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Meta-analyses

# Prediction of resting energy expenditure in healthy older adults: A systematic review

Iolanda Cioffi [a,*], Maurizio Marra [a], Fabrizio Pasanisi [a], Luca Scalfi [b]

[a] Department of Clinical Medicine and Surgery, Federico II University Hospital, Pansini 5, 80131 Naples, Italy
[b] Department of Public Health, Federico II University Hospital, Naples, Pansini 5, 80131 Italy

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SUMMARY

*Background & aims:* Estimates of energy requirements, based on measured or predicted resting energy expenditure (REE), are needed to avoid undernutrition or overnutrition (and their clinical consequences) in elderly subjects. The aims of this systematic review were to evaluate the prediction accuracy of REE in healthy elderly subjects and to ascertain which equation is more reliable at group level and/or individual level.

*Methods:* Studies assessing prediction of REE in general elderly population were systematically searched using PubMed, EMBASE, Web of Science and CINAHL until March 2020. Prediction accuracy of REE was assessed at both group (bias) and individual (precision) level for each equation.

*Results:* Fourteen studies met the inclusion criteria of this systematic review. Bias was reported in 8 papers and calculated in another 5 from absolute values. There was a prevalent tendency towards an overestimation of REE across the studies. The least bias was observed for the Mifflin (−0.3%) and Harris–Benedict (+2.6%) equations, with values above 5% for the FAO/WHO/UNU, Fredrix and Muller equations. Precision widely varied between studies for the same equation. The higher precision was observed using the Harris–Benedict equation (~70%), while the Henry and Mifflin equations provided estimates within 10% of measured values in 65% and 61% of elderly individuals, respectively.

*Conclusions:* None of the prediction equations considered provides accurate and precise REE estimates in healthy older adults. However, the best prediction is given by the Mifflin equation at group level and by the Harris–Benedict equation at individual level. Further studies with strong quality design are needed to evaluate the variability and accuracy of REE in the elderly general population.



## 1. Introduction

Due to increasing in life expectancy, more attention is paid to the energy and nutrient requirements of elderly subjects, i.e. individuals aged 60–65 years or older [1,2]. The knowledge of energy requirements is essential to avoid undernutrition or overnutrition and for the targeted nutritional support of both healthy elderly people and those who are frail, malnourished, sarcopenic or affected by chronic diseases such as heart failure, stroke, chronic obstructive pulmonary disease, etc. [3,4].

Energy requirement is defined as the amount of energy needed to balance energy expenditure, with some adjustments for specific metabolic demands or excess body fat and is therefore based on measures of total energy expenditure (TEE). Energy needs decline gradually with aging due to a decrease in both resting energy expenditure (REE) and physical activity level (PAL). Indeed, REE is by far the largest component and the most important determinant of TEE not only in adults but also in elderly people [4]. Generally, in public health and clinical nutrition, energy requirements are routinely calculated by multiplying estimated or measured REE plus physical activity and disease coefficients [1].

Although REE can be efficiently measured by indirect calorimetry, the cost of equipment, the time required for the measurement as well as the need of specific experience and skills have limited the use of this technique to specialized settings [1,5]. As an alternative, predictive equations based on demographic, anthropometric and/or body composition variables and derived from healthy individuals are applied in public health nutrition and in the clinical setting to estimate REE in population groups, groups of subjects or single individuals [5].

* Corresponding author. Department of Clinical Medicine and Surgery Federico II University, Via S. Pansini 5, 80131 Naples, Italy. Fax: +390817462376.
*E-mail address:* iolanda.cioffi@unina.it (I. Cioffi).

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So far, a small number of predictive equations for REE have been developed for elderly people (age >60 years) such as the Schofield [6] and the FAO/WHO/UNU equations [7] from data retrieved all over the world (but small samples), and the Henry one [8] in a much larger sample, again from different countries. In addition, the Fredrix [9] and the Luhrmann [10] equations were generated and validated for healthy aged people in single center studies. Besides, the equations developed for the general population such as the Harris–Benedict (HB) [11] and Mifflin [12] equations are frequently applied in subjects aged >60 years. The accuracy of predictive equations in elderly is therefore questioned, mainly because the commonly used formulas developed in the healthy adult population may result unsuitable in subjects age >60–65 years [4]. Facing this background and considering some more recent papers published on the issue in the last decade [15–20], we implemented a systematic review aiming: 1) to evaluate the prediction accuracy of REE in healthy elderly subjects and 2) to assess which of the validated equations gave the best results at both group and/or individual level.

## 2. Materials and methods

A systematic review of the literature was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [21].

### 2.1. Search strategy

The following electronic databases were queried using a combination of search terms until the 4th of March 2020: PubMed, EMBASE, Web of Science and Cumulative Index to Nursing and Allied Health Literature (CINAHL). The construction of the search strategy was performed using database specific subject headings and keywords. Both medical subject headings (MeSH) and free text search terms were employed in different databases. The search strategy was performed using the combination of the following terms (resting energy expenditure OR resting metabolic rate OR basal metabolic rate OR basal energy expenditure) AND (elderly OR older subject) AND (prediction equation OR predictive equation).

The limits for search included data from aged participants and human subjects, whereas no filters were applied for study design and publication date. The search strategy was implemented by hand searching the references of all the included studies and systematic reviews or meta-analysis on the field.

### 2.2. Eligibility criteria and study selection

The eligibility of the studies was set according to the PICOS (Population, Intervention, Comparison, Outcomes, and Study design) criteria and reported in Fig. 1.

Two authors (I.C., L.S.) separately screened abstracts for their inclusion or exclusion; retrieving full text articles from potentially relevant abstracts. Any disagreement about inclusion was resolved by discussing with a third review author (M.M.).

We selected studies with the following characteristics: 1) including subjects aged ≥60 years in good health (or defined "free from illness and disease"); 2) comparing predicted REE (PREE) with measured REE (MREE) by indirect calorimetry or other validated methods (metabolic cart or other measurement of oxygen uptake and carbon dioxide production using externally calibrated equipment); 3) reporting a detailed description of standardized condition adopted before performing the measurement such as an overnight fasting and bed rest before the measure; and 4) showing data on REE accuracy at the group level and/or at the individual level.

Studies were excluded for the following reasons: 1) inclusion of acutely ill patients (including mechanically ventilated patients) or with diseases such as thyroid dysfunction, diabetes mellitus, hypertension, psychiatric diseases and cancer that might influence metabolic rate; 2) exclusive enrollment of subjects with overweight and/or obesity; 3) the use of specific medications known to affect REE; 4) the employment of predictive methods for estimating energy expenditure (e.g. calculated from accelerometry, heart rate monitoring) or equipment that had not been externally calibrated (e.g. hand-held devices).

### 2.3. Data extraction and analysis

Two authors (I.C., L.S.) independently examined key participant characteristics and reported data from papers which met the inclusion criteria using standard data extraction templates. From each included study, the following information were extracted: 1) first author name and year of publication; 2) study design and aims; 3) inclusion and exclusion criteria of participants; 4) number of subjects; 5) age, gender and body mass index (BMI) of participants; 6) REE measurement and type of calorimeter used; 7) predictive equations used for estimating REE and 8) data on REE accuracy at the group and/or at the individual level. Specifically, as measure of accuracy at the group level was used the average percent difference between PREE and MREE, i.e. bias. While the percentage of patients with a PREE within ±10% of MREE was adopted as a measure of accuracy at the individual level or precision.

To simplify calculation of accuracy prediction, equations were excluded from the analysis if they were evaluated by fewer than three studies. However, a table of all equations used by included studies was made from the original publications and reported in the supplementary material (Table S1). The authors of original papers that met the inclusion criteria were contacted if any clarification about the data was required. For each selected study, results were reported for the entire populations as well as, if possible, for male/female subgroups. Data on accuracy at group level (bias) and/or at individual level (precision) were summarized manually to allow for analysis by participants, which took account of the number of subjects in the group by weighting mean values, and by study groups (without any adjustment), as previously done [22,23].

### 2.4. Risk of bias assessment

The validity of studies was independently assessed by two authors (I.C., L.S.) using the "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies" developed jointly by methodologists from the National Heart, Lung and Blood Institute (NHLBI) and Research Triangle Institute International [24]. The tools included fourteen items for assessing potential flaws in study methodology, including sources of bias (e.g., patient selection, performance, attrition, and detection), confounding, study power, and other factors. A judgment of "good" indicated a low risk of bias, "poor" indicated a significant risk of bias and "fair" meant that the study was susceptible to some bias deemed not sufficient to invalidate its results. The possible disagreements were resolved by consensus, or with consultation with a third author (M.M.).

## 3. Results

### 3.1. Description of the studies included

The initial literature search identified 2196 records. After removing duplicates, 483 records were screened for titles and abstracts, and then, after excluding articles not meeting the inclusion criteria, 64 full papers were assessed for eligibility. After further

| Criteria | Inclusion criteria | Exclusion criteria |
|---|---|---|
| **Population** | Elderly individuals | Elderly participants who were affected by diseases or took medications known to affect REE |
| **Intervention** | The use of predictive equations for estimating REE | Different predictive methods for estimating energy expenditure (e.g. calculated from accelerometry, heart rate monitoring) |
| **Comparison** | The measurement of REE by indirect calorimetry or other validated methods (metabolic cart or other measurement of oxygen uptake and carbon dioxide production using externally calibrated equipment) | The use of equipment for measuring REE that had not been externally calibrated (e.g. hand-held devices) and the lack of standardized procedures such as fast, bed rest etc. before REE measurement. |
| **Outcome** | The accuracy of REE prediction at both group (bias) and/or individual (precision) level | None |
| **Study design** | All types of studies | None |

**Fig. 1.** PICOS criteria for inclusion and exclusion of studies.

analysis and quality assessment, a total of 14 studies met the inclusion criteria for this systematic review (Fig. 2).

All identified studies had an observational/cross-sectional design, and the main characteristics are shown in Table 1. Data relative to group of participants with obesity [16] or assessing TEE [25] or derived from alternative methods for measuring REE [26] were not considered, because not pertinent to the aims of this review.

### 3.2. Characteristics of the studies

The accuracy of predictive equations was reported by studies including between 20 and 335 elderly subjects. In Table 1 was indicated that ten studies recruited both males and females, while two only females [19,27] and two only males [18,25]. All studies enrolled elderly individual with no physical disabilities and no evidence of diseases known to affect energy expenditure or mental

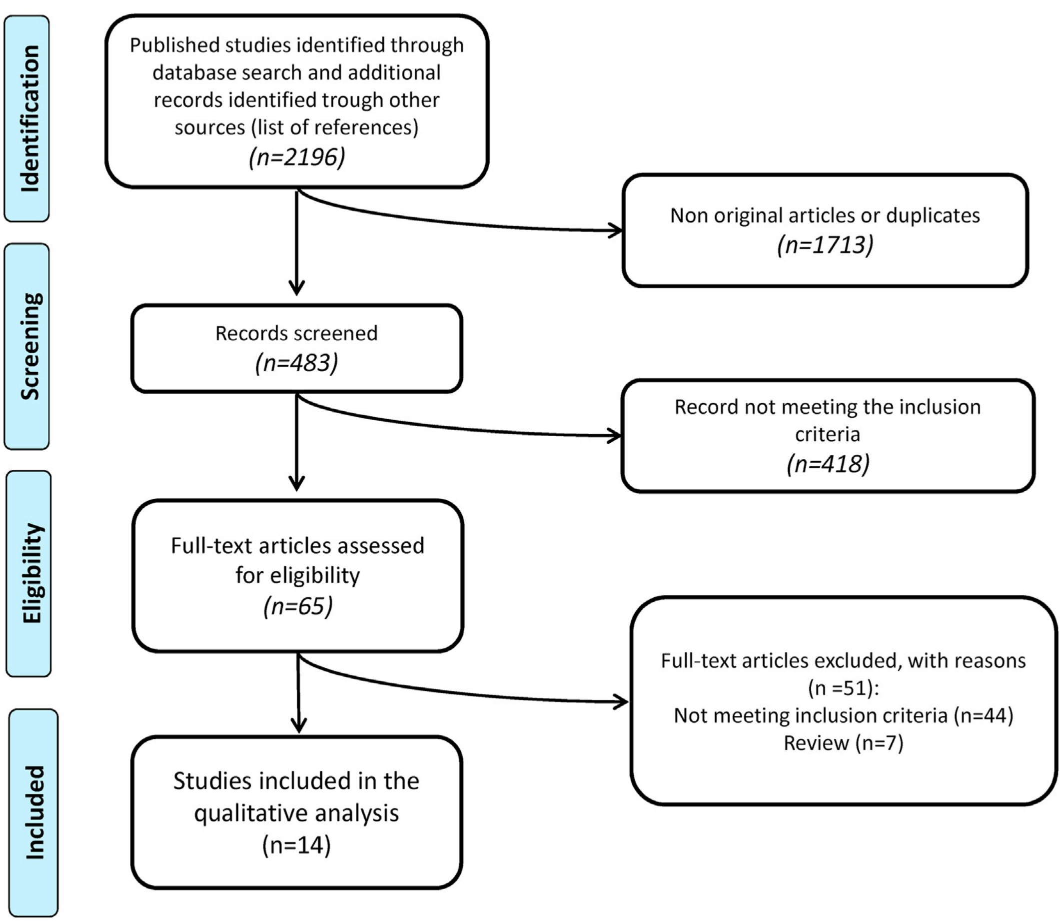


**Fig. 2.** Flow diagram of the literature search process.

**Table 1**
Characteristics of the included studies.

| Author, year, [ref] | Study design | Participants | N | Age (years) | Gender M/F | BMI (kg/m$^2$) | REE measurement (equipment used; fast; rest; measurement time) | Measured REE (Kcal/die) |
|---|---|---|---|---|---|---|---|---|
| Fredrix et al. (1990) [9] | Cross-sectional | Healthy elderly volunteers<br>Age 51–82 y<br>BMI = 21–31 kg/m2<br>Stable body weight<br>Absence of mental and metabolic diseases | 40 | M = 63 ± 8<br>F = 66 ± 7 | 18/22 | M = 26.4 ± 2.4<br>F = 25.5 ± 2.6 | Mijnhardt Servomex metabolic cart; 10-h overnight fast; 30 min rest; 30 min measurement. | REE = 1512 kcal/d<br>M = 1733 kcal/d<br>F = 1330 kcal/d |
| Fuller et al. (1996) [25] | Cross-sectional | Free-living elderly men<br>Age 76-88y<br>Absence of mental and metabolic diseases<br>Adequate physical capacity | 23 | Median = 82 | 23/0 | 24.8 ± 3.0 | Deltatrac™ MBM- 100; fast, rest and time measurement not specified. | M = 1433 kcal |
| Itoi et al. (2017) [17] | Cross-sectional | Community-dwelling elderly subjects<br>Age 64–78 y<br>BMI = 17–27.5 kg/m2<br>No evidence of disease or prescription medications known to affect REE<br>No history of alcohol abuse | 32 | 73.9 ± 6.2 | 14/18 | 22.2 ± 2.5 | Minato Medical Science metabolic cart; 12-h overnight fast; 20 min rest; 30 min measurement. | REE = 1132 kcal/d |
| Karlsson et al. (2017) [18] | Cross-sectional | Octogenarian men<br>Age ≥82y<br>BMI = 22.2–32.5 kg/m2<br>Not specified | 22 | 82.6 ± 0.3 | 22/0 | 27.0 ± 2.8 | DeltaTrac II; 12-h overnight fast; 15–20 min rest; 15–30 min measurement. | M = 1440 kcal |
| Khalaj-Hedayati et al. (2009) [26] | Cross-sectional | Free-living elderly subjects<br>Age 61–83 y<br>BMI = 22.3–31.3 kg/m2<br>Nonsmoker<br>Adequate physical capacity<br>Absence of metabolic diseases | 50 | M = 68.4 ± 4.1<br>F = 68.6 ± 4.7 | 24/26 | M = 26.2 ± 2.59<br>F = 25.7 ± 3.49 | Vmax Spectra 29n Sensormedics; overnight fast;<br>10 min rest; 30 min measurement. | M = 1558 kcal*<br>F = 1227 kcal* |
| Luhrmann et al. (2002) [10] | Cross-sectional | Free-living elderly subjects<br>Age 60–85 y<br>Adequate physical capacity<br>No evidence of diseases known to affect REE | 285 | M = 66.9 ± 5.1<br>F = 67.8 ± 5.7 | 106/179 | M = 26.3 ± 3.1<br>F = 26.4 ± 3.7 | Deltatrac™MBM-100; fast and rest not specified; 25–35 min measurement. | M = 1633 kcal*<br>F = 1315 kcal* |
| Luhrmann et al. (2004) [31] | Cross-sectional | Free-living elderly subjects<br>Age 60–85 y<br>BMI = 18.3–40.1 kg/m2<br>Adequate physical capacity<br>No evidence of diseases known to affect REE | 335 | M = 67.4 ± 5.4<br>F = 67.7 ± 5.5 | 130/225 | M = 26.7 ± 3.2<br>F = 26.7 ± 3.9 | Deltatrac™MBM-100; fast and rest not specified; 25–35 min measurement. | M = 1661 kcal*<br>F = 1334 kcal* |
| Melzer et al. (2007) [28] | Cross-sectional | Healthy elderly subjects<br>Age 70–98 y<br>Adequate physical capacity<br>No evidence of diseases known to affect REE | 119 | M = 78.4 ± 5.6<br>F = 78.6 ± 5.3 | 64/55 | M = 26 ± 7.31<br>F = 25.5 ± 5.0 | Deltatrac II Metabolic Monitor; overnight fast; 30 min rest; 30 min measurement | REE = 1370 kcal<br>M = 1462 kcal<br>F = 1139 kcal |
| Nhung et al. (2007) [30] | Cross-sectional | Healthy elderly subjects<br>Age 60–70 y<br>BMI = 18.5–24.9kg/m2<br>No evidence of any metabolic or mental diseases known to affect REE | 75 | M = 65 ± 4.0<br>F = 66.5 ± 4.6 | 35/40 | M = 22.9 ± 2.04<br>F = 21.9 ± 1.8 | Oxycon Delta metabolic cart; 12-h overnight fast; 30 min rest; > 15 min measurement | M = 1361 kcal*<br>F = 1142 kcal* |
| Noreik et al. (2014) [16] | Cross-sectional | Healthy elderly subjects divided in 2 groups:<br>BMI 21–28.9 kg/m2<br>BMI > 29kg/m2 Age ≥65 y | 20<br>20 | 82.1 ± 6.6<br>79.8 ± 8.1 | 9/11<br>5/15 | 24.9 ± 2.5<br>33.7 ± 4.5 | Vmax Spectra 29, Sensormedics; overnight fast;<br>30 min rest; > 10 min measurement | REE = 1315 kcal<br>REE = 1526 kcal |

(continued on next page)

**Table 1** (*continued*)

| Author, year, [ref] | Study design | Participants | N | Age (years) | Gender M/F | BMI (kg/m$^2$) | REE measurement (equipment used; fast; rest; measurement time) | Measured REE (Kcal/die) |
|---|---|---|---|---|---|---|---|---|
| | | Absence of metabolic and mental diseases Sufficient physical capacity | | | | | | |
| Reidlinger et al. (2015) [29] | Cross-sectional | Healthy elderly subjects Age >70 y No evidence of any metabolic or mental diseases known to affect REE | 34 | M = 74 ± 3.4 F = 75.6 ± 5 | 14/20 | M = 27.7 ± 2.2 F = 24.7 ± 3.2 | Europa GEM metabolic cart; overnight fast; 30 min rest; 30 min measurement | REE = 1253 kcal M = 1415 kcal F = 1139 kcal |
| Sgambato et al. (2019) [19] | Cross-sectional | Healthy elderly women Age 60–97 y BMI = 17.3–39.9 kg/m2 No evidence of any metabolic or mental diseases known to affect REE | 79 | 69.7 ± 6.5 | 0/79 | 27.2 ± 4.6 | Vmax Encore29, Sensormedics; 12-h overnight fast; 15 min rest; 25 min measurement | F = 1001 kcal* |
| Siervo et al. (2014) [15] | Cross-sectional | Healthy elderly subjects Age 60–94 y BMI = 18.1–48.1 kg/m2 No evidence of diseases known to affect REE Absence of weight changes (±5 kg) in the last year | 68 | 74.4 ± 9.3 | 13/55 | 26.3 ± 5 | Vmax 29 Sensormedics; overnight fast; rest not specified; 30–40 min measurement | REE = 1298 kcal M = 1654 kcal F = 1214 kcal |
| Taaffe et al. (1995) [27] | Cross-sectional | White elderly women Age 60–82 y BMI = 18.9–39.4 kg/m2 Apparently healthy and free of systemic disease and metabolic disorders known to affect REE. | 116 | 67.1 ± 4.4 | 0/116 | 26.7 ± 4.2 | Douglas bag metabolic cart; 10-h overnight fast; rest not specified; > 10 min measurements | F = 1285 kcal |

Data are expressed as mean ± standard deviation, unless otherwise specified. BMI = body mass index; F = females; M = males; REE = resting energy expenditure; y = year.
* Transformed in kcal.

or neurological disorders. However, no information in this regard was available in the paper by Karlsson et al. [18].

As reported in Table 1, most subjects aged ≥60 years, with some exceptions: two studies [28,29] enrolled individuals aged ≥70 years and one [18] included only octogenarians, while in the study by Fredrix et al. [9] the age of participants varied between 51 and 82 years.

Mean BMI of participants ranged from 22.2 to 27.7 kg/m$^2$ (Table 1). In the study by Nhung et al. [30] subjects had a BMI 18.5–24.9 kg/m$^2$, whereas in the others papers, BMI showed a huge variability, varying from normal weight to overweight/obesity or even severe obesity [15,19,27]. In other words, elderly subjects with normal-weight, overweight and obesity were included in most study samples.

Finally, studies considered in the present review were performed in different countries: 4 in Germany [10,16,26,31]; 3 in UK [9,25,29], and one each in Italy [15], Sweden [18], Switzerland [28], USA [27], Brazil [19], Vietnam [30] and Japan [17].

### 3.3. Risk of bias

The risk of bias is reported in the supplementary material (Table S2). Quality rating was fair for many studies, most of them being at moderate risk of bias. Overall, the sample size was small without being justified, and some differences emerged in the assessment of REE prediction and data reporting. Two studies [18,29] were rated as poor with a significant risk of bias (less than 50% of eligible people participated in the study), whereas four studies had an overall good quality rating [10,26,30,31]. It should be highlighted that some questions, included in this study quality assessment tool, cannot be applied for cross-sectional, due to the type of study design.

### 3.4. Resting energy expenditure

In all the studies selected for this review, indirect calorimetry was performed for measuring REE according to the following standardized conditions: i) overnight fast (at least 10–12 h); ii) bed rest from 10 until 30 min before starting the measurement and iii) measurement of energy expenditure after an adjustment period for 10–15 min [16,27,30] until 30–40 min [9,10,15,17,18,26,28,29,31], discarding the first 5–10 min from the analysis. The metabolic carts with canopy system were: Deltatrac [10,18,25,28,31], Minato Medical Science [17], Mijnhardt Servomex [9], Vmax SensorMedics [15,16,19,26], Oxycon Delta [30] and Europa GEM [29]. In the study by Taaffe et al. [27] REE was determined by indirect calorimetry but expired air was collected using Douglas bags.

### 3.5. Prediction accuracy

As reported above, to make more reliable the evaluation of prediction accuracy across the studies, only the equations assessed in at least three studies were selected for this systematic review (Table 2). They were those derived from the general population such as the HB [11], Mifflin [12], Muller [32] and Owen [33] equations as well as those specifically developed for the elderly

**Table 2**
Predictive equations for resting energy expenditure (REE) evaluated for accuracy by studies included in the systematic review.

| Equations developed for the general population | Study evaluating accuracy | |
|---|---|---|
| | At group level | At individual level |
| **Harris Benedict 1919**<br>Male $REE\ (kcal) = 13.7516 \times BW + 5.0033 \times H\ (cm) - 6.7550 \times age + 66.4730$<br>Female $REE\ (kcal) = 9.5634 \times BW + 1.8496 \times H\ (cm) - 4.6756 \times age + 655.0955$ | Fredrix et al. [9], Itoi et al. [17], Khalaj-Hedayati et al. [26], Melzer et al. [28], Noreik et al. [16], Reidlinger et al. [29], Siervo et al. [15], Fuller et al. [25], Luhrmann et al. [31], Sgambato et al. [19], Taaffe et al. [27]. | Itoi et al. [17], Khalaj-Hedayati et al. [26], Karlsson et al. [18] Melzer et al. [28], Reidlinger et al. [29], Siervo et al. [15]. |
| **Mifflin 1990**<br>$REE\ (kcal) = 9.99 \times BW + 6.25 \times H\ (cm) - 4.92 \times age + 166 \times sex\ (M = 1; F = 0) - 161$ | Itoi et al. [17], Khalaj-Hedayati et al. [26], Melzer et al. [28], Noreik et al. [16], Reidlinger et al. [29], Siervo et al. [15], Sgambato et al. [19], Taaffe et al. [27]. | Itoi et al. [17], Khalaj-Hedayati et al. [26], Melzer et al. [28], Reidlinger et al. [29], Siervo et al. [15]. |
| **Muller 2004**<br>$REE\ (MJ) = 0.047 \times BW + 1.009 \times sex\ (M = 1; F = 0) - 0.01452 \times Age + 3.21$ | Itoi et al. [17], Khalaj-Hedayati et al. [26], Reidlinger et al. [29], Siervo et al. [15], Sgambato et al. [19]. | Itoi et al. [17], Khalaj-Hedayati et al. [26], Reidlinger et al. [29], Siervo et al. [15]. |
| BMI 25–30 kg/m2: $REE\ (MJ) = 0.04507 \times BW + 1.006 \times sex + 0.01553 \times age + 3.407$ | Noreik et al. [16]. | |
| **Owen 1986**<br>Male $REE\ (kcal) = 879 + 10.2\ BW$<br>Female $REE\ (kcal) = 795 + 7.18\ BW$ | Fredrix et al. [9], Itoi et al. [17], Noreik et al. [16], Siervo et al. [15], Taaffe et al. [27]. | Itoi et al. [17], Melzer et al. [28], Siervo et al. [15] |
| **Equations developed for the elderly population** | **At group level** | **At individual level** |
| **FAO/WHO/UNU 1985**<br>>60 y Male $REE\ (kcal) = 13.5 \times BW + 487$<br>>60 y Female $REE\ (kcal) = 10.5 \times BW + 596$ | Itoi et al. [17], Khalaj-Hedayati et al. [26], Melzer et al. [28], Luhrmann et al. [10,31]; Noreik et al. [16], Nhung et al. [30], Siervo et al. [15], Taaffe et al. [27]. | Itoi et al. [17], Nhung et al. [30] Siervo et al. [15]. |
| >60 y Male $REE\ (kcal) = 8.8 \times BW + 1128 \times H\ (m) - 1071$<br>>60 y Female $REE\ (kcal) = 9.2 \times BW + 637 \times H\ (m) - 302$ | | Khalaj-Hedayati et al. [26], Melzer et al. [28]. |
| **Fredrix 1990**<br>>51 y $REE\ (kcal) = 1641 + 10.7 \times BW - 9.0 \times age - 203 \times sex\ (M = 1; F = 2)$ | Itoi et al. [17], Khalaj-Hedayati et al. [26], Siervo et al. [15], Taaffe et al. [27] | Itoi et al. [17]. Khalaj-Hedayati et al. [26], Siervo et al. [15]. |
| **Luhrmann 2002**<br>>60 y $REE\ (kJ) = 3169 + 50.0 \cdot BW - 15.3 \cdot age + 746 \cdot sex\ (M = 1; F = 0)$ | Itoi et al. [17], Khalaj-Hedayati et al. [26], Melzer et al. [28], Noreik et al. [16], Reidlinger et al. [29], Siervo et al. [15], Sgambato et al. [19]. | Itoi et al. [17], Khalaj-Hedayati et al. [26], Melzer et al. [28], Reidlinger et al. [29], Siervo et al. [15]. |
| **Henry 2005 (Oxford)**<br>>60 y Male $REE\ (kcal) = 13.5 \times BW + 514$<br>>60 y Female $REE\ (kcal) = 10.1 \times BW + 569$ | Sgambato et al. [19] | |
| 60-70 y Male $REE\ (kcal) = 13 \times BW + 567$<br>60-70 y Female $REE\ (kcal) = 10.2 \times BW + 572$ | Itoi et al. [17], Siervo et al. [15] | Itoi et al. [17], Siervo et al. [15] |
| >70 y Male $REE\ (kcal) = 13.7 \times BW + 481$<br>>70 y Female $REE\ (kcal) = 10 \times BW + 577$ | Itoi et al. [17], Siervo et al. [15 | Itoi et al. [17], Siervo et al. [15 |
| >60 y Male $REE\ (kcal) = 11.4 \times BW + 541 \times H\ (m) - 256$<br>>60 y Female $REE\ (kcal) = 8.52 \times BW + 421 \times H\ (m) + 10.7$ | Khalaj-Hedayati et al. [26], Reidlinger et al. [29] | Khalaj-Hedayati et al. [26], Reidlinger et al. [29] |
| **Schofield 1985**<br>>60 y Male $REE\ (kcal) = 13.5 \times BW + 487$<br>>60 y Female $REE\ (kcal) = 10.5 \times BW + 596$ | Fredrix et al. [9], Noreik et al. [16], Siervo et al. [15], Luhrmann et al. [31], Sgambato et al. [19] | |
| >60 y Male $REE\ (MJ) = 0.038\ BW + 4.068H\ (m) - 3.491$<br>>60 y Female $REE\ (MJ) = 0.033\ BW + 1.917H\ (m) + 0.074$ | Luhrmann et al. [31] | |

BMI: Body Mass Index; BW: body weight; H: height; y: years.

population (age >60 years), i.e. the Fredrix [9], Luhrmann [10], FAO/WHO/UNU [7], Schofield [6] and Henry [8] equations. As reported in Table 2, the HB equation [11] was the most frequently assessed, followed by the FAO/WHO/UNU [7], Luhrmann [10] and Mifflin [12] equations.

### 3.5.1. Accuracy at group level (bias)

The accuracy at group level was assessed by calculating bias, i.e. the average percent predicted-measured difference. Bias was reported in eight papers and calculated in another five from absolute values. The bias for each equation varied considerably between studies. Considering the Mifflin equation [12], it ranged from an underestimate of −12% to an overestimate of +9%, while less marked variations were observed for the other equations. There was a prevalent tendency towards an overestimation of REE (Table 3) except for the study by Siervo et al. [15]. Indeed, as reported in Fig. 3, substantial differences between equations emerged in the analysis by groups or by participants (i.e. weighted mean bias of different studies), with the least bias for the Mifflin [12] (−0.3%) and HB [11] (+2.6%) equations, and values above 5% for the equations proposed by FAO/WHO/UNU [7], Fredrix [9] and Muller [32]. Similar findings were observed for the study group analysis.

Seven studies analyzed results separately by gender, with similar findings to those just described (Table S3). The only exception was the study by Sgambato et al. [19] in elderly Brazilian females, which showed a remarkable overestimation for all the equations used, ranging from +13% for the Mifflin equation [12] up to + 30% for the Luhrmann equation [10].

**Table 3**
Accuracy at group level, assessed by bias, among included studies.

| | Age range | N | Bias (%)[a] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | HB | FAO/WHO/UNU | Fredrix | Henry | Luhrmann | Mifflin | Muller | Owen | Schofield |
| Fredrix et al. [9] | 51-82 y | 40 | +7 | | | | | | | +4 | +6 |
| Itoi et al. [17] | 64-78 y | 32 | −1 | +5 | +9 | +4 | +6 | −8 | +8 | +15 | |
| Khalaj-Hedayati et al. [26] | 61-83 y | 50 | +4 | +8[b] | +9 | +4[b] | +7 | +1 | +7 | | |
| Melzer et al. [28] [c] | 70-98 y | 119 | +3 | +4[b] | | | +3 | +6 | | +7 | |
| Noreik et al. [16] [c] | ≥65y | 20 | +4 | +3 | | | −2 | +9 | +5^ | +8 | +0.8 |
| Reidlinger et al. [29] [c] | ≥70 y | 34 | +6 | | | +9[b] | +12 | +1 | +12 | | +11 |
| Siervo et al. [15] [c] | 60-94 y | 68 | −2 | +8 | +1 | −0.7 | −1 | −12 | +0.2 | −2 | −0.6 |

[a] Data are presented as the difference between mean predicted and mean measured REE expressed as a percentage of mean measured REE. HB= Harris–Benedict.
[b] The equations used both body weight and height; ^ Equation for BMI 25–30 kg/m$^2$.
[c] Bias has been calculated by the absolute values reported in the text.

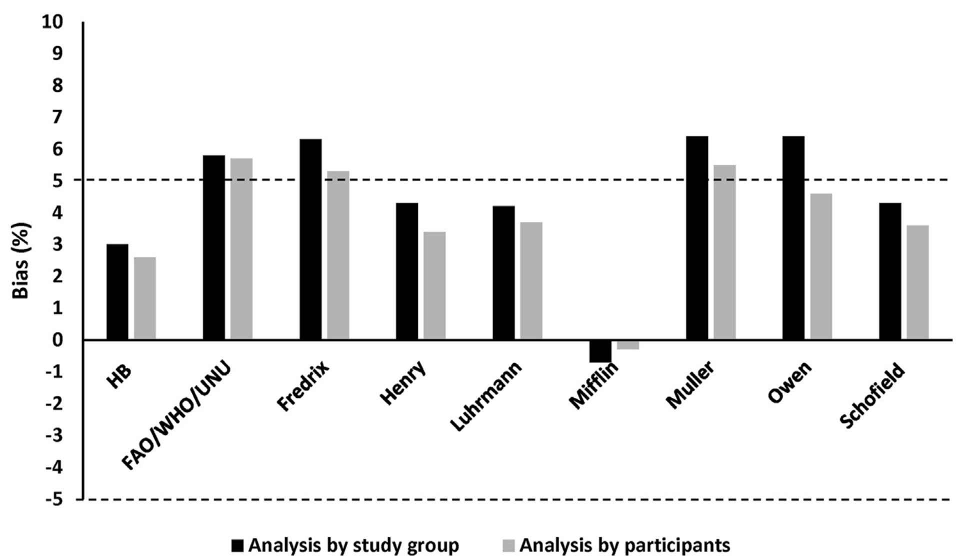


**Fig. 3. Accuracy at group level (bias).** Data are presented as the difference between mean predicted and mean measured REE expressed as a percentage of mean measured REE. Analysis by participants consisted of weighted means of bias, whereas analysis by study group had not adjustment of mean values.

**Table 4**
Accuracy at individual level, assessed by accuracy within 10%, among included studies.

| | Age range | N | Accuracy within ±10% | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | HB | FAO/WHO/UNU | Fredrix | Henry | Luhrmann | Mifflin | Muller | Owen |
| Itoi et al. [17] | 64-78 y | 32 | 88 | 72 | 66 | 81 | 72 | 56 | 69 | 31 |
| Khalaj-Hedayati et al. [26] | 61-83 y | 50 | 72 | 60[a] | 52 | 76[a] | 64 | 74 | 64 | |
| Melzer et al. [28] | 70-98 y | 119 | 72 | 64[a] | | | 64 | 60 | | 51 |
| Reidlinger et al. [29] | ≥70 y | 34 | 50 | | | 44[a] | 35 | 70 | 44 | |
| Siervo et al. [15] | 60-94 y | 68 | 64 | 42[b] | 66 | 60[b] | 58[b] | 38[b] | 63 | 50 |

Data are presented as the percentage of predicted REE values within 10% of measured REE. HB= Harris–Benedict.
[a] The equation used both body weight and height.
[b] Data was extracted by Fig. 1B of Siervo et al. [15].

### *3.5.2. Accuracy at individual level (precision)*

The accuracy at individual level (precision) was reported in eight studies as percentage of elderly subjects with a predicted REE between 90 and 110% of the measured one, showing very different results (Table 4). Precision widely varied between studies for the same equation and among mean values of different equations (by groups between 47 and 69% and by individuals between 44 and 69%). The Owen equation [33] gave the least precise estimates (44% as mean of three studies, range 31–51%). Based on the analysis by participants or by groups, the highest accuracy at individual level was observed using the HB equations (69%) [11], while the Henry [11] equations provided estimates within 10% of measured values in around 65% and the other equations in around 60% of participants (Fig. 4).

In 5 studies, precision was reported separately by gender or only for males or females (Table S4). The Mifflin equation [12] provided the highest precision in females (85%), but not in males (43%), as reported by Reidlinger et al. [29]. On the other hand, the study by Karlsson et al. [18], evaluating REE prediction in octogenarian men, showed that the Mifflin equation [12] provided the highest accuracy compared to other formulas. Precision values reported by Sgambato et al. [19] were very low in both genders for all the equations used.

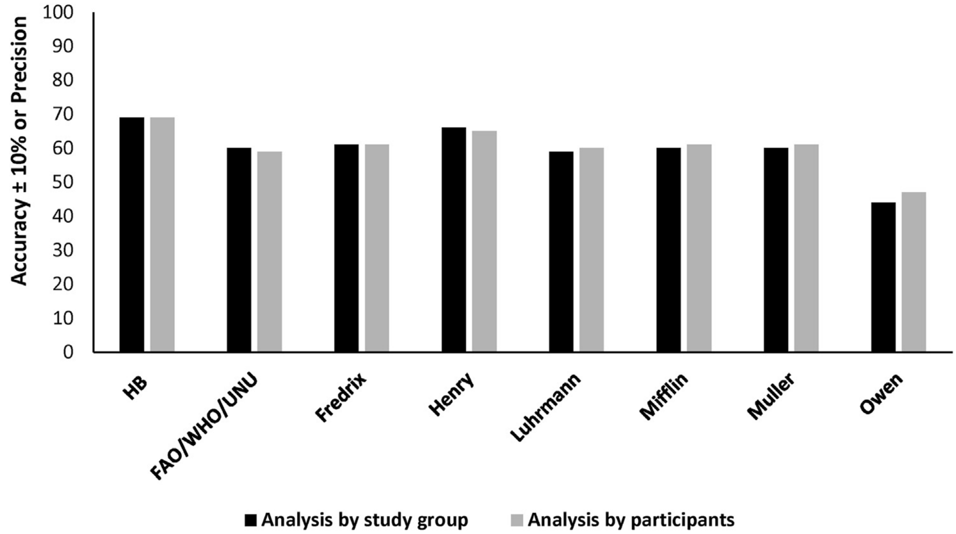


**Fig. 4. Accuracy at individual level (precision).** Data are presented as the percentage of predicted REE values within 10% of measured REE. Analysis by participants consisted of weighted means of precision, whereas analysis by study group had not adjustment of mean values.

## 4. Discussion

The aims of this systematic review were to assess prediction accuracy of REE in healthy older adults, and specifically to identify the equation giving the most reliable estimates of REE at group and/or individual level. Overall, we found a great heterogeneity and variability of accuracy prediction across the selected studies, with a clear trend towards an overestimation of REE. Based on the present findings, the most accurate equations in groups of elderly subjects are those proposed by Mifflin [12] and HB [11] since they showed the lowest bias. While, the highest individual accuracy was observed for the HB equation [11], followed by the Henry [8] and Mifflin [12] equations.

To date, only few attempts have been made to explore the predictive accuracy of equations for REE in aged people. The previous systematic review by Frankenfield et al. [13] was performed in subjects with and without obesity including various ethnic and age groups. Four prediction equations were identified as the most used in clinical practice; and only the accuracy prediction within ±10%, but not bias, was assessed. The authors suggested the use of the Mifflin equation due to the consistent results observed in adults but did not specifically consider data in older adults. Before Frankenfield et al., a narrative review by Gaillard et al. [14], which was focused on energy needs in the elderly, was published. The authors used four equations to determine the accuracy of REE prediction (with a not well defined approach) and stated that the HB equation [11] was accurate in both healthy and sick elderly people, while the Fredrix equation [9] was accurate only in the sick population.

For the present systematic review, we selected those studies exclusively focused on healthy older adults that provided consistent data on prediction accuracy at group level (bias) and/or individual level (precision), using equations evaluated at least in three different papers. We identified 8 predictive equations as the most used. Bias was the mean percent difference between predicted and measured REE for a given group of subjects and is used to detect the occurrence (and extent) of a systematic over- or underestimation. Our results indicate that, in elderly people, the Mifflin equation [12] provided the most accurate prediction at the group level, while the Henry and Schofield equations did the same among those specifically designed for that age group. Overall, it is worth noting that all the equations considered led to an overestimation of REE, which was even more marked when the somewhat diverging values reported by Siervo et al. [15] were not considered. In such a case, the Mifflin equation [12] still showed the smallest mean bias (+2.8%), with this latter increasing to more than 5% for several equations. These findings are in line with those reported by Porter et al. [20], who calculated the measured-predicted differences of REE in elderly subjects but not the percent bias. Finally, even though no definite conclusion can be drawn due to scarcity of data, the results available on the two genders separately seem to be similar to those just discussed for both genders combined.

Although the accuracy at group level provides useful information to public health nutrition and community dietetics, data on precision, i.e. the percentage of subjects with predictive values between 90 and 110% of measured REE, are required for assessing the accuracy in single individuals. In the present study, the HB equations [11] had the best precision (69%), while, the age-specific equations proposed by FAO/WHO/UNU [7], Luhrmann [10], Henry [8] or Fredrix [9] had a slightly lower precision (from 60 to 65%) and no data were provided for the Schofield equations [6].

Previous reviews [13,14] gave neither information on precision nor clear indication of which predictive formula for REE was the most reliable in elderly people. No one equation could be recommended in the elderly population because of limited data; but Frankenfield et al. [13] suggested the use of the Mifflin equation [12] without providing any data on its precision. Conversely, our findings showed that the Mifflin equation had a precision of approximately 61%, which was similar to those provided by age-specific equations and lower compared to the HB equations, resulting inaccurate in approximately 40% of older adults.

In the present systematic review, the number of studies giving bias and precision varied depending on the equation chosen, making the comparison not so definite but still interesting from a practical point of view. Actually, some general considerations can reasonably be drawn. The first one is that prediction accuracy is not higher for those equations that were developed specifically for elderly people. Of note, some of them were derived on very small samples of subjects (FAO/WHO/UNU [7], Schofield [6] and Fredrix [9]). In most cases there was a substantial positive mean bias (overestimation), which varied by a few percentage points between equations; and it was substantially influenced by including the paper by Siervo et al. [15], which gave disagreeing results – no immediate explanation for this – compared to the other ones. The second point to consider is that aging affects body composition with a decrease of lean tissues and an increase of adipose tissue. Since fat-free mass (FFM) is the major determinant of REE, changes in both quantity and quality of FFM can influence REE measurement in older subjects and consequently the accuracy of prediction. Unfortunately, none of the selected studies showed any data on body composition, potentially contributing to the inaccuracy of results. Finally, although the HB formula provides the most precise equations for predicting REE in this sample of older adults, the equation is still imprecise in approximately 31% of individuals, indicating that REE prediction was higher than measured, leading to a slight overestimation of energy needs, and highlighting the importance of measuring REE by IC to provide adequate requirements.

Minor inconsistencies between studies are also expected, but cannot be clearly identified, due to the use of different instruments, calibration procedures and sample characteristic. Unfortunately, there are not enough data to provide reliable information on older subjects or potential differences between genders.

Therefore, to simply and improve future evaluations on REE prediction, it would be useful to analyse and present data on accuracy at both group (bias) and individual (precision) level, possibly by taking gender differences into account. As further step, more attention should be paid on the sample characteristics, especially for age and body weight, to minimize the variability within and between groups. Last, but not least, because of aging, prediction of REE in the elderly should be assessed by considering the presence of diseases able to affect FFM, such as sarcopenia, in order to improve its accuracy.

### 4.1. Strength and limitations

To the best of our knowledge, this is the first systematic review assessing the prediction accuracy of REE in healthy older adults at both group and individual level. A strength of this review is the use of clear inclusion criteria, with the exclusion of studies involving sick elderly people, and the identification of standardized conditions (fasting state, bed rest, etc.) for REE measurement.

However, several limitations should be considered when examining the results of this review. Firstly, most of the selected studies did not have a strong experimental design (for instance, because of small sample sizes), and were only partially adequate and representative of the target population. Secondly, there was a wide variability in ethnicity and individual characteristics: participants' age ranged from 52 to over 80 years and their BMI varied from normal weight to severe obesity, without reporting data separately. As a result, this large heterogeneity, observed within and between studies, could impact differently on REE prediction and consequently on summarizing the results of this systematic review. Lastly, studies differed in the way data regarding bias and precision were reported.

## 5. Conclusion

In conclusion, none of the prediction equations considered provides accurate and precise REE estimates in healthy older adults. Findings systematically shows a great heterogeneity and variability of prediction accuracy of REE in the older population, with a considerable tendency towards an overestimation of measured values. The most accurate prediction is given by the Mifflin equation at group level and by the Harris–Benedict equation at individual level. Further studies with strong quality design are needed to evaluate the variability of REE in the elderly general population, to assess the accuracy of the currently available predictive equations and possibly to derive new equations that are specific for population subgroups such as frail and/or very old subjects.

## Credit author statement

Iolanda Cioffi: Conceptualization, Data curation, Writing- Original draft preparation, Writing - Review & Editing. Maurizio Marra: Visualization, Writing - Review & Editing. Fabrizio Pasanisi: Visualization, Writing - Review & Editing. Luca Scalfi: Conceptualization, Writing - Review & Editing, Supervision.

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## Conflict of interest

Authors declare no conflict of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2020.11.027.

## References

[1] Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr 2019;38:10–47. https://doi.org/10.1016/j.clnu.2018.05.024.
[2] Shenkin SD, Harrison JK, Wilkinson T, Dodds RM, Ioannidis JPA. Systematic reviews: guidance relevant for studies of older people. Age Ageing 2017;46:722–8. https://doi.org/10.1093/ageing/afx105.
[3] Ritz P. Factors affecting energy and macronutrient requirements in elderly people. Publ Health Nutr 2001;4:561–8. https://doi.org/10.1079/PHN2001141.
[4] Manini TM. Energy expenditure and aging. Ageing Res Rev 2010;9:1–11. https://doi.org/10.1016/j.arr.2009.08.002.
[5] Marra M, Cioffi I, Sammarco R, Montagnese C, Naccarato M, Amato V, et al. Prediction and evaluation of resting energy expenditure in a large group of obese outpatients. Int J Obes 2017;41:697–705. https://doi.org/10.1038/ijo.2017.34.
[6] Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. Hum Nutr Clin Nutr 1985;39(Suppl 1):5–41.
[7] Energy and protein requirements. Report of a joint FAO/WHO/UNU Expert Consultation. World Health Organ Tech Rep Ser 1985;724:1–206.
[8] Henry C. Basal metabolic rate studies in humans: measurement and development of new equations. Publ Health Nutr 2005;8:1133–52. https://doi.org/10.1079/PHN2005801.
[9] Fredrix E, Soeters P, Deerenberg I, Kester A, Vonmeyenfeldt M, Saris W. Resting and sleeping energy-expenditure in the elderly. Eur J Clin Nutr 1990;44:741–7.
[10] Luhrmann P, Herbert B, Krems C, Neuhauser-Berthold M. A new equation especially developed for predicting resting metabolic rate in the elderly for easy use in practice. Eur J Nutr 2002;41:108–13. https://doi.org/10.1007/s003940200016.
[11] Harris JA, Benedict FG. A biometric study of human basal metabolism. Proc Natl Acad Sci USA 1918;4:370–3. https://doi.org/10.1073/pnas.4.12.370.
[12] Mifflin M, Stjeor S, Hill L, Scott B, Daugherty S, Koh Y. A new predictive equation for resting energy-expenditure in healthy-individuals. Am J Clin Nutr 1990;51:241–7.
[13] Frankenfield D, Roth-Yousey L, Compher C. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: a systematic review. J Am Diet Assoc 2005;105:775–89. https://doi.org/10.1016/j.jada.2005.02.005.
[14] Gaillard C, Alix E, Salle A, Berrut G, Ritz P. A practical approach to estimate resting energy expenditure in frail elderly people. J Nutr Health Aging 2008;12:277–80. https://doi.org/10.1007/BF02982634.

[15] Siervo M, Bertoli S, Battezzati A, Wells JC, Lara J, Ferraris C, et al. Accuracy of predictive equations for the measurement of resting energy expenditure in older subjects. Clin Nutr 2014;33:613–9. https://doi.org/10.1016/j.clnu.2013.09.009.
[16] Noreik M, Maurmann M, Meier V, Becker I, Röhrig G, Polidori MC, et al. Resting energy expenditure (REE) in an old-old population: implications for metabolic stress. Exp Gerontol 2014;59:47–50. https://doi.org/10.1016/j.exger.2014.06.009.
[17] Itoi A, Yamada Y, Yokoyama K, Adachi T, Kimura M. Validity of predictive equations for resting metabolic rate in healthy older adults. Clinical Nutrition ESPEN 2017;22:64–70. https://doi.org/10.1016/j.clnesp.2017.08.010.
[18] Karlsson M, Olsson E, Becker W, Karlström B, Cederholm T, Sjögren P. Ability to predict resting energy expenditure with six equations compared to indirect calorimetry in octogenarian men. Exp Gerontol 2017;92:52–5. https://doi.org/10.1016/j.exger.2017.03.013.
[19] Sgambato MR, Wahrlich V, Anjos LAD. Validity of basal metabolic rate prediction equations in elderly women living in an urban tropical city of Brazil. Clin Nutr ESPEN 2019;32:158–64. https://doi.org/10.1016/j.clnesp.2019.03.003.
[20] Porter J, Nguo K, Collins J, Kellow N, Huggins CE, Gibson S, et al. Total energy expenditure measured using doubly labeled water compared with estimated energy requirements in older adults ($\geq$65 y): analysis of primary data. Am J Clin Nutr 2019;110:1353–61. https://doi.org/10.1093/ajcn/nqz200.
[21] Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097. https://doi.org/10.1371/journal.pmed.1000097.
[22] Madden AM, Mulrooney HM, Shah S. Estimation of energy expenditure using prediction equations in overweight and obese adults: a systematic review. J Hum Nutr Diet 2016;29:458–76. https://doi.org/10.1111/jhn.12355.
[23] Chima L, Mulrooney HM, Warren J, Madden AM. A systematic review and quantitative analysis of resting energy expenditure prediction equations in healthy overweight and obese children and adolescents. J Hum Nutr Diet 2020;33:373–85. https://doi.org/10.1111/jhn.12735.
[24] National Institution of Health: U. S Department of Health and Human Services. Quality assessment tool for observational cohort and cross-sectional studies. 2014.
[25] Fuller NJ, Sawyer MB, Coward WA, Paxton P, Elial M. Components of total energy expenditure in free-living elderly men (over 75 years of age) : measurement, predictability and relationship to quality-of-life indices. Br J Nutr 1996;75:161–73. https://doi.org/10.1017/BJN19960122.
[26] Khalaj-Hedayati K, Bosy-Westphal A, Müller MJ, Dittmar M. Validation of the BIOPAC indirect calorimeter for determining resting energy expenditure in healthy free-living older people. Nutr Res 2009;29:531–41. https://doi.org/10.1016/j.nutres.2009.08.001.
[27] Taaffe DR, Thompson J, Butterfield G, Marcus R. Accuracy of equations to predict basal metabolic rate in older women. J Am Diet Assoc 1995;95:1387–92. https://doi.org/10.1016/S0002-8223(95)00366-5.
[28] Melzer K, Karsegard WL, Genton L, Kossovsky MP, Kayser B, Pichard C. Comparison of equations for estimating resting metabolic rate in healthy subjects over 70 years of age. Clin Nutr 2007;26:498–505. https://doi.org/10.1016/j.clnu.2007.05.002.
[29] Reidlinger DP, Willis JM, Whelan K. Resting metabolic rate and anthropometry in older people: a comparison of measured and calculated values. J Hum Nutr Diet 2015;28:72–84. https://doi.org/10.1111/jhn.12215.
[30] Nhung BT, Khan NC, Hop LT, Lam NT, Khanh NLB, Lien DTK, et al. Resting metabolic rate of elderly Vietnamese. Ann Nutr Metabol 2007;51:7–13. https://doi.org/10.1159/000100815.
[31] Luhrmann PM, Neuhauser-Berthold M. Are the equations published in literature for predicting resting metabolic rate accurate for use in the elderly? J Nutr 2004;8:7.
[32] Müller MJ, Bosy-Westphal A, Klaus S, Kreymann G, Lührmann PM, Neuhäuser-Berthold M, et al. World Health Organization equations have shortcomings for predicting resting energy expenditure in persons from a modern, affluent population: generation of a new reference standard from a retrospective analysis of a German database of resting energy expenditure. Am J Clin Nutr 2004;80:1379–90. https://doi.org/10.1093/ajcn/80.5.1379.
[33] Owen OE, Kavle E, Owen RS, Polansky M, Caprio S, Mozzoli MA, et al. A reappraisal of caloric requirements in healthy women. Am J Clin Nutr 1986;44:1–19. https://doi.org/10.1093/ajcn/44.1.1.