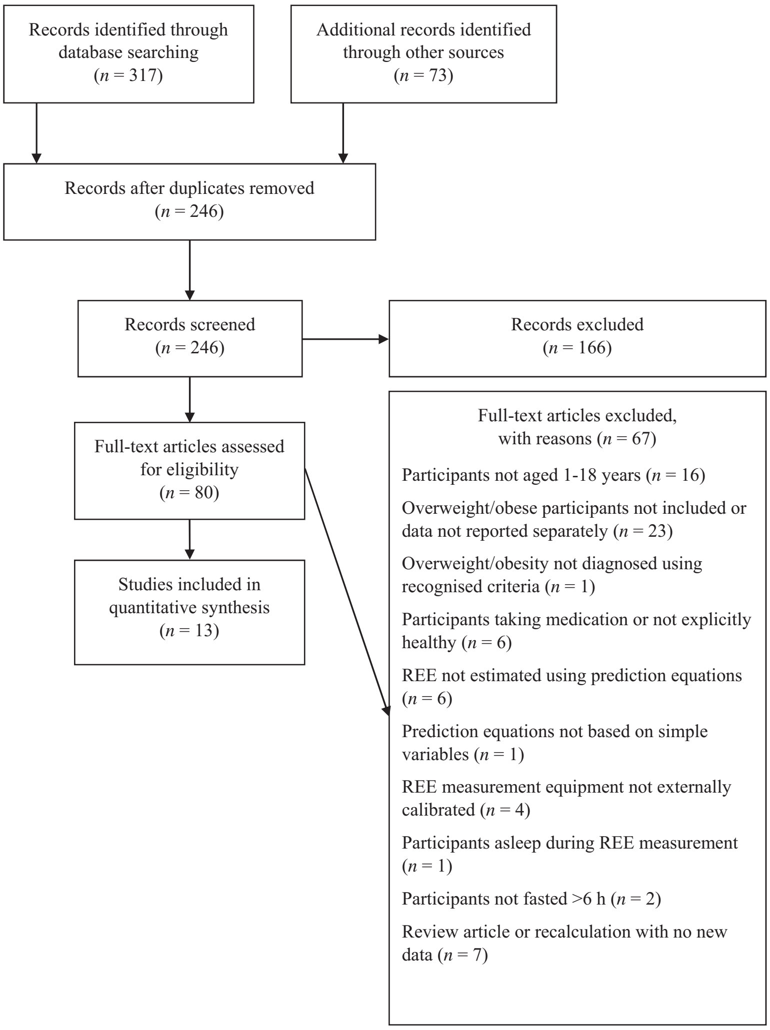

Figure 1 Flow and identification of studies for evaluation of equations predicting resting energy expenditure in overweight and obese children. REE, resting energy expenditure.

Table 1 Studies evaluating prediction of resting energy expenditure in healthy overweight and obese children and adolescents included† in the systematic review

Authors (year), reference number	Country and context of study	Participants included in the quantitative synthesis (number; sex; age; overweight/ obesity category)‡	REE measurement (fast; conditions; equipment; measurement duration)
Derumeaux-Burel et al. (2004)[45]	France, Clermont-Ferrand: participants visiting a paediatric nutritionist for the first time	Cohort 1: 191 boys and 280 girls; 3–18 years; BMI Z-score ≥2 Cohort 2: 62 boys and 149 girls; 3–18 years; BMI Z-score ≥2	Overnight fast; monitored to prevent movement or sleeping; Deltatrac II; ≥45 min measured (first 10 excluded)
Dietz et al. (1991)[46]	USA, Massachusetts and Illinois: participants recruited from weight control clinics	Cohort 2: 13 girls; 15.1 (1.5) years [mean (SD); weight ≥120% ideal body weight	Overnight fast; rested for 30 min; open circuit indirect calorimeter with ventilated hood; 30 min measured
Hofsteenge et al. (2010)[47]	Netherlands, Amsterdam: participants recruited from a paediatric obesity outpatient clinic	51 boys and 70 girls; 12–18 years; overweight or obese according to Cole et al. (2000)	Overnight fast; supine and awake; Vmax Encore n29; 30 min measured (first 5 excluded)
Klein et al. (2011)[48]	USA, Washington, D.C: participants enrolled in a weight loss trial	31 boys and 27 girls; 7–15 years; BMI ≥95th percentile	Overnight fast (12 h); rested for 20–30 min; Ultima CardiO2 system; 30 min measured (first 5 excluded)
Lazzer et al. (2010)[43]	Italy; participants enrolled before beginning a weight-reduction programme	589 boys and 823 girls; 7–18 years; BMI >97th percentile	Overnight fast; supine and at rest; Vmax 29; ≥45 min measured (first 10 excluded)
Lazzer et al. (2006)[23]	Italy; participants enrolled before beginning a weight reduction programme	Group 2: 19 boys and 34 girls; 12–18 years; BMI >99th percentile	Overnight fast; lying position; Vmax 29; 30 min measured (first 5–10 excluded)
Lazzer et al. (2007)[42]	Italy, Piancavallo: participants recruited from the Division of Auxology	121 boys and 166 girls; 7–18 years; BMI >97th percentile	Overnight fast; steady state achieved in lying position; Vmax 29; 30 min measured (first 5–10 excluded)
Lazzer et al. (2014)[49]	Italy, Piancavallo: participants enrolled before beginning a weight reduction programme.	341 boys and 507 girls; 7–18 years; BMI >97th percentile	Overnight fast; supine and at rest; Vmax 29; ≥45 min measured (first 10 excluded)
Marra et al. (2015)[50]	Italy, Naples: measurements performed before initiation of a weight reduction programme	109 boys and 155 girls; 14–18 years; BMI 30.0–70.0	Overnight fast (12–14 h); lying down, 15-min adaptation period; Vmax 29; 45 min measured
Molnár et al. (1995)[51]	Hungary, Pecs: participants referred to paediatric obesity clinic	Cohort 1: 77 boys and 59 girls; 10–16 years; body weight ≥120% expected weight for height Cohort 2: 49 boys and 30 girls; 10–16 years; body weight ≥120% expected weight for height	Overnight fast (11 h); rested for 30 min; Deltatrac indirect calorimeter; 45 min measured
Schmelzle et al. (2004)[52]	Germany, Greifswald: participants admitted to paediatric clinic	49 boys and 33 girls; 4–15 years; BMI >95th percentile	Overnight fast (12 h); rested for 15–30 min; Detatrac II metabolic monitor; ≥30 min measured
Steinberg et al. (2017)[53]	Canada, Toronto. Participants recruited from an outpatient weight management clinic	84 boys and 142 girls; 12–18 years; BMI ≥120% of 95th percentile	Overnight fast; rested, awake and supine; Vmax 29; 20–25 min measured
Tverskaya et al. (1998)[39]	USA, New York: paediatric patients	50 boys and 60 girls; 3–18 years; BMI> 28	Preprandial, early morning; resting awake state; Deltatrac MBM-100 indirect calorimeter; 30 min measured

BMI, body mass index in kg m^{-2}; REE, resting energy expenditure.
†Included studies met *a priori* criteria defined to minimise risk of bias in individual studies.
‡Overweight/obesity categories as described by the authors.

The precision of predicted values was reported by studies comprising between 226 and 1759 participants. There were insufficient data to report on children aged <7 years. Precision also varied with the proportion of predicted values within 10% of measured REE varying between 28–63% (Table 4). The highest precision in the 11–18 years group was observed using the equations of Mifflin [38] (62% of individual observations), whereas Schofield and

Table 2 Prediction equations based on simple anthropometric and demographic variables evaluated for accuracy and precision by studies included in the systematic review

Equation†	Studies evaluating precision	Studies evaluating accuracy
Harris & Benedict (1919)[54] Male REE (kcal) = 66.4730 + 13.7516 weight + 5.0033 height (cm) – 6.7550 age Female REE (kcal) = 655.0955 + 9.5634 weight + 1.8496 height (cm) – 4.6756 age	Hofsteenge *et al.* (2010)[47] Steinberg *et al.* (2017)[53]	Derumeaux-Burel *et al.* (2004)[45] Hofsteenge *et al.* (2010)[47] Lazzer *et al.* (2007)[42] Schmelzle *et al.* (2004)[52] Tverskaya *et al.* (1998)[39] Steinberg *et al.* (2017)[53]
Henry (1999)[55] Male REE (kJ) = 66.9 weight + 2876 Female REE (kJ) = 47.9 weight + 3230	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]
Henry (2005)[56] Male REE (kcal) = 18.4 weight + 581 Female REE (kcal) = 11.1 weight + 761	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]
IOM healthy weight (Institute of Medicine, 2005)[57] Male REE (kcal) 68 – 43.3 age + 712 height + 19.2 weight Female REE (kcal) = 189 – 17.6 age + 625 height + 7.9 weight	Klein *et al.* (2011)[48] Steinberg *et al.* (2017)[53]	Klein *et al.* (2011)[48] Steinberg *et al.* (2017)[53]
IOM overweight and obese (Institute of Medicine, 2005)[57] Male REE (kcal) = 420 – 33.5 age + 418.9 height + 16.7 weight Female REE (kcal) = 516 – 26.8 age + 347 height + 12.4 weight	Klein *et al.* (2011)[48] Steinberg *et al.* (2017)[53]	Klein *et al.* (2011)[48] Steinberg *et al.* (2017)[53]
Lazzer *et al.* (2006)[23] REE (kJ) = 54.96 weight + 1816.23 height + 892.68 sex‡ – 115.93 age + 1484.50	Hofsteenge *et al.* (2010)[47] Steinberg *et al.* (2017)[53]	Hofsteenge *et al.* (2010)[47] Lazzer *et al.* (2006)[23] Lazzer *et al.* (2007)[42] Steinberg *et al.* (2017)[53]
Mifflin *et al.* (1990)[38] Male REE (kcal) = 9.99 weight + 6.25 height – 4.92 age + 5 Female REE (kcal) = 9.99 weight + 6.25 height – 4.92 age – 161	Hofsteenge *et al.* (2010)[47] Lazzer *et al.* (2010)[43] Steinberg *et al.* (2017)[53]	Hofsteenge *et al.* (2010)[47] Lazzer *et al.* (2010)[43] Steinberg *et al.* (2017)[53]
Molnár *et al.* (1995)[51] Male REE (kJ) = 50.9 weight + 25.3 height (cm) – 50.3 age + 26.9 Female REE (kJ) = 51.2 weight + 24.5 height (cm) – 207.5 age + 1629.8	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50] Steinberg *et al.* (2017)[53]	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50] Molnár *et al.* (1995)[51] Steinberg *et al.* (2017)[53]
Molnár single (Molnár *et al*, 1995)[51] Male and female REE (kJ) = 50.2 weight + 29.6 height (cm) – 144.5 age – 550 sex§ + 594.3		Hofsteenge *et al.* (2010)[47] Molnár *et al.* (1995)[51]
Müller *et al.* (2004)[24] REE (MJ) = 0.02606 weight + 0.04129 height (cm) + 0.311 sex‡ – 0.08369 age – 0.808	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]
Schmelzle (*et al.* 2004)[52] Male REE (kcal) = 6.6 weight + 13.1 height (cm) – 794 Female REE (kcal) = 11.9 weight + 0.84 height (cm) + 579	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]
Schofield (1985)[25] *Age 3–10 years* Male REE (MJ) = 0.082 weight + 0.545 height + 1.736 Female REE (MJ) = 0.071 weight + 0.677 height + 1.553 *Age 10–18 years* Male REE (MJ) = 0.068 weight + 0.574 height + 2.157 Female REE (MJ) = 0.035 weight + 1.948 height + 0.837	Hofsteenge *et al.* (2010)[47] Marra *et al.* (2015)[50]	Derumeaux-Burel *et al.* (2004)[45] Hofsteenge *et al.* (2010)[47] Lazzer *et al.* (2007)[42] Marra *et al.* (2015)[50] Schmelzle *et al.* (2004)[52]
WHO weight & height‖ (World Health Organization, 1985)[58] *Age 10–18 years* Male REE (kcal) = 16.6 weight + 77 height + 572 Female REE (kcal) = 7.4 weight + 482 height + 217	Hofsteenge *et al.* (2010)[47] Steinberg *et al.* (2017)[53]	Derumeaux-Burel *et al.* (2004)[45] Dietz *et al.* (1991)[46] Hofsteenge *et al.* (2010)[47] Lazzer *et al.* (2007)[42] Molnár *et al.* (1995)[51] Steinberg *et al.* (2017)[53]

Table 2 Continued

Equation†	Studies evaluating precision	Studies evaluating accuracy
WHO weight (World Health Organization, 1985)[58]	Hofsteenge *et al.* (2010)[47]	Dietz *et al.* (1991)[46]
Age 3–10 years	Marra *et al.* (2015)[50]	Hofsteenge *et al.* (2010)[47]
Male REE (MJ) = 95 weight + 2071/1000	Steinberg *et al.* (2017)[53]	Marra *et al.* (2015)[50]
Female REE (MJ) = 94 weight + 2088/1000		Molnár *et al.* (1995)[51]
Age 10–18 years		Schmelzle *et al.* (2004)[52]
Male REE (kcal) = 17.5 weight + 651		Steinberg *et al.* (2017)[53]
Female REE (kcal) = 12.2 weight + 746		

REE, resting energy expenditure.
†Unless otherwise stated, weight (kg), height (m), age (years).
‡Female = 0, male = 1.
§Male = 0, female = 1.
||WHO weight and height equation for age 10–18 also used in participants age 3–10 (no weight and height equation published for this age group).

Table 3 Accuracy of equations predicting resting energy expenditure in three age groups, analysed by participant and by study subgroup

	Analysis by participants			Analysis by study subgroup		
Age subgroup (years)	Equation	Participants (*n*)	Bias (%)	Equation	Subgroups (*n*)	Bias (%)
3–18	Müller	385	–13.9	Müller	3	–14.0
	Mifflin	1759	–6.1	IOM hw	3	–12.1
	Schmelzle	385	–4.3	IOM oo	3	–11.9
	Molnár	690	–3.7	Mifflin	4	–5.1
	Molnár single	200	–2.5	Schmelzle	3	–4.5
	Harris & Benedict	1508	–1.0	Molnár	6	–4.1
	WHO wt & ht	**2636**	**0.8**	Molnár single	3	–2.6
	Schofield	**1436**	**0.8**	Harris & Benedict	16	–2.5
	Henry 1999	385	1.2	**Schofield**	**13**	**zz0.4**
	Henry 2005	385	2.2	WHO wt & ht	13	1.3
	IOM hw	284	3.0	Henry 1999	3	1.7
	IOM oo	284	4.5	Henry 2005	3	3.4
	Lazzer	687	5.2	Lazzer	5	3.7
	WHO wt	970	9.2	WHO wt	10	8.7
11–18	Müller	385	–13.9	Müller	3	–14.0
	Schmelzle	385	–4.3	Molnár	4	–4.7
	Molnár	611	–3.7	Schmelzle	3	–4.5
	Mifflin	347	–2.4	Mifflin	2	–2.9
	Molnár single	121	–2.0	Molnár single	1	–2.0
	Schofield	**744**	**0.0**	Harris & Benedict	8	–0.7
	Harris & Benedict	778	0.7	**WHO wt & ht**	**7**	**–0.3**
	WHO wt & ht	719	1.1	Schofield	7	0.5
	Henry 1999	385	1.2	Henry 1999	3	1.7
	Henry 2005	385	2.2	Henry 2005	3	3.4
	Lazzer	400	7.6	Lazzer	4	4.2
	WHO wt	624	9.2	WHO wt	5	8.8
	IOM hw	226	9.4	IOM hw	1	9.4
	IOM oo	226	11.6	IOM oo	1	11.6
3–10	Harris & Benedict	166	–3.6	Harris & Benedict	4	–4.8
	Schofield	**128**	**1.1**	**Schofield**	**2**	**0.0**
	WHO wt	128	9.2	WHO wt	2	8.4

wt, weight; ht, height; hw, healthy weight; oo, overweight and obese.
Bias is the difference between mean measured resting energy expenditure (REE) and mean predicted REE expressed as a percentage of mean measured REE. The most accurate equations have the smallest magnitude bias indicated by bold text. Negative bias indicates a tendency to underestimate REE. Positive bias indicates a tendency to overestimate REE.
The bold text identifies the most accurate equation/s in each sub-group.

WHO weight and height provided estimates within 10% of measured values with 43% and 45% of individual observations; values for analysis by studies were similar. In the 7–18 years group, the highest precision was observed using the equations of Schmelzle [52], Harris Benedict [54] and Henry [55] (57%, 54% and 56% of individual observations) compared to 43% and 44% from Schofield and WHO weight and height; again, values for analysis by studies were similar.

Removing the large datasets from the single study centre in Northern Italy [23,42,43] had no impact on the observations of accuracy but resulted in the Mifflin equations giving the most precise estimates in the 7–18 group (62%-63%) (see Supporting Information Tables S1 and S2).

The assessed risk of bias of this review was considered to be low when evaluated using the ROBIS [44] tool (see Supporting Information Data S1).

Discussion

The aims of this systematic review were to identify the prediction equations based on simple anthropometric and demographic variables that provide the most accurate and precise estimates of REE in healthy overweight and obese young people aged 1–18 years. Data from studies that met the inclusion criteria indicate that, at a population level, the most accurate equations for 11–18 years are those of Schofield [25] and WHO [26] based on weight and height as they showed minimal bias. The equations of Schofield also provided the most accurate predictions for children aged 3–10 years. Although the accuracy of the Schofield and WHO weight and height equations for children aged 3–18 years provide useful guidance for those working with groups of young people, those working with individuals will be equally interested in the precision data and this is less reliable. Less than 50% of REE predictions derived using the Schofield and WHO weight and height were within 10% of measured values regardless of age group or whether analysed per participant or per study. The best precision in 11–18 years olds was observed with the Mifflin [38] equations and this finding is comparable to that of a systematic review undertaken in adults [37] which is surprising because these equations were derived in a population aged 19–78 years. A possible explanation for this is that, although the Mifflin equations [38] were derived from an adult population with a mean age of 45 years, their participants were stratified by age and comprised approximately 20% aged ≤29 years. In addition, approximately 47% of their participants weighed ≥120% of ideal body weight compared to just 16% weighing <100%. It is possible that the better precision observed using the Mifflin equations in those aged 11–18 years in the present analysis reflects these participants being potentially post-pubertal and therefore closer in body composition to the Mifflin adults compared to when the wider age group of 7–18 years was considered. In the present study, if a wider age group of 7–18 years was considered, the equations of Schmelzle [52], Harris Benedict [54] and Henry [55] all performed with comparable precision. However, with increased precision, accuracy is compromised and so practitioners who need estimations of REE should consider what is important for their situation when selecting an equation, as well as be aware that no equations provide accurate and precise predictions in all groups and that it is not realistic to expect this.

There are a number of challenges associated with investigating the prediction of REE in young people. These include the dynamic changes occurring in relation to growth and variation in body composition and the effects of puberty [59] in those aged 11–18 years, as explained above. Obesity has been reported to increase the likelihood of early onset of puberty in girls with less clarity about its impact on boys [60,61]. In addition, differences in physical activity levels between children and adolescents may impact upon body composition and thus influence REE. Physical activity levels are generally low in UK children and boys are more active than girls (23% of boys and 20% of girls met the recommendations [62] for physical activity in 2015 ([63])). Activity levels in girls fall with age, while hours spent in sedentary activities increase with age [64]. In addition, obese children are likely to be less active than non-obese children [65–68]. Physical activity has been shown to affect anthropometric measurements with differential effects by sex; in girls apart from body mass index (BMI), all anthropometric measures were affected, whereas, in boys, BMI *Z*-score and fat-free mass only were affected [69]. The possible effects of physical activity are separate from but related to the effects of puberty, but may help to explain why REE prediction equations perform less well than might be expected. The equations examined in the included studies do not take these factors into account and this may contribute to the lower levels of precision observed in children in the present review compared to adults [37].

There was insufficient information to evaluate the accuracy of equations in children aged <3 years or of precision of equations in those <7 years. Because there is increasing awareness of the risks of overweight and obesity in very young children [70], more research is needed in this age group to provide guidance about their energy requirements. There are methodological complexities associated with measuring REE using indirect calorimetry in younger children [71] and, where this has been undertaken, it is primarily in those who are critically ill and

Table 4 Precision of equations predicting resting energy expenditure in two age groups, analysed by participant and by study subgroup

	Analysis by participant			Analysis by study subgroup		
Age subgroup (years)	Equation	Participants (*n*)	Precision (%)	Equation	Subgroups (*n*)	Precision (%)
11–18	Mifflin	347	62	Mifflin	2	63
	Schmelzle	385	57	Harris & Benedict	2	58
	Henry 1999	385	56	Schmelzle	3	57
	Harris & Benedict	347	54	Henry 1999	3	56
	Molnár	611	51	Lazzer	2	54
	Lazzer	347	49	Molnár	4	52
	WHO wt & ht	347	45	WHO wt & ht	2	47
	WHO wt	611	44	WHO wt	4	46
	Schofield	385	43	Schofield	3	43
	IOM hw	226	41	IOM hw	1	41
	Müller	385	35	Müller	3	36
	IOM oo	226	34	IOM oo	1	34
	Henry 2005	385	29	Henry 2005	3	32
7–18*	Schmelzle	385	57	Harris & Benedict	2	58
	Henry 1999	385	56	Schmelzle	3	57
	Harris & Benedict	347	54	Henry 1999	3	56
	Molnár	611	51	Mifflin	4	56
	Mifflin	1759	51	Lazzer	2	54
	Lazzer	347	49	Molnár	4	52
	WHO wt & ht	1759	44	WHO wt	4	46
	WHO wt	611	44	WHO wt & ht	4	45
	Schofield	385	43	Schofield	3	43
	IOM hw	284	37	Müller	3	36
	Müller	385	35	Henry 2005	3	32
	IOM oo	284	33	IOM oo	3	32
	Henry 2005	385	29	IOM hw	3	28

Precision expressed as the percentage of participants with predicted resting energy expenditure (REE) within 10% of measured REE; wt, weight; ht, height; hw, healthy weight; oo, overweight and obese
*Data not available for children aged <7 years.

where respiratory gases are being monitored for clinical purposes [72], as well as of interest for determining energy requirements. In addition, different criteria for identifying overweight and obesity are used in very young children than those who are older [73,74], which adds further complexity as a child grows and transitions from one to the other.

Based on the numbers in Table 3, it appears that equations which have been widely tested tend to have better accuracy [with the exception of the WHO (wt) equation]. Older equations perform better and this may reflect the fact that they have been tested more and in more diverse populations than newer equations. The exception of the WHO (wt) equation may reflect the fact that this equation relies on a single parameter (body weight) that does not adequately reflect the complexities of different body composition in this group. A single body weight may reflect a range of different body compositions, and the relative proportions of fat and fat-free mass will impact upon REE. Several studies have developed new equations in a calibration population and tested them in a separate validation group and recommended their use over previously published equations [39,45]. This is perhaps unsurprising because participants for calibration and validation were commonly recruited from the same population. However, to minimise the potential impact of this on the conclusions, this review excluded equations that had been evaluated in less than two studies.

Strengths

The eligibility criteria of the review were used to ensure the studies included provided high quality data. The protocol was published in advance and adhered to throughout [41]. All decisions were made in duplicate and a third investigator was consulted on the few occasions when they did not agree. The review team included researchers with experience of undertaking systematic reviews, measuring REE and using REE prediction in clinical paediatric practice and so, collectively, they were able to evaluate a range of relevant aspects. The risk of bias of the review was assessed using the ROBIS tool [44] and indicated that robust mechanisms were used throughout and, where methods deviated from the published protocol, full explanations were given. Risk of bias was considered to be low.

Limitations

A range of definitions of obesity were accepted, providing these were explicitly stated, and included different cut-offs for percentiles of normal data or relative values (e.g. percentage ideal body weight). This variation between studies means that degree of excess weight was not explored (i.e. as in adults using simply BMI categories to define overweight and obesity). It is likely that different degrees of excess body weight impact differently on total REE and REE per kg body weight, although it was not possible to take this into account. The 13 studies included in the data analysis were undertaken in Europe (nine) and North America (four). This means that large sections of the world population have not been represented. Studies from other continents were retrieved by the search strategy but were subsequently excluded as a result of not meeting inclusion criteria, including methodology, which may have impacted on the results (e.g. fasting for <6 h and REE not measured using an externally calibrated indirect calorimeter) [75,76]. This geographical limitation is important because ethnicity is known to impact on REE through differences in body composition and the review has not been able to address this. McDuffie *et al.* [77] reported on the impact on ethnicity in black and white overweight and normal weight children but did not meet the inclusion criteria for the review because data for overweight and obese children were not reported separately.

Conclusions

No single equation provided both accurate and precise REE estimations in this population and it is important to recognise that all calculated values are just estimates. The Schofield equations provided the most accurate REE predictions so are recommended for those working with *groups* of overweight or obese young people aged 3–18 years where, collectively, a least biased REE value is required. However, the Schofield equations are not optimum for those seeking a precise REE value for *individuals* because only 43% of predictions are likely be within 10% of measured REE.

In clinical practice, where precision is often more important than accuracy, the Mifflin equations are recommended for estimating REE in young people aged 11–18 years. However, practitioners should be aware that these equations, although the most precise in this age group, are imprecise in approximately 40% of individuals and tend to provide underestimates of REE. Although the Mifflin equations did not provide the most precise estimations of REE in the wider age group of 7–18 years, they are recommended in preference to those of Henry [56], which currently form the basis of the UK Dietary Reference Values for Energy [35] but which demonstrated poor precision in those who are overweight or obese.

Further studies of prediction of REE are required in children under 7 years, and particularly in those aged <3 years, to enable recommendations to be made in these groups.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting is compliant with the PRISMA guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned in the published protocol (PROSPERO 2016 CRD42016042790) have been explained.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.
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Lucy Chima undertook the database searches, data extraction and analysis, and contributed to the manuscript. Hilda Mulrooney co-designed the study, undertook data extraction and analysis, and contributed to the manuscript. Janet Warren suggested the original idea, advised on aspects relating to paediatric nutrition and contributed to the manuscript. Angela Madden co-designed and supervised the overall study, duplicated the searches, and contributed to data analysis and the writing of the manuscript.

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Supporting information

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

Data S1. Assessment of risk of bias using the ROBIS(44) tool.

Table S1. Accuracy of equations predicting resting energy expenditure in three age groups, analysed by participant and by study subgroup without studies 23, 42 & 43.

Table S2. Precision of equations predicting resting energy expenditure in two age groups, analysed by participant and by study subgroup without studies 23, 42 & 43.