

Total energy expenditure measured using doubly labeled water compared with estimated energy requirements in older adults (≥ 65 y): analysis of primary data

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ABSTRACT

Background: Contemporary energy expenditure data are crucial to inform and guide nutrition policy in older adults to optimize nutrition and health.

Objective: The aim was to determine the optimal method of estimating total energy expenditure (TEE) in adults (aged ≥ 65 y) through 1) establishing which published predictive equations have the closest agreement between measured resting metabolic rate (RMR) and predicted RMR and 2) utilizing the RMR equations with the best agreement to predict TEE against the reference method of doubly labeled water (DLW).

Methods: A database consisting of international participant-level TEE data from DLW studies was developed to enable comparison with energy requirements estimated by 17 commonly used predictive equations. This database included 31 studies comprising 988 participant-level RMR data and 1488 participant-level TEE data. Mean physical activity level (PAL) was determined for men (PAL = 1.69, $n = 320$) and women (PAL = 1.66, $n = 668$). Bland–Altman plots assessed agreement of measured RMR and TEE with predicted RMR and TEE in adults aged ≥ 65 y, and subgroups of 65–79 y and ≥ 80 y. Linear regression assessed proportional bias.

Results: The Ikeda, Livingston, and Mifflin equations most closely agreed with measured RMR and TEE in all adults aged ≥ 65 y and in the 65–79 y and ≥ 80 y subgroups. In adults aged ≥ 65 y, the Ikeda and Livingston equations overestimated TEE by a mean \pm SD of 175 ± 1362 kJ/d and 86 ± 1344 kJ/d, respectively. The Mifflin equation underestimated TEE by a mean \pm SD of 24 ± 1401 kJ/d. Proportional bias was present as energy expenditure increased.

Conclusions: The Ikeda, Livingston, or Mifflin equations are recommended for estimating energy requirements of older adults. Future research should focus on developing predictive equations to meet the requirements of the older population with consideration given to body composition and functional measures. *Am J Clin Nutr* 2019;110:1353–1361.

Keywords: doubly labeled water, total energy expenditure, elderly, resting energy expenditure, nutrition

Introduction

The average human life expectancy continues to increase in most developed countries, associated with improved food and water quality, immunization, and enhanced medical care (1). The UN forecast that between 2015 and 2030, the number of people aged ≥ 60 y will increase by 56%, from 901 million to 1.4 billion, and then to 2.1 billion by 2050 (2).

Policies are needed to support these global population changes; at their core are population and individual food and nutrition requirements. These are set out in dietary reference values at a national and international level, e.g., by the National Health and

The Women's Health Initiative program is funded by the National Heart, Lung, and Blood Institute, NIH, US Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN268201600002C, HHSN268201600003C, HHSN268201600004C, and R01 CA119171. We also acknowledge the contributions of Joshua Chang and Alvin Tjahyo funded by an Eastern Health Foundation grant and Monash University Vacation Scholarship for completion of the quality assessments.

Supplemental Tables 1–5 and Supplemental Figure 1 are available from the “Supplementary data” link in the online posting of the article and from the same link in the online table of contents at <https://academic.oup.com/ajcn/>.

Data described in the article will not be made available because these were obtained through an agreement with third parties (e.g., Women's Health Initiative). Data can be sought directly from the authors of individual articles.

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Abbreviations used: DLW, doubly labeled water; PAL, physical activity level; RMR, resting metabolic rate; TEE, total energy expenditure; WHI, Women's Health Initiative.

Received January 29, 2019. Accepted for publication July 25, 2019.

First published online August 28, 2019; doi: <https://doi.org/10.1093/ajcn/nqz200>.

Medical Research Council and the FAO/WHO (3, 4). However, research and understanding of the energy needs in the older population are limited. Applying evidence for energy expenditure derived from younger populations to older adults fails to account for the differences in body composition, activity, and health status. The studies presented and synthesized in this analysis were conducted in the older adult population (≥ 65 y) and crucially utilized the gold-standard doubly labeled water (DLW) methodology for measurement of total energy expenditure (TEE).

The DLW technique (5) is safe and noninvasive, requiring only periodic sampling of bodily fluids while individuals engage in usual activities. This technique is based on the ingestion of water labeled with 2 stable isotopes, deuterium and oxygen-18, and the fact that the oxygen and hydrogen atoms will have different routes of biological elimination (6).

Predictive equations currently used to derive estimated energy requirements are based on international data collected over the past century. Commonly used equations to predict resting metabolic rate (RMR) include the Schofield (7) and Harris-Benedict (8) equations. Using the factorial method, a value for energy expended by physical activity is applied to predicted RMR to derive TEE. Such equations do not recognize the range of influences leading to varying energy requirements in the elderly population. Body composition, health and cognitive status, and medication use vary considerably within the 60 to ≥ 100 y old age group. What is clearly lacking is further age bracketing for those in their 70s, 80s, or 90s and beyond. The US dietary guidelines (2015–2020) equally do not subgroup the energy needs of adults beyond 76 y (9). Current predictive equations are based on data unlikely to be representative of contemporary older individuals.

Our study utilized the 17 predictive equations for RMR of older adults compiled by Itoi et al. (10). Equations for the present analyses were sourced from the original publications. Specifically, the aim was to determine the optimal equation for estimating TEE in adults aged ≥ 65 y (all adults, 65–79 y old, and ≥ 80 y old) through

- 1) establishing which published predictive equations have the highest level of agreement between measured RMR and predicted RMR; and
- 2) utilizing the RMR equations with the closest agreement to predict TEE against the reference method of DLW.

Methods

Our recently published systematic review (11) collated the extent of the international evidence for TEE using DLW in older adults. Systematic review methods were applied to finalize a library of DLW studies in those aged ≥ 65 y, classified as the retirement age internationally (12). The Monash University Human Research Ethics Committee (project number 8025) provided an exemption from ethics approval for contacting authors and for requesting the collection of these data for this primary analysis. Participant-level data were obtained either from the original source publication or by contacting authors of articles and requesting data to be shared. Since this review was published (11), investigators from the US Women's Health Initiative (WHI) have contributed TEE data from a further 694 participants (13, 14).

A quality assessment of the included studies was completed by duplicate reviewers using the Quality Criteria Checklist for Primary Research (Academy of Nutrition and Dietetics) (15) included in **Supplemental Table 1**. Additional statements to assess the quality of the RMR and DLW method used in each study were developed for this evaluation, with findings included in **Supplemental Table 2**.

The outcome of the systematic review process was a large international database containing TEE, RMR, anthropometry, and demographic information at the participant level for adults aged ≥ 65 y. This database is used for this analysis. The characteristics of participants contributing to this database are reported in **Supplemental Table 3**. Data from 48 publications (31 studies), mostly from developed countries, are included.

The Bland–Altman method (16) was utilized to assess the level of agreement between 2 measures (i.e., predicted compared with measured RMR and predicted TEE compared with measured TEE by DLW). The difference between measured and predicted RMR or TEE (y-axis) was compared with measured RMR or TEE (rather than the mean of the 2 variables as is traditionally used), given these are the gold-standard measures. The difference between measured and predicted RMR and TEE was calculated as “measured minus predicted,” therefore a negative difference means the equation overestimated measured RMR or TEE and a positive difference means the equation underestimated measured RMR or TEE. A 1-sample *t* test was applied to assess whether the difference between the 2 measurements varied significantly from zero ($P < 0.05$). The upper and lower limits of agreement were calculated as the mean difference $\pm 1.96 \times SD$. A linear regression was conducted to assess for proportional bias ($P < 0.05$) to determine whether there was a trend of more data points being above or below the mean difference (**Table 1**).

There were 2 parts to this analysis, which were completed with data from all participants (aged ≥ 65 y) (referred to throughout as “main analysis”) and repeated for participants aged 65–79 y and ≥ 80 y (referred to throughout as “subgroup analysis”). In Step 1, we aimed to establish which 3 equations showed the highest level of agreement between measured RMR and predicted RMR. Consensus was reached within the research team before finalizing the database that these 3 equations would then be utilized to compare measured TEE and predicted TEE (Step 2).

Participants who contributed data on RMR measured by the accepted reference methods of indirect calorimetry or Douglas bag, performed using standardized laboratory conditions, were included in the Step 1 analysis ($n = 988$). Predicted RMR was generated for each participant by entering their data (weight, height, sex, and age) into each of the 17 predictive equations. These calculations were performed in Microsoft Excel (2013). Participants with disease states likely to affect energy expenditure (chronic kidney disease, chronic obstructive pulmonary disease, and thyroid illnesses), those with missing data, or whose RMR data were greater than TEE (attributed to data entry error) were excluded from the analysis. The flow diagram for participant selection is shown in **Figure 1**.

Before Bland–Altman analyses, descriptive analyses were undertaken to determine the distribution of data (provided as histograms in **Supplemental Figure 1**). The assumptions that data were normally distributed (Kolmogorov–Smirnov $P > 0.05$) and that comparison between the 2 measures did not vary from zero were unable to be met (1-sample *t* test), despite

TABLE 1 Performance of equations against the assumptions of Bland–Altman analyses (Step 1)¹

Equation (<i>n</i> = 17)	One-sample <i>t</i> test <i>P</i> > 0.05	Mean of the difference (bias) ²	SD of the difference	Lower LOA	Upper LOA	Regression coefficient <i>P</i> < 0.05 (proportional bias)
Bernstein (17)	No	734	787	– 809	2277	Yes
De Lorenzo (18)	No	– 422	762	– 1916	1072	Yes
EU (19)	No	– 497	722	– 1912	918	Yes
Fredrix (20)	No	– 509	766	– 2010	992	Yes
Ganpule (21)	No	– 140	782	– 1673	1393	Yes
Harris–Benedict (8)	No	– 265	746	– 1727	1197	Yes
Henry (22)	No	– 398	770	– 1907	1111	Yes
Ikeda (23)	No	– 59	740	– 1509	1391	Yes
Korth (24)	No	– 569	865	– 2264	1126	Yes
Livingston (25)	Yes	– 16	740	– 1466	1434	Yes
Lüthmann (26)	No	– 511	780	– 2040	1018	Yes
Mifflin (27)	Yes	45	761	– 1447	1537	Yes
Müller (28)	No	– 509	789	– 2055	1037	Yes
Owen (29)	No	– 612	805	– 2190	966	Yes
Schofield (7)	No	– 362	752	– 1836	1112	Yes
Weijjs-Kruizenga (30)	No	– 1095	807	– 2677	487	Yes
WHO (31)	No	– 516	773	– 2031	999	Yes

¹Main analysis, *n* = 988 participants. Assumptions of the Bland–Altman analysis are that the 1-sample *t* test >0.05 and that the regression coefficient >0.05 (i.e., no proportional bias). Bland–Altman analyses were conducted with RMR expressed as kJ/d. Normal distribution was tested for the following variables: RMR derived from equations (kJ/d); RMR measured (kJ/d); difference of RMR measured and RMR derived from equations (kJ/d); and mean of RMR measured and RMR derived from equations (kJ/d). LOA, limit of agreement; RMR, resting metabolic rate.

²A negative “mean of the difference” means the equation overestimated measured RMR and a positive “mean of the difference” means the equation underestimated measured RMR.

transformation attempts. We proceeded with Bland–Altman analyses noting the skewed distribution. From the 17 Bland–Altman plots comparing measured RMR and predicted RMR, the 3 equations demonstrating the least bias (the smallest mean of the mean difference between the 2 methods) were selected for further analysis in Step 2.

In Step 2, participants with measured TEE data (*n* = 1488) were included in the analysis. Participants with disease states likely to affect TEE (chronic kidney disease, chronic obstructive pulmonary disease, those in intensive care) and those with missing data were excluded. DLW measurements were accepted as reported, except 1 clear outlier (verified with the author as a data entry error) with a TEE of 28.6 MJ. The flow diagram for participant selection is shown in **Figure 2**. Participant characteristics are also described in Supplemental Table 3.

To account for differences in body size, physical activity level (PAL) was calculated to characterize energy expenditure above the RMR of the population (32). The mean male and female PALs derived from our total database were calculated from TEE measured using DLW divided by RMR measured using indirect calorimetry in original studies. Applying a predefined group PAL value reflects the process undertaken in clinical practice. For the main analysis, the mean PAL calculated for men was 1.69 ± 0.26 (*n* = 320) and mean PAL for women was 1.66 ± 0.31 (*n* = 668). For the subgroup analysis, the mean PAL for men aged 65–79 y was 1.71 ± 0.26 (*n* = 219) and for women was 1.69 ± 0.31 (*n* = 514), and the mean PAL for men aged ≥ 80 y was 1.65 ± 0.25 (*n* = 101) and for women was 1.60 ± 0.30 (*n* = 154).

These PAL values were applied to the RMR derived from the predictive equations to generate predicted TEE in the main and the subgroup analyses. Agreement between predicted TEE and measured TEE was explored in a series of Bland–Altman plots

(16), 1 plot for each of the 3 predictive equations identified in Step 1.

All statistical analyses were conducted using IBM SPSS Statistics version 25.0.

Results

Step 1: The composite database contained data from 988 adults aged ≥ 65 y with the majority of participants being women (68%), Caucasian/white (60%), with a median age of 74 y (**Table 2**). For the subgroup analysis there were 733 participants aged 65–79 y [70% women, 58% Caucasian/white, mean BMI (in kg/m²) 27.3 ± 5.3] and 255 aged ≥ 80 y (60% women, 65% Caucasian/white, mean BMI 25.4 ± 4.4). Data for Bland–Altman plots for the main analysis and subgroup analysis are reported in **Table 1** and **Supplemental Table 4**, respectively.

For the main analysis, the Mifflin equation demonstrated the closest agreement (least bias) (**Figure 3**, **Table 1**) compared with measured RMR. It underestimated measured RMR by a mean \pm SD of 45 ± 761 kJ/d. The Ikeda and Livingston equations also showed close agreement, but with the Ikeda equation violating the assumption of the 1-sample *t* test. The Ikeda and Livingston equations overestimated measured RMR by a mean \pm SD of 16 ± 740 kJ/d and 59 ± 740 kJ/d, respectively. All equations showed proportional bias.

The Ikeda, Livingston, and Mifflin equations also demonstrated the least bias among both the 65–79 y olds and the ≥ 80 y olds in the subgroup analysis (Supplemental Table 4). In the 65–79 y old age group, the Livingston equation showed the least bias with an overestimation of measured RMR by a mean \pm SD of 5 ± 754 kJ/d. In the ≥ 80 y age bracket, the Livingston and Mifflin equations performed similarly, with an overestimation

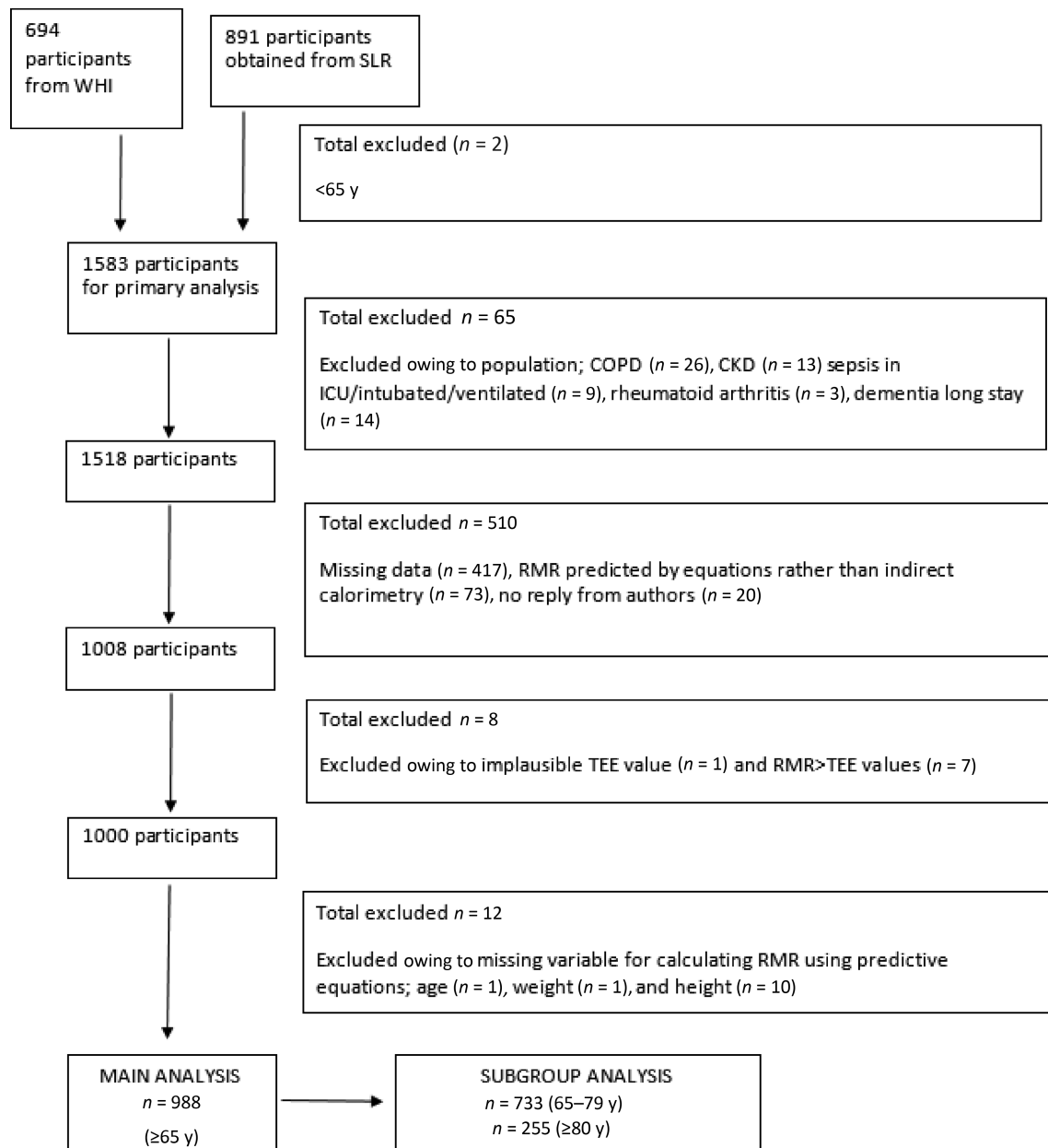


FIGURE 1 Flowchart of selection of data from individual participants aged ≥ 65 y (main analysis) and 65–79 y and ≥ 80 y (subgroup analysis) used to compare RMR measured in original studies using indirect calorimetry with RMR calculated from a series of predictive equations (Step 1). CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; RMR, resting metabolic rate; SLR, systematic literature review; TEE, total energy expenditure; WHI, Women’s Health Initiative.

of measured RMR by 45 ± 697 kJ/d and underestimation of measured RMR of 44 ± 739 kJ/d, respectively. Like the main analyses, the 3 equations showed proportional bias in both age groups.

Step 2: There were 1488 participants who contributed TEE data for analysis after excluding data from 95 participants (6%) (Figure 2). The majority of participants providing data for the main TEE analyses were women (75%), Caucasian/white (68%), with a median age of 73 y (Table 2). For the subgroup analysis 1184 participants were aged 65–79 y (77% women, 68% Caucasian/white, mean BMI: 27.6 ± 5.3) and 304 were

aged ≥ 80 y (65% women, 67% Caucasian/white, mean BMI: 25.6 ± 4.4).

Based on the analysis in Step 1, the Ikeda, Livingston, and Mifflin equations were selected in both the main and subgroup analyses, and the derived sex-specific PAL values were applied to determine predicted TEE. Predicted and measured TEE were compared using Bland–Altman plots. These analyses demonstrated variable patterns of agreement between predicted and measured TEE for adults aged ≥ 65 y in the main analysis (Figure 4, Table 3) and subgroup analysis (Supplemental Table 5).

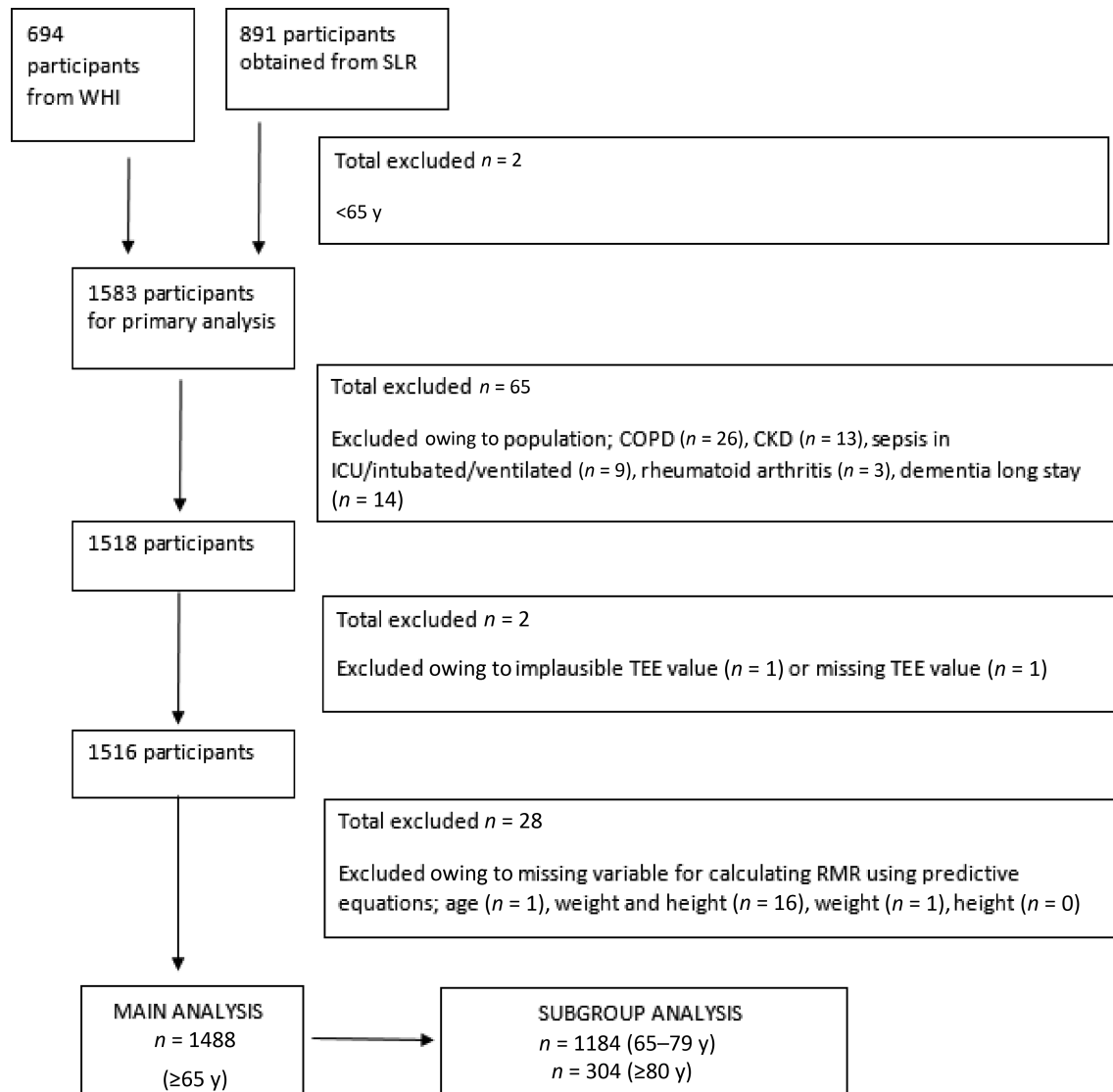


FIGURE 2 Flowchart of selection of data from individual participants aged ≥ 65 y (main analysis) and 65–79 y and ≥ 80 y (subgroup analysis) used to compare TEE measured in original studies using doubly labeled water with estimated TEE (Step 2). CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; RMR, resting metabolic rate; SLR, systematic literature review; TEE, total energy expenditure; WHI, Women's Health Initiative.

For the ≥ 65 y analysis in Step 2, the bias between predicted and measured TEE was -86 ± 1344 kJ/d and -175 ± 1362 kJ/d for the Livingston and Ikeda equations, respectively. TEE calculated by the Mifflin equation had the smallest bias (24 ± 1401 kJ/d) but the largest variability (SD). The Ikeda and the Livingston equations violated the assumption for the 1-sample *t* test and for all 3 equations, proportional bias was observed, as shown by the regression line (dotted line), R^2 , and *P* value in Figure 4.

The Mifflin equation showed the least bias among the ≥ 80 y age group (-245 ± 1413 kJ/d), whereas the Livingston equation showed the least bias among the 65–79 y age group (-5 ± 1336 kJ/d). In the ≥ 80 y age group all 3 equations overestimated measured TEE, and had larger bias than in the 65–79 y age group. All equations for both age groups showed

proportional bias, as shown by the regression line (dotted line), R^2 , and *P* value in Figure 4.

The Bland–Altman graphs showed a clear positive trend. Data points extended beyond both the upper and lower limits of agreement—more so beyond the upper limits (Figure 4). This indicates that the higher an individual's TEE (in kilojoules per day) the more likely the equations will underestimate TEE, and vice versa.

Discussion

The systematic process undertaken and reported here has led to the development of a large international database of TEE measurements using the DLW method in people aged ≥ 65 y. We aimed to determine which published predictive equations have

TABLE 2 Descriptive characteristics of individual participants aged ≥ 65 y providing RMR data used in Step 1 and TEE data used in Step 2 (main analysis)¹

Characteristic	RMR data (<i>n</i> = 988)	TEE data (<i>n</i> = 1488)
Gender, <i>n</i> (%)		
Female	668 (68)	1108 (75)
Male	320 (32)	380 (25)
Ethnicity, <i>n</i> (%)		
Caucasian/white	593 (60)	1005 (68)
Asian	30 (3)	32 (2)
African	184 (19)	227 (15)
Hispanic	37 (4)	60 (4)
Other	59 (6)	74 (5)
Missing	85 (9)	90 (6)
Age, y	74, 69–80, 65–101	73, 68–78, 65–101
BMI, kg/m ²	25.9, 23.2–29.8, 14.6–47.8	26.3, 23.5–30.3, 14.6–47.8
Fat-free mass, ² %	63.7, 57.8–69.4, 43.4–92.6	63.7, 57.8–69.4, 34.9–100
RMR measured, kJ/d	5215, 4559–5960, 2370–8780	N/A
RMR measured, kJ · kg BW ⁻¹ · d ⁻¹	74, 66–84, 39–132	N/A
RMR measured, ² kJ · kg FFM ⁻¹ · d ⁻¹	118, 108–130, 74–175	N/A
TEE measured, kJ/d	N/A	8600, 7540–9750, 3540–19,320

¹Values are *n* (%) or median, IQR, min–max. Step 1 involved individual participant data for RMR measured in original studies using indirect calorimetry compared with RMR calculated from a series of predictive equations; Step 2 involved individual participant data for TEE measured in original studies using doubly labeled water compared with TEE calculated from a series of predictive equations. BW, body weight; FFM, fat-free mass; N/A, not applicable; RMR, resting metabolic rate; TEE, total energy expenditure.

²*n* = 623.

the closest agreement with measured RMR in adults aged ≥ 65 y and to utilize these RMR equations to predict TEE against the reference method of DLW, to determine the optimal equation for estimating TEE in adults aged ≥ 65 y.

Of the 17 equations included in the analysis, the equations by Ikeda, Livingston, and Mifflin had the closest agreement with measured RMR in the main and subgroup analyses. Although all equations showed proportional bias, Mifflin had the lowest mean difference across the ≥ 65 y age cohort, with the Livingston equation showing the least bias in the 65–79 y age group. However, across all 3 of the equations tested, concerning the mean difference and SD of the difference, along with the presence of proportional bias, the variation that has been identified is likely to be insignificant in the clinical context. In the absence of any better-performing predictive equation, this analysis suggests that any of these 3 equations can be used. Clinicians and policy makers should beware of the proportional bias that applies as participant energy expenditure increases.

Commonly cited equations (Schofield and Harris–Benedict) showed proportional bias and overestimated RMR. This is not surprising given that these equations were developed using very limited participant numbers in the target older population. Only 2 of the equations currently in use were developed specifically for older adults: the equations of Fredrix et al. (developed from 40 healthy individuals aged 51–82 y) and Lührmann et al. (developed from 286 free-living individuals aged 60–85 y). There was proportional bias for both equations and they overestimated RMR.

The large SD of 1344–1401 kJ across the 3 equations is also likely to be clinically relevant over time. A deficit or excess of 1 SD at 1400 kJ/d would lead to notable weight change in the clinical setting. Because of the proportional bias, analysis of larger data sets may yield equations that provide more accurate estimates of TEE than those currently in use. This will be

important for clinical practice given the forecasts for large populations of older adults into the future.

The analysis of a large DLW database across the life span undertaken by Black et al. (32) described the importance of considering PAL rather than the addition of standard activity energy expenditure. Because PAL provides a ratio of BMR rather than a defined value, it incorporates a scaling factor for body size/requirements. In the Black et al. analysis across the life span, mean \pm SD PAL for women aged 65–74 y was 1.62 ± 0.28 , whereas for those aged ≥ 75 y it was 1.48 ± 0.23 . The figures for men showed a similar pattern of decline into older age, with a mean \pm SD PAL for men aged 65–74 y of 1.61 ± 0.28 , whereas for those aged ≥ 75 y it was 1.54 ± 0.24 . We suggest that the higher mean PAL calculated within the present database both for men and for women (including the subgroup analyses) may be attributable to the addition of more recent studies, the larger database size in the older age categories, and potentially a more active aged population having been sampled.

All predictive energy equations rely on chronological rather than biological age, itself a potential limitation on accuracy. There is an increasing body of literature regarding the differences between these measures of age, attributable to the hallmarks of ageing: genomic instability, loss of proteostasis, mitochondrial dysfunction, altered intercellular communication, deregulated nutrient sensing, stem cell exhaustion, epigenetic alterations, and telomere attrition (1). A range of clinical biomarkers that reflect physiological systems that are measurable in a clinical setting can predict accelerated aging (33). However, at a population level it is unlikely that these biomarkers could be measured for incorporation into predictive energy equations. Ethnicity may be another variable that warrants consideration in equation development, with limited analysis of large data sets to understand differences in body composition and how these affect energy expenditure. Rather, it seems likely that age, gender, and

Main analyses

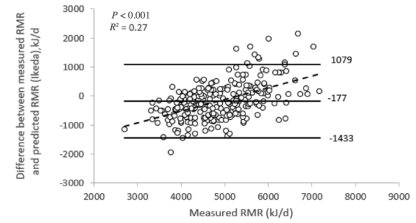
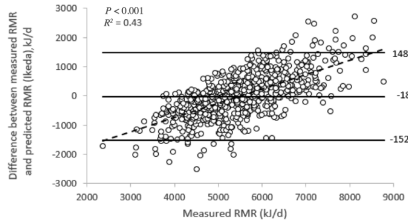
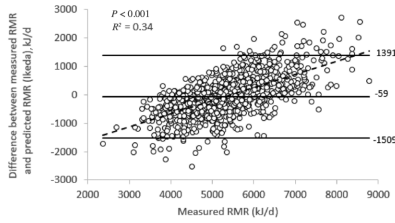
≥65 y (n = 988)

Subgroup analyses

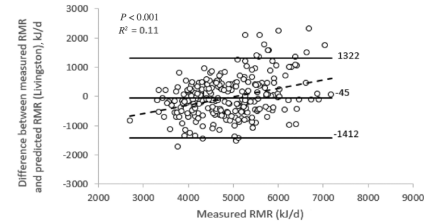
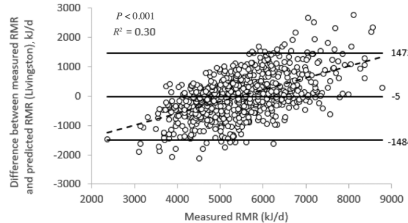
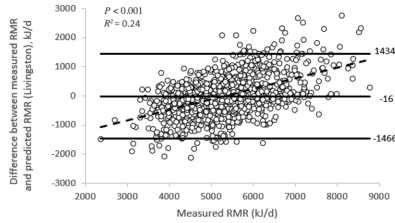
65–79 y (n = 733)

≥80 y (n = 255)

A Ikeda



B Livingston



C Mifflin

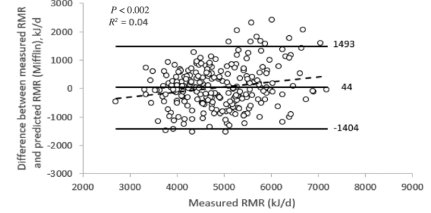
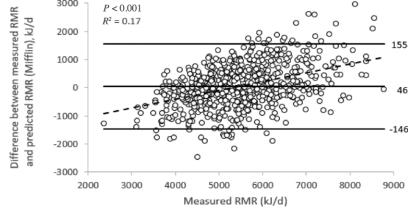
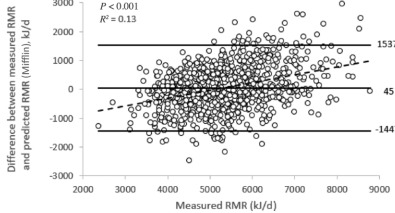


FIGURE 3 Bland–Altman analysis testing agreement between measured RMR and RMR derived from the 3 best-performing equations, Ikeda, Livingston, and Mifflin (main analysis, n = 988; subgroup analysis: n = 733, 65–79 y; n = 255, ≥80 y). Solid lines indicate the means + 95% limits of agreement (bias). Dotted line indicates the regression line, with P value and R² for the regression line (proportional bias). RMR, resting metabolic rate.

anthropometric indexes will continue to provide the levers for future predictive equation development.

The development of predictive equations into the future should consider the importance of functional measures in addition to those of chronological age. These measures may reduce the proportional bias identified in this analysis, but importantly should be bedside measures so that equations can be utilized in clinical practice. Examples of functional measures that may be considered are the Short Physical Performance Battery (34), a

validated and well-established measure for mobility disability, the Mini Nutritional Assessment (35), and the SarQoL, a sarcopenia-specific health-related quality of life instrument (36). Other more technical but accurate measures of body composition collected within nutrition laboratory studies (e.g., fat and fat-free mass) for older adults should also be considered.

One of the strengths of this analysis is the development of a comprehensive participant-level database in older adults who are free of significant chronic diseases. Several limitations

TABLE 3 Performance of equations against the assumptions of Bland–Altman analyses (Step 2)¹

Study (n = 3)	One-sample t test P > 0.05	Mean of the difference (i.e., bias) ²	SD of the difference	Lower LOA	Upper LOA	Regression coefficient P < 0.05 (proportional bias)
Ikeda et al. (23)	No	−175	1362	−2845	2495	Yes
Livingston and Kohlstadt (25)	No	−86	1344	−2720	2548	Yes
Mifflin et al. (27)	Yes	24	1401	−2722	2770	Yes

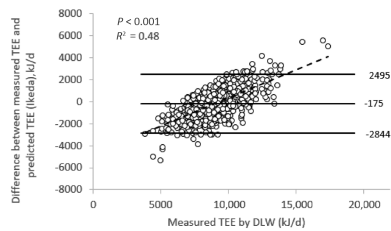
¹Main analysis, n = 1488. Assumptions of the Bland–Altman analysis are that the 1-sample t test P > 0.05 and that the regression coefficient P > 0.05 (i.e., no proportional bias). Bland–Altman analyses were conducted with TEE expressed as kJ/d; physical activity level was applied as 1.69 for men, 1.66 for women. Normal distribution was tested for the following variables: TEE derived from equations (kJ/d); TEE measured (kJ/d); and difference of TEE measured and TEE derived from equations (kJ/d). LOA, limit of agreement; TEE, total energy expenditure.

²A negative “mean of the difference” means the equation overestimated measured TEE and a positive “mean of the difference” means the equation underestimated measured TEE.

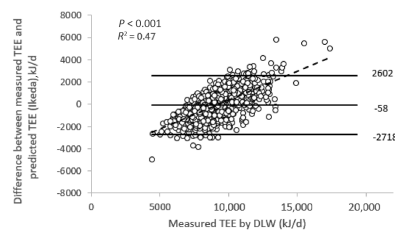
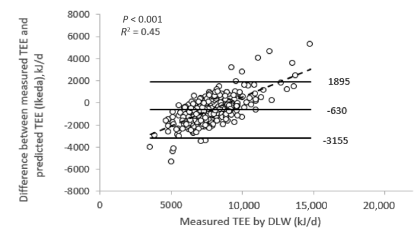
Main analyses

 ≥ 65 y ($n = 1488$)

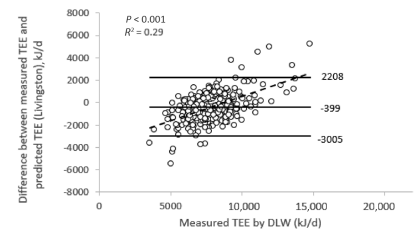
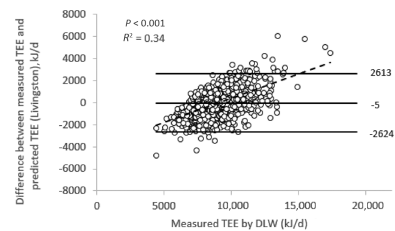
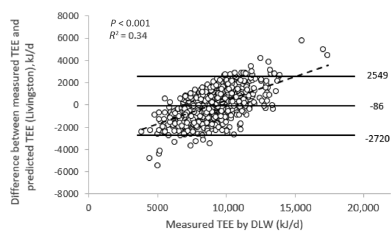
A Ikeda



Subgroup analyses

65–79 y ($n = 1184$) ≥ 80 y ($n = 304$)

B Livingston



C Mifflin

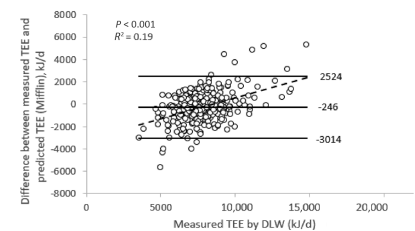
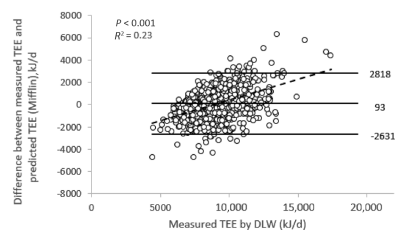
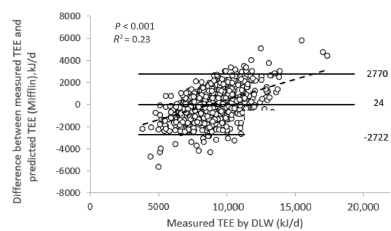


FIGURE 4 Bland–Altman analysis testing agreement between TEE measured using DLW and TEE derived from the Ikeda, Livingston, and Mifflin equations (main analysis, $n = 1488$; subgroup analysis: $n = 1184$, 65–79 y; $n = 304$, ≥ 80 y). Solid lines indicate the means + 95% limits of agreement (bias). Dotted line indicates the regression line, with P value and R^2 for the regression line (proportional bias). DLW, doubly labeled water; TEE, total energy expenditure.

should be acknowledged. These include the skew that existed for variables included in the Bland–Altman analyses. Also, there was a gender distribution with more women than men included, due to the demographics of ageing generally, and the contribution of the large data set of women from the WHI (13, 14). Another potential bias was that much of the data were obtained from developed countries (likely associated with the cost of running DLW studies), which limits their generalizability. It should also be noted that this analysis applies to only “healthy” older adults and inclusion criteria did not mandate that individuals within studies were required to be weight stable.

In conclusion, this analysis has identified that the 3 existing predictive equations with the closest alignment to this large international TEE database in older adults are the Ikeda, Livingston, and Mifflin equations. We recommend that any of these equations should be used in estimating the RMR and TEE for the population aged ≥ 65 y. However, given the proportional bias, the use of these equations has limitations particularly when used for individuals with higher energy expenditures. In the future, given the large population growth forecast in the later decades of life and their illness profiles, greater accuracy

of predictive equations should be expected. The inclusion of functional measures of ageing into new predictive equations for older adults may lead to closer estimates of energy expenditure. Future research efforts should also focus on the further refinement of predictive equations that meet the requirements of subsets of the aging population, such as those with various chronic diseases.

The authors’ responsibilities were as follows—JP, KN, CEH, DS, RP, and HT: designed the research; KN, JC, and NK: analyzed the data; JP, KN, JC, and HT: wrote the paper; JP: has primary responsibility for the final content; and all authors: contributed to data interpretation and read and approved the final manuscript. None of the authors reported a conflict of interest related to the study.

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