Determination of the applicability of the Fitmate in the assessment of resting energy expenditure and diet induced thermogenesis in outpatients with Chronic Obstructive Pulmonary Disease visiting the nutrition center for nutritional depletion and/or involuntary weight loss

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Foreword

This thesis is written in the context of a graduation report for the education: Nutrition and Dietetics at the Hogeschool van Amsterdam. The subject of my graduation report is: Determination of the applicability of the Fitmate in the assessment of resting energy expenditure and diet induced thermogenesis in outpatients with Chronic Obstructive Pulmonary Disease visiting the nutrition center for nutritional depletion and/or involuntary weight loss.

The motivation for this graduation report is outpatients with COPD. Previous studies showed that the resting energy expenditure (REE) predictive formulas give different values for REE in comparison with the REE measured by indirect calorimetry. The purpose of this graduation report was to determine the applicability of the Fitmate, a device for measuring your REE, which you can take to the bedside of the patient and is less costly and laborious for use.

I would like to pay tribute to my sponsor and supervisors Nicolaas E.P. Deutz and M.P.K.J. Engelen of the Center for Translational Research in Aging & Longevity for their support, involvement, feedback and valuable time they have put in my graduation report.

Furthermore I want to pay tribute to my teacher tutor P.J.M. Weijs of the Hogeschool van Amsterdam for his time, guidance and feedback during my graduation report.

A.M. Klopman
Abstract

Keywords: COPD; Diet induced thermogenesis; Fat-free mass; Resting energy expenditure

Objective: This study investigates the applicability of the Fitmate in the assessment of resting energy expenditure and diet-induced thermogenesis in outpatients with Chronic Obstructive Pulmonary Disease.

Methods: 14 healthy subjects between 21 and 57 years old were studied. All subjects underwent a resting energy expenditure (REE) measurement using the Fitmate and a ventilated hood system. Fat-free mass (FFM) was measured by Dual energy X-ray Absorptiometry (DEXA).

Results: There was a variance coefficient found between two test days with the Fitmate (REE) of 18.7 %. The Fitmate underestimated the ventilated hood system and prediction equations of Harris & Benedict and FAO/WHO/UNU (average: 203, 90 and 59 kcal/day), whereas the ventilated hood system overestimated the prediction equations of Harris & Benedict and FAO/WHO/UNU (average: 113 and 145 kcal/day). For healthy subjects the Fitmate provided 43% accurate measurement, the RMSE was 261 kcal/day, and the percentage bias was -11.8%. The Harris & Benedict and the FAO/WHO/UNU both provided 57% accurate prediction, with an RMSE of 203 kcal/day and a percentage bias(%) of ~6.5 % for the Harris & Benedict. The RMSE for the FAO/WHO/UNU was 233 kcal/day and the bias(%) was ~8.4%. The diet induced thermogenesis (DIT) in subject A and B ranged from 2.0 to 7.8% of the energy content of the meal.

Conclusions: The Fitmate is applicable in the assessment of resting energy expenditure and diet induced thermogenesis, but it needs to be taken in account that both the Fitmate and the ventilated hood system have their limitations. The Fitmate underestimates REE in comparison with the ventilated hood system and the prediction equations of Harris & Benedict and FAO/WHO/UNU. The Ventilated hood overestimates the REE when compared to the prediction equations of Harris & Benedict and FAO/WHO/UNU. Unfortunately it was not possible to test the applicability of the Fitmate in outpatients with COPD.

More research is needed about the reproducibility and accuracy of the ventilated hood system, used in our data, so we can be sure that the ventilated hood system may be used as the “gold standard”.

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1.0 Introduction

1.1 Weight loss and COPD
COPD is a collective name for Chronic Obstructive Pulmonary Disease including emphysema and chronic bronchitis. In recent years, systemic COPD is no longer seen as only a local organ disease, but rather viewed as a systemic condition in which inflammation, changes in intermediary metabolism and skeletal muscle weakness play an important role. The main symptoms patients with COPD experience are shortness of breath and a reduced exercise tolerance.

A poor nutritional status is common among these individuals with COPD and is an independent predictor of increased mortality and morbidity. Landbo et al [1] even described that in mild to moderate COPD, the best prognosis were found in normal-weight and overweight individuals, whereas in severe COPD, overweight and obese patients had a better survival. These patients may be somehow protected from weight loss because of higher energy reserves [1]. Weight loss is commonly present in patients with COPD, resulting in loss of fat mass as well as fat-free mass (FFM). About 25-60% of the COPD patients are characterized by malnutrition [2]. Depletion of FFM has been reported in 20% of COPD outpatients [3] and in 35% of those eligible for pulmonary rehabilitation [4]. Several factors are responsible for nutritional depletion in COPD such as a negative energy balance, disuse atrophy of the muscles, hypoxemia, systemic inflammation, oxidative stress and hypogonadism in some patients [4].

1.2 Energy expenditure and COPD (REE)
Total daily energy expenditure consists of 3 components: resting energy expenditure (REE), diet-induced thermogenesis (DIT) and activity induced thermogenesis (AIT)

Healthy subjects: COPD patients:

- 25-35% Activity induced thermogenesis
- 5-10% diet induced thermogenesis
- 60-65% resting energy expenditure
- REE increased in 25%
- Increased AIT
- No information available about DIT and COPD
1.2.2 Resting energy expenditure
REE is the energy needed for the ongoing processes in the body in the resting state when no food is digested and no energy is needed for temperature regulation [5].

Hypermetabolism is normally defined by measured/predicted REE ratio ($\frac{REE_m}{REE_p} > 110\%$), using a ventilated hood to determine the measured REE and the Harris & Benedict equation for the calculated REE [6, 7]. Previous studies done in COPD patients have also defined hypermetabolism as $\frac{REE_m}{REE_p} > 110\%$ [8-10]. Sergi [9] showed that REE, both in absolute values and when adjusted for their fat-free mass (FFM) was significantly higher in COPD patients than in healthy age-matched controls. Hypermetabolism defined as $\frac{REE_m}{REE_p} > 110\%$ was found in 60% of COPD cases and 13.7% (<0.01) of healthy subjects. No relationship was found between measured/predicted REE ratio ($\frac{REE_m}{REE_p}$) and the severity of airflow obstruction as reflected by the forced expiratory volume in 1 second (FEV$_1$) in COPD. These results are consistent with other studies, in which FEV$_1$ was higher in hypermetabolic than in normometabolic COPD patients [10]. The main cause of the increased REE in stable COPD is an increased oxygen cost of breathing related to the presence of hyperinflation of the thorax and flattened of the diaphragm, resulting in an inefficient breathing pattern. The changes in energy balance may partially be reversed by reducing hyperinflation with medication, breathing techniques or lung volume reduction (predominantly in the emphysema group). This could reduce their oxygen cost of breathing and increase oxygen availability, which favors carbohydrate metabolism and recovery in body composition [11-13].

The presence of low-grade chronic inflammation, both locally and systemically, is also an important factor contributing to the elevated REE in COPD patients [14, 15]. Furthermore COPD patients often experience acute exacerbations of their symptoms mostly related to the presence of an acute respiratory tract infection, which further increases their REE (to 120-135%). In addition COPD patients are using various medications (such as oral or systemic corticosteroids, theophyllines, hormones, benzodiazepines and antipsychotic) that have shown to have a dose-dependent stimulating effect on REE [9]. There is also evidence that high catecholamine levels in COPD may induce a hypermetabolic response in these patients [16, 17].

1.2.3 Activity Induced Thermogenesis (AIT)
Activity induced Thermogenesis (AIT) is the energy expenditure needed for physical activity. AIT can be estimated from the difference between total energy expenditure (TEE) (by doubly-labelled water technique), and resting energy expenditure (REE), as assessed by indirect calorimetry, after subtracting TEE by 10% to account for diet-induced thermogenesis.

Limited data are available on AIT in COPD patients [5]. However there is some evidence that AIT is elevated in COPD patients [18];[19]. Static as well as dynamic hyperinflation of the thorax are important determinants of an increased work of breathing in daily life, and therefore may contribute to the increased AIT as observed in COPD. In addition, the increased energy expenditure for daily life activities (AIT) in COPD may be related to disturbances found in skeletal muscle energy metabolism [18, 19].
1.2.4. Diet Induced Thermogenesis (DIT)
Diet induced thermogenesis (DIT) is the increase in energy expenditure above resting energy expenditure associated with digestion, absorption, and storage of food. The design of most studies on DIT is a measurement of resting energy expenditure before and after a test meal, with a ventilated hood system. The DIT can be calculated as the area under the curve. In previous studies several researches reported within-subject variability in DIT, determined with a respiratory chamber, of 43% to 48% [20-24]. Kinabo and Weststrate [21, 25] point out numerous studies showing discrepancies concerning the influence of various factors on DIT (such as: age, exercise, nutritional status, energy content of a meal, and meal composition). Many of these discrepancies may be the result of methodological differences, particularly differences in the time taken to measure DIT.

However, it is generally accepted that the main determinants of DIT are the energy content and the protein fraction of food. The thermogenic effect of separate nutrients is highest for protein (20%-30%), followed by CHO (5%-10%) and fat (0%-3%) [22, 26-31]. In healthy subjects with a mixed diet, DIT represents about 10% of the total amount of energy ingested over 24h. For protein there was a tendency for an increased DIT, from 7.1 to 8.3% when 20 en% of the meal was exchanged with protein [15]. In a second study, with similar energy exchange with protein, there was a significant increase in DIT, from 10.5 to 14.6% of the energy content of the meal [22]. For carbohydrate and fat, one study showed no effect [15], one study showed an increase after exchange of 65 en% fat for carbohydrate [32], and one study showed the opposite, a decrease after the exchange of 28 en% fat for carbohydrate [33].

Figure 1: Diet induced thermogenesis as an increase in energy expenditure during and after 3 different lunch types [34].
In conclusion, several studies have shown that the DIT needs to be performed for at least 3 to 4 hours, with a meal/drink content of at least 400 to 450 kcal and a high percentage of protein (10-20%) [15, 21, 22, 39].

Until yet, no information is present whether diet induced thermogenesis is increased in patients with COPD and whether the Fitmate is able to assess it.

1.2.5. Methodology to measure REE

Many methods are available for measurement or estimation of REE, but they all have their limitations.

<table>
<thead>
<tr>
<th>Study</th>
<th>Group</th>
<th>N</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weststrate [21]</td>
<td>Obese and non-obese men and women</td>
<td>N=103</td>
<td>DIT can accurately be assessed within 3h for a meal providing ≈ 2508 kJ</td>
</tr>
<tr>
<td>Kinabo [25]</td>
<td>Healthy, adult, non-obese female</td>
<td>N=16</td>
<td>DIT did not return to baseline after 5h for a meal providing ≈ 5016 kJ</td>
</tr>
<tr>
<td>Belko et al [35]</td>
<td>Healthy male subjects, 23-30 yr of age</td>
<td>N=8</td>
<td>DIT returned to baseline after 3h for meals containing 15% of energy requirements but not for meals containing 30% and 45% of energy requirement.</td>
</tr>
<tr>
<td>D’Alessio et al [36]</td>
<td>Lean and obese men</td>
<td>N=10</td>
<td>DIT could last as long as 8h after meals providing ≈ 6688 kJ. DIT did not return to baseline after 4h for meals providing ≈ 2090 kJ</td>
</tr>
<tr>
<td>Welle et al [37]</td>
<td>Healthy male subjects</td>
<td>N=7</td>
<td>DIT did not return to baseline after 4 h for a 1672 kJ meal</td>
</tr>
<tr>
<td>Reed [38]</td>
<td>Healthy subjects</td>
<td>N=131</td>
<td>A 3-h DIT measurement can exclude &gt; 40% of the total DIT, and a 4-h measurement can exclude 22.5% of the total DIT, 10% of the 6-h DIT is left between 4 and 6 hours, based on a meals providing ≈ 3953 KJ (15% protein)</td>
</tr>
</tbody>
</table>

Table 1: results of DIT, expressed in kJ/meal and the needed time to measure the DIT
1.2.5.A. Prediction equations

Standardized equations are often used to assess REE and TEE, such as the Harris & Benedict equation, modified by various stress and activity factors to account for the clinical state of the patient.

<table>
<thead>
<tr>
<th>Reference</th>
<th>REE predictive equations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy subjects</td>
<td>Harris &amp; Benedict 1984[40]</td>
</tr>
<tr>
<td></td>
<td>♂: 13.397 x Weight + (4.799 x Height (cm)) – (5.677 x Age) + 88.362</td>
</tr>
<tr>
<td></td>
<td>♀: 9.247 x Weight + (3.098 x Height (cm)) – (4.33 x Age) + 477.593</td>
</tr>
<tr>
<td>Healthy subjects</td>
<td>FAO/WHO/UNU (MJ/d) [41]</td>
</tr>
<tr>
<td></td>
<td>♂: age 18-30y: 15.4 x Weight – (27 x Height (m)) + 717</td>
</tr>
<tr>
<td></td>
<td>♀: age 18-30y: 11.3 x Weight – (16 x Height (m)) + 901</td>
</tr>
<tr>
<td></td>
<td>♀: age ≥60y: 8.8 x Weight + (1128 x Height (m)) - 1071</td>
</tr>
<tr>
<td></td>
<td>♀: age 18-30y: 13.3 x Weight + (334 x Height (m)) + 35</td>
</tr>
<tr>
<td></td>
<td>♀: age 30-60y: 8.7 x Weight – (25 x Height (m)) + 865</td>
</tr>
<tr>
<td></td>
<td>♀: age ≥60y: 9.2 x Weight + (637 x Height (m)) - 302</td>
</tr>
<tr>
<td>COPD specific</td>
<td>Moore [42]</td>
</tr>
<tr>
<td></td>
<td>♂: 11.5 x Weight + 952</td>
</tr>
<tr>
<td></td>
<td>♀: 14.1 x Weight + 515</td>
</tr>
</tbody>
</table>

Table 2: Predictive equations

Although easy to use, inexpensive and universally available, these equations have been shown to be inaccurate in a variety of clinical settings. Furthermore, these equations often differ considerably from measured values as obtained by the ventilated hood system. REE prediction equations also systematically misclassify obese children and adults, critically ill patients, and individuals with eating disorders [43-46].

A previous study by Weijs [47] in 48 outpatients and 45 inpatients has shown that the predictive equations have a prediction error ranging from 223 to 426 kcal/day, which is 16-28% of the REE. He concluded that measuring REE is preferable above the use of prediction equations in individual patient care. However when the required equipment is not available, the FAO/WHO/UNU and the Harris and Benedict 1984 equations are the most practical and accurate equations for predicting REE in adult outpatients, inpatients and underweight patients. But it needs to be taken in account that the percentage of patients that had an acceptable prediction was only about 50%. In outpatients, the equation of Harris & Benedict predicted as high as two-thirds of the group within 10% of indirect calorimetry measurement, but in the inpatients group the Harris & Benedict equation only predicted well in one-third of the patients. [47].

Slinde et al. [48] examined the energy expenditure in underweight patients with severe COPD. He showed that the equation of FAO/WHO/UNU underestimated the REE in half of the patients. Using the disease-specific equation of Moore, REE was underestimated in three out of the 10 patients. Schols [8] also showed that the prediction equation of Moore was invalid, because REE was overestimated in most of the patients. Furthermore, a large inter-individual variation in resting energy expenditure in patients was found when measured REE was expressed as a percent of predicted REE. The results demonstrate that REE in COPD patients needs to be measured rather than predicted [8]. In another study by Moore [42], it has been shown that equations derived from normal populations (Harris and Benedict) underestimate REE in patients with COPD by 300-400kcal [42].
In the present study, the prediction equations developed by FAO/WHO/UNU, Moore, and Harris and Benedict will be used to determine if the Fitmate gives comparable results for resting energy expenditure in healthy subjects and in patients with COPD.

1.2.5.B. Ventilated hood system
Measurement of REE by ventilated hood indirect calorimetry is generally considered as the “gold standard”. This method although accurate, is technically demanding, time consuming, involves the use of expensive, specialized equipment that is not universally available, and requires trained personnel to perform it. The ventilated hood system uses CO2 and O2 for the calculation of REE. Oxygen consumption and carbon dioxide production will be calculated from the airflow and the difference in the concentration of oxygen and carbon dioxide between the incoming and outgoing air. For the measurement with the ventilated hood system the SensorMedics Vmax 29n is often used. The equipment needs to be calibrated before each measurement with gas mixtures with known O2 and CO2 contents according to the manufacturer’s instructions. A transparent Plexiglas hood will be placed over the patient’s head and room air will be drawn through the hood at a fixed flow rate. The expired air of the patient mixes with the room air in the hood from which samples are taken. A limitation of the ventilated hood system is the bad applicability on the bedside.

1.2.5.C. Fitmate
Recently, a new device (the Fitmate) has been introduced that seems well applicable in clinical practice (See appendix 1 for a short manual of the Fitmate). In contrast to the ventilated hood system that request data of both VO2 consumption and VCO2 production, the Fitmate calculates the REE by using the standard metabolic equation of Weir with a fixed RQ of 0.85 and only the measured VO2:

\[ \text{REE (kcal \cdot day}^{-1}) = (3.941 \times \text{VO2 L/day}) + (1.106 \times 0.85 \times \text{VO2 L/day}). \]

Data from a previous study shed light on the use of an assumed or fixed RQ of 0.85 for the conversion of oxygen uptake to measure REE in kcal/day. The mean and standard deviation for RQ, across the Douglas bag trials, was 0.801 +/- 0.053. Conversion via the Weir equation, using an oxygen uptake of 241 mL/min (as measured by the BodyGem), and the actual fixed RQ (0.85), results in estimated REE’s of 1.653 and 1.672 kcal/day, respectively. Therefore, the use of the constant RQ of 0.85 in the modified Weir equation introduced a mean error of 1.2% or 19 kcal/day in a healthy subject group [50].

Segal et al. [51] have shown that in healthy individuals similar results are obtained from the ventilated hood system, mask and mouthpiece. A total of 18 healthy men and women underwent three measurement techniques: the ventilated canopy, the Hans-Rudolph face mask (model 7900) and a rubber mouthpiece and nose clip used with a Hans-Rudolph nonrebreathing valve (Hans-Rudolph, Inc, Kansas, City, MO) in three consecutive 20-min measurement periods in a Latin square design. No significant effects (<0.05) were found for either period (first,
second, or third 20-min measurement period), or method of measurement. The subject also was asked to rate the methods for the most to the least comfortable. Eight subjects preferred the ventilated hood system, seven found the mask most comfortable, one subject preferred the mouthpiece, and two had no preference. Three subjects reported a feeling of claustrophobia while lying under the hood. Special attention must be given to sick people or individuals for whom the tightly fitting mask or mouthpiece and nose clips cause significant apprehension and discomfort. These methods may not be tolerated. It was concluded that the facemask and mouthpiece are acceptable alternatives to the ventilated hood system for estimation of resting energy expenditure [51].

As mentioned above, the Fitmate can be used at the bedside of the patient. Furthermore, it is laborious to use and less costly than the ventilated hood system. Still it is unclear yet whether the Fitmate is applicable as a tool to evaluate energy expenditure in the clinical setting.
2.0 Hypotheses and specific aims

Resting energy expenditure is often elevated in patients with a chronic wasting disease. It is still unclear whether the Fitmate can be used as an alternative to the ventilated hood system in the assessment of energy expenditure in these patients. If this is the case, the Fitmate will be the preferable technique in the clinical setting as it is laborious to use and less costly than the ventilated hood system.

In this study we will test the following hypothesis: The Fitmate is applicable in the assessment of energy expenditure in patients with a chronic wasting disease.

2.1. General aim
Determination of the applicability of the Fitmate in the assessment of REE in outpatients with Chronic Obstructive Pulmonary Disease visiting the nutrition center for nutritional depletion and/or involuntary weight loss.

2.2. Specific aims
Specific aim 1: To determine the day-to-day reproducibility of the Fitmate in healthy subjects.

Specific aim 2: To determine the validity of the Fitmate by comparing REE obtained by the ventilated hood system, as reference method, and using general prediction equations in healthy subjects.

Specific aim 3: To determine whether the Fitmate is able to pick up differences in energy expenditure after intake of a protein rich supplement in healthy subjects.

Specific aim 4: To measure the day-to-day reproducibility of the Fitmate in patients with COPD.

Specific aim 5: To determine the validity of the Fitmate by comparing REE obtained using general- and COPD specific prediction equations in cachectic outpatients with COPD.

The knowledge gained from this study will benefit our insight in the validity and reproducibility of the Fitmate. This information will determine whether the Fitmate is applicable in the clinical setting to measure REE in patients visiting the nutrition center for nutritional depletion and/or involuntary weight loss.
3.0. Materials and methods

For the complete study, we enrolled 14 healthy subjects (age range 21-57 years) and we were intended to measure 10 COPD patients (age >50 years) to determine validity and reproducibility of the Fitmate (compared with the ventilated hood system and existing prediction equations). Unfortunately it was not possible to include patients with COPD in our study. Although we had obtained IRB approval, and started the recruitment process, the remaining time period was too short to actually enroll COPD patients who fulfilled the in- and exclusion criteria.

3.1. Study population

The healthy population (aim 1, 2 and 3) were recruited from the staff at the UAMS, Donald W. Reynolds Institute on Aging. Subjects were included when they were 21 years and older. All 10 COPD patients (age >50 years) that we intended to measure (aim 4 and 5), had to suffer from chronic airflow limitation, defined as measured forced expiratory volume in one second (FEV₁) less than 70% of reference FEV₁. All had to be in a clinically stable condition and not suffering from respiratory tract infection or exacerbation of their disease at least 4 weeks prior to the study. Cachexia was present based on the following criteria: Body mass index < 21 kg/m² and/or FFM-Index: FFM/height² < 16 (males), 15 (females) kg/m² and/or recent involuntary weight loss (> 5% in preceding 3 months or > 10% in preceding 6 months). Exclusion criteria were as follows: Established diagnosis of malignancy, Diabetes Mellitus, untreated metabolic diseases including hepatic or renal disorder, Chronic Respiratory failure with Cor pulmonale and unstable heart disease requiring therapy or recent myocardial infection.

The COPD subjects were intended to be recruited at the UAMS clinics or responded to distributed flyers in the COPD community. These flyers were distributed at several places in Little Rock (i.e. bulletin boards, waiting rooms of pharmacies, grocery stores) and provided to physicians, residents, dieticians/nutritionists to hand out to eligible patients. When interested, these patients contacted the PI or research staff for further information and were subsequently screened. In addition, HIPAA recruitment authorization forms were provided to physicians, residents, and dieticians/nutritionists to hand out to eligible patients. This HIPAA recruitment authorization forms authorized the use/disclosure of information to the PI and research staff to determine whether a subject qualifies for a research project. The investigator documented subject screening, using a screening log where history examination was performed. Body weight and muscle mass was determined by Dual-energy X-ray absorptiometry (DEXA), and FEV₁ measurement was done using a digital handheld FEV₁ meter (Microlife), if the results from a recent one were not already available.

3.2. Study design

3.2.1. Anthropometry

All subjects came to the laboratory early in the morning between 8:00 and 9:00 am after an overnight of fast (12h). Weight and height were measured using standard techniques. Weight was measured to 1 decimal, placed in pounds. Height was measured to the last completed millimeter using a stadiometer.

3.2.2. Body composition (Dual-energy X-ray absorptiometry (DEXA))

Body composition (including FFM) was estimated from Bioelectrical Impedance Analysis by using Dual-energy X-ray absorptiometry (Hologic Delphi W). The DEXA measurement exposes subjects to a very low dose of radiation equivalent to measure a three compartment model, consisting of bone, fat, and lean tissue mass. This three-compartment model will be used for the analysis, with lean tissue assumed to
be all muscle. The information obtained by the DEXA is important to see if there is a relation between REE and FFM. For more information about the DEXA, see appendix 2.

3.2.3. Resting energy expenditure
For the energy expenditure measurement at rest, the Fitmate equipment and the ventilated hood system were used. Furthermore, REE was measured and expressed as absolute values. The prediction equations developed by FAO/WHO/UNU, Moore, and Harris and Benedict were used to determine if the Fitmate gives comparable results for resting energy expenditure in healthy subjects and in patients with COPD. (see table 1).

3.2.3.A. The Fitmate
For the energy expenditure measurement at rest, the Fitmate equipment was used. For measurement, the instantaneous values of Oxygen uptake (VO$_2$), Respiratory frequency (Rf) and fraction of O$_2$ expired (FeO$_2$) were measured. Measurements were done with a mask placed on the mouth and nose of the subject.

For the purpose of this study, additional data were required, so the Fitmate was connected to the serial port of a computer for downloading of data files that included information on oxygen consumption and REE. The Fitmate unit was auto-calibrated prior to each test.

3.2.3.B. Ventilated hood system
For the measurement with the ventilated hood system the SensorMedics Vmax 29n was used to measure the REE for 30 minutes. For more details see appendix 3.

*Half of the subjects performed the ventilated hood system test first while the other half performed the Fitmate test first.*
3.2.4. Research question 1: To determine the minimal measurement period necessary to obtain reliable values in REE by the Fitmate

Before starting with the aims, the minimal measurement period necessary to obtain reliable values was determined first. This was determined in the post absorptive state and after 30 minutes rest in supine position. In total 14 healthy subjects have been measured.

3.2.5. Research design for Specific aim 1: To determine the day-to-day reproducibility of the Fitmate in healthy subjects

day 1

<table>
<thead>
<tr>
<th>Time frame (minutes)</th>
<th>T=0</th>
<th>T=10</th>
<th>T=20</th>
<th>T=30</th>
<th>T=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy expenditure (10 minutes)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Day 2

(Subsequent day)

<table>
<thead>
<tr>
<th>Time frame (minutes)</th>
<th>T=0</th>
<th>T=10</th>
<th>T=20</th>
<th>T=30</th>
<th>T=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy expenditure (10 minutes)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To determine the day-to-day reproducibility, two 10-minutes measurements were done on two separate days. Before each test, the subjects had to lie in a supine position for 30 minutes. In total 6 healthy subjects have been measured.

3.2.6. Research design for Specific aim 2: To determine the validity of the Fitmate by comparing REE obtained by the ventilated hood system, as reference method, and using general prediction equations in healthy subjects.

<table>
<thead>
<tr>
<th>Time frame</th>
<th>T=0</th>
<th>T=30min</th>
<th>T=60min</th>
<th>T=90min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometry X</td>
<td>Fitmate or</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilated hood system</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
After lying in supine position for 30 minutes, REE was determined by the ventilated hood system as well as by the Fitmate for 30 minutes. At random, half of the subjects started with the Fitmate and the other half started with the ventilated hood system. The Harris and Benedict and FAO/WHO/UNU prediction equations were used for comparison. In total 14 healthy subjects have been measured.

3.2.7. Research design for Specific aim 3: To determine whether the Fitmate is able to pick up differences in energy expenditure after intake of a protein rich supplement in healthy subjects

<table>
<thead>
<tr>
<th>Time frame (Hours)</th>
<th>T=0</th>
<th>T=½</th>
<th>T=1</th>
<th>T=1½</th>
<th>T=2</th>
<th>T=2½</th>
<th>T=3</th>
<th>T=3½</th>
<th>T=4</th>
<th>T=4½</th>
</tr>
</thead>
<tbody>
<tr>
<td>REE</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinks</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIT (20min)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

On two different days, REE was measured for 30 minutes with a ventilated hood system or the Fitmate to determine baseline REE. Subsequently, two protein rich drinks with a total of 480kcal and 30 grams of protein (Boost© high protein) were consumed within 10 minutes. During the study, the subject had the metabolic hood or Fitmate mask placed on their face at various time periods throughout the study for measurement of diet-induced thermogenesis. Measurements were taken using the Hood/mask for 20 minutes at a time, with a resting period of 10 minutes between two measurement periods. Subjects remained in bed for the total duration of the study, with bathroom breaks (with a wheelchair) offered to them in between the measurement periods to ensure that metabolic measurements were as accurate as possible. The study was completed within 3 hours.

3.2.8. Research design for Specific aim 4: To measure the day-to-day reproducibility of the Fitmate in cachectic outpatients with COPD

**Day 1**

<table>
<thead>
<tr>
<th>Time frame (hours)</th>
<th>T=0</th>
<th>T=1</th>
<th>T=2</th>
<th>T=3</th>
<th>T=4</th>
<th>T=5</th>
<th>T=6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometry</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy expenditure</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Day 2**

<table>
<thead>
<tr>
<th>Time frame (hours)</th>
<th>T=0</th>
<th>T=1</th>
<th>T=2</th>
<th>T=3</th>
<th>T=4</th>
<th>T=5</th>
<th>T=6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometry</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy expenditure</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
On two test days, REE was measured for 10 minutes using the Fitmate, after lying in supine position for 30 minutes. Individuals were instructed to maintain the same diet and activity and dietary patterns throughout the 2 days of reliability testing. To check the dietary pattern of the subject a dietary 24 hr recall was intended to be obtained. Unfortunately no subjects have been measured.

3.2.9. Research design for Specific aim 5: To determine the validity of the Fitmate by comparing REE obtained using general and COPD specific prediction equations in cachectic outpatients with COPD.

<table>
<thead>
<tr>
<th>Time frame (minutes)</th>
<th>T=0</th>
<th>T=10</th>
<th>T=20</th>
<th>T=30</th>
<th>T=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropometry</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy expenditure</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

On both test days, REE was measured for 10 minutes using the Fitmate, after lying in a supine position for 30 minutes. Individuals were instructed to maintain the same diet and activity and dietary patterns throughout the 2 days of reliability testing. The data obtained by Fitmate were compared to those calculated using general and COPD specific prediction equations. Unfortunately no subjects have been measured.

3.3. Statistical analysis
The relationship between REE and FFM were determined using linear-regression analysis. Linear regression analysis was also used to determine the relationship between the two methods of measuring REE, namely the Fitmate and the ventilated hood system. Oxygen consumption and REE measurements were compared using paired t tests with Bland Altman plots showing the absolute differences between the two methods over the complete range of measured oxygen uptakes and REE. Test-to-test reliability was calculated using Pearson Product-moment coefficients. Statistical significance was set at the P < 0.05 level, and values were expressed as mean ± SD. The accuracy of the Fitmate and the equations of Harris & Benedict and FAO/WHO/UNU were evaluated on the basis of the percentage of subjects predicted within 10% of the REE measured [52]. The root mean squared prediction error (RMSE), and the mean percentage difference (bias) were used to indicate how well the model predicted in our data set [47, 53].
4.0 Results

4.1. Results research question 1: To determine the minimal measurement period necessary to obtain reliable values in REE by the Fitmate

The Pearson Product-moment coefficient was used to analyze the relationships between different time periods of measurement.

As shown in figure 2, 3 a strong correlation was found between the time periods 5-10 minutes and 5-30 minutes, and between 5-15 minutes and 5-30 minutes. In conclusion, a Fitmate measurement lasting at least 10 minutes gives reliable values for REE.
4.2. Results specific aim 1: To determine the day-to-day reproducibility of the Fitmate in healthy subjects
Bland-Altman plot was used to show the different scores between measurements, and the Pearson product correlation was used to show the correlation between the two days.

As shown in figure 4, there was no significant correlation found between the REE (kcal/day) of both test days, over a time period of 10 minutes. There was an interday difference of -91 kcal/day. There was a variance coefficient found in REE of 18.7% between both days and a \( R^2 = 0.34 \) and \( r = 0.58 \).

4.3. Results specific aim 2: To determine the validity of the Fitmate by comparing the data obtained with those from the ventilated hood system, as reference method, and when using general prediction equations in healthy subjects.
Healthy subject characteristics and body composition are shown in table 3, with the data summarized for age, weight, height, BMI and FFM. Aged ranged from 21 to 57 y. All subjects and patients met the inclusion and exclusion criteria.

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Woman</th>
<th>ALL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>6</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.0 ± 12.6</td>
<td>31.4 ± 8.6</td>
<td>36.4 ± 11.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>85.6 ± 20.5</td>
<td>67.3 ± 5.6</td>
<td>75.2 ± 16.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.0 ± 6.8</td>
<td>171.0 ± 6.8</td>
<td>173.7 ± 9.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.6 ± 4.5</td>
<td>23.4 ± 2.7</td>
<td>24.8 ± 3.8</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>64.2 ± 9.3</td>
<td>46.3 ± 1.8</td>
<td>54.0 ± 10.9</td>
</tr>
<tr>
<td>FFM-Index (FFM/height²)</td>
<td>20.0 ± 1.7</td>
<td>16.1 ± 1.2</td>
<td>17.8 ± 2.4</td>
</tr>
</tbody>
</table>

Table 3: Subject characteristics summarized for age, weight, height, BMI and FFM
Table 4: difference between REE and oxygen consumption shown as mean ± SD

<table>
<thead>
<tr>
<th>Title</th>
<th>P value</th>
<th>Mean difference in REE</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitmate vs. ventilated hood 5-30 min.</td>
<td>&lt;0.001</td>
<td>-203</td>
<td>-301 to –105</td>
</tr>
<tr>
<td>Fitmate vs. ventilated hood 0-10 min.</td>
<td>&lt;0.001</td>
<td>-211</td>
<td>-314 to –108</td>
</tr>
<tr>
<td>Fitmate vs. ventilated hood 10-30 min.</td>
<td>&lt;0.001</td>
<td>-196</td>
<td>-290 to –101</td>
</tr>
<tr>
<td>Fitmate vs. ventilated hood 15-30 min.</td>
<td>&lt;0.001</td>
<td>-194</td>
<td>-284 to –104</td>
</tr>
<tr>
<td>Fitmate O₂ vs. ventilated hood O₂ 5-30 min.</td>
<td>&lt;0.01</td>
<td>-0.02</td>
<td>-0.04 to -0.004</td>
</tr>
<tr>
<td>Fitmate O₂ vs. ventilated hood O₂ 0-10 min.</td>
<td>&lt;0.01</td>
<td>-0.03</td>
<td>-0.04 to -0.01</td>
</tr>
<tr>
<td>Fitmate O₂ vs. ventilated hood O₂ 10-30 min.</td>
<td>&lt;0.01</td>
<td>-0.03</td>
<td>-0.04 to -0.01</td>
</tr>
<tr>
<td>Fitmate O₂ vs. ventilated hood O₂ 15-30 min.</td>
<td>&lt;0.001</td>
<td>-0.03</td>
<td>-0.04 to -0.01</td>
</tr>
<tr>
<td>Fitmate 5-30 vs. HB 1984</td>
<td>NS</td>
<td>-90</td>
<td>-184 to 3</td>
</tr>
<tr>
<td>ventilate hood 5-30 vs. HB 1984</td>
<td>&lt;0.05</td>
<td>113</td>
<td>12 to 214</td>
</tr>
</tbody>
</table>

Table 5: Paired t-test to show if the measurements were significantly different from each other.

As shown in figure 5, there was a significant correlation found between the REE (kcal/day) between the Fitmate and ventilated hood system over a time period of 30 minutes, with the first 5 minutes not included. There was a significant intermethod difference of -208 kcal/day (p<0.001), however this difference did not change when the measuring period was reduced to shorter periods (see table 5). The Fitmate underestimated REE in comparison with the ventilated hood system with 11.7%, there was a difference found on individual level between 5.5% and –28.5%. No significant difference was present in intermethod difference in REE between males and females, and no significant relationship was found between intermethod difference and age. Therefore, the Fitmate underestimated REE as compared to the ventilated hood technique with 208 kcal/day, independent of the length of the measurement period, gender and age.
There was a significant correlation found between the \( \text{O}_2 \) (l/min) as determined by the Fitmate and ventilated hood system during a time period of 30 minutes, with the first 5 minutes not included. There was a significant intermethod difference of 0.02 l/min (p<0.05). The Fitmate underestimated the \( \text{O}_2 \) as compared to the ventilated hood technique by 0.02 l/min (9.8%). There is a difference found on individual level between 5.4 and 27.8%. No significant difference was present in intermethod difference in REE between males and females, and no significant relationship was found between intermethod difference and age (see figure 6).

As shown in figure 7, there was no significant correlation found between the measured REE (kcal/day) with the Fitmate and the estimated REE (kcal/day) with the Harris & Benedict equation. The Fitmate underestimated the REE as compared to the H&B equation by on average 90 kcal/day (7%). There is a difference found on individual level between 18.7% and –11.4%. No significant difference was present in intermethod difference in REE between males and females, and no significant relationship was found between intermethod difference and age.
Figure 8: Estimated REE (kcal/day) by indirect calorimetry with the ventilated hood system and prediction equation (HB) in 14 healthy subjects. $R^2 = 0.66$ (p<0.05), the intermethod difference in REE between the ventilated hood system and Harris & Benedict 1984 is 113 kcal/day. The limits of agreement (dashed lines) are -230 to 456 kcal/day.

As shown in figure 8, there was a significant correlation found between the measured REE (kcal/day) using the ventilated hood system and the estimated REE (kcal/day) using the Harris & Benedict equation. The Harris & Benedict underestimated the REE as compared to the ventilated hood system by on average of 113 kcal/day (6.1%). There is a difference found on individual level between 10.1% and –21.5%. No significant difference was present in intermethod difference in REE between males and females, and no significant relationship was found between intermethod difference and age.

Figure 9: Estimated REE (kcal/day) by indirect calorimetry with the Fitmate and prediction equation (FAO/WHO/UNU) in 14 healthy subjects. $R^2 = 0.63$ (p=ns), the intermethod difference in REE between the Fitmate and Harris & Benedict 1984 is -59 kcal/day. The limits of agreement (dashed lines) are -439 to 322 kcal/day.
As shown in figure 9, there was no significant correlation found between the measured REE (kcal/day) using the Fitmate system and the estimated REE (kcal/day) using the FAO/WHO/UNU equation. The Fitmate underestimated the REE as compared to the FAO/WHO/UNU by on average of 59 kcal/day (2.1%). There is a difference found on individual level between 7.1% and −7.4%. No significant difference was present in intermethod difference in REE between males and females, and no significant relationship was found between intermethod difference and age.

![REE Ventilated hood vs. FAO/WHO/UNU](image.png)

Figure 10: Estimated REE (kcal/day) by indirect calorimetry with the ventilated hood system and prediction equation (FAO/WHO/UNU) in 14 healthy subjects. $R^2 = 0.63$ (p<0.05), the intermethod difference in REE between the ventilated hood system and Harris & Benedict 1984 is 145 kcal/day. The limits of agreement (dashed lines) are -226 to 515 kcal/day.

As shown in figure 10, there was a significant correlation found between the measured REE (kcal/day) using the ventilated hood system and the estimated REE (kcal/day) using the FAO/WHO/UNU equation. The FAO/WHO/UNU underestimated the REE as compared to the ventilated hood system by on average of 145 kcal/day (8.0%). There is a difference found on individual level between 6.7% and −27.3%. No significant difference was present in intermethod difference in REE between males and females, and no significant relationship was found between intermethod difference and age.

<table>
<thead>
<tr>
<th>Instrument</th>
<th>REE (Kcal/d)</th>
<th>SD</th>
<th>Bias (%)</th>
<th>RMSE (Kcal/d)</th>
<th>Accurate prediction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>REE measured</td>
<td>1726</td>
<td>193</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fitmate</td>
<td>1523</td>
<td>304</td>
<td>-11.8</td>
<td>261</td>
<td>43</td>
</tr>
<tr>
<td>HB 1984 [40]</td>
<td>1613</td>
<td>279</td>
<td>-6.5</td>
<td>203</td>
<td>57</td>
</tr>
<tr>
<td>FAO/WHO/UNU [41]</td>
<td>1581</td>
<td>299</td>
<td>-8.4</td>
<td>233</td>
<td>57</td>
</tr>
</tbody>
</table>

Table 6: Evaluation of resting energy expenditure (REE) in 14 healthy adults based on bias, root mean squared prediction error (RMSE), and percentage accurate prediction.

As measured by the ventilated hood system (SensorMedics Vmax 29n)

For healthy subjects the Fitmate provided 43% accurate measurement, the RMSE was 261 kcal/day, and the percentage bias was −11.8%. The Harris & Benedict and the FAO/WHO/UNU both provided 57% accurate prediction, with an RMSE of 203 kcal/day and a bias(%) of −6.5 % for the Harris & Benedict. The RMSE for the FAO/WHO/UNU was 233 and the bias(%) was −8.4%.
There was no significant correlation found between the REE (kcal/day) of the Fitmate and the FFM measured with the DEXA, and there was also no significant correlation found between the REE (kcal/day) measured with the ventilated hood system and the FFM using DEXA.

4.4. Results specific aim 3: To determine whether the Fitmate is able to pick up differences in energy expenditure after intake of a protein rich supplement in two healthy subjects

![REE ventilated hood and FFM DEXA](image)

**Figure 11:** REE (kcal/day) by indirect calorimetry with the Fitmate and FFM by the DEXA in 14 healthy subjects. $R^2 = 0.72$

![REE Fitmate and FFM DEXA](image)

**Figure 11:** REE (kcal/day) by indirect calorimetry with the ventilated hood system and FFM by the DEXA in 14 healthy subjects. $R^2 = 0.51$

![DIT Fitmate (kcal/day) subject A](image)

**Figure 12:** Response in REE (kcal/day) after intake of a high protein drink, measured by the Fitmate. The first 30 minutes values were averaged and used as baseline value.

![DIT ventilated hood (kcal/day) subject A](image)

**Figure 13:** Response in REE (kcal/day) after intake of a high protein drink, measured by the ventilated hood system. The first 30 minutes values were averaged and used as baseline value.
After intake of two high protein drinks (Boost© high protein, see appendix 4) with a total energy content of 480 kcal and 30 gram protein, for a period of 3 hours, the area under the curve for subject A was 34 kcal/day with the Fitmate and 37 kcal/day for the measurement with a ventilated hood system. The area under the curve for subject B was 13 kcal/day with the Fitmate and 9 kcal/day with a ventilated hood system. DIT assessed in subject A and B ranged from 2.0 to 7.8% of the energy content of the meal.

4.5. Results specific aim 4: To measure the day-to-day reproducibility of the Fitmate in patients with COPD
Until yet no results have been obtained.

4.6. Results specific aim 5: To determine the validity of the Fitmate by comparing the data obtained using general and COPD specific prediction equations in cachectic outpatients with COPD
Until yet no results have been obtained
5.0 Discussion

Resting energy expenditure (REE) is the major component of total daily energy expenditure and therefore accurate assessment is of importance when estimating energy requirements. Breakthroughs in technology initiated the development of new devices to measure resting energy expenditure comparable to metabolic carts. The new devices are easier to use than traditional instruments and therefore can measure resting energy expenditure outside the laboratory and are also more affordable. But validation of these new devices needs to be tested in more detail.

The purpose of this study was to compare the new device, the Fitmate with the classic ventilated hood system for the assessment of Resting energy expenditure and Diet induced thermogenesis (DIT) in healthy subjects and in outpatients with Chronic Obstructive Pulmonary Disease (COPD) visiting the nutrition center for nutritional depletion and/or involuntary weight loss.

In the present study, we measured REE in 14 healthy subjects. All of them were colleagues from our research team at the Institute on Aging. Unfortunately it was not possible to include patients with COPD in our study. Although we had obtained IRB approval, and started the recruitment process, the remaining time period was too short to actually enroll COPD patients who fulfilled the in- and exclusion criteria.

Differences in practical application between the Fitmate and the ventilated hood system

In the present study, the Fitmate was evaluated because the system is mobile and less costly and laborious to use than a ventilated hood system, the so-called “gold standard” for measuring REE.

One of the main differences between the Fitmate and a ventilated hood system is that the Fitmate uses a facemask, while the ventilated hood system uses a hood. The hood needs to be applied when the subject is in supine position whereas the Fitmate can also be used when the subject is sitting in a chair. However, previous research has shown that a sitting position will increase the REE with 70kcal/day [54]. To exclude this effect, all subjects in the present study were studied in supine position. Alteration in the subject’s natural breathing pattern sometimes occurred due to the tightly fitting mouthpiece of the Fitmate and was less frequently present during the ventilated hood measurement. The breathing sound that the Fitmate makes during the measurement sometimes influenced the subject’s breathing pattern. In previous studies, numerous authors believe that this alteration in the subject’s breathing pattern may result in an increased REE value [55-57]. However, the ventilated hood can give subjects a claustrophobic feeling, which can also result in an increased REE due to the change in the subjects breathing pattern. Both the ventilated hood and the Fitmate systems are prone to air leaks. Using the Fitmate, the facemask needs to fit tightly on the subject’s face and a sealant may be needed to avoid air leaks. In the present study, the Fitmate detected an air leak between 3-6 times during a 30 min measurement period and responded to this leak with a beep. No insight is provided by the Ventilated hood technique whether air leaks occurred during the measurement period. However, to decrease the measurement noise, the RQ of the ventilated hood system can serve as a tool to detect some inaccurate measurements or REE protocol violations. If RQ is 0.7 or >1, prolonged starvation or excessive recent energy consumption should be suspected. If these metabolic reasons for an aberrant RQ does not exist, then air leaks, hypoventilation, hyperventilation, or inaccurate gas sensors should be suspected. Two subjects had an RQ >1, these data are removed from study results. The estimated RQ of the Fitmate is in agreement with the RQ determined with the ventilated hood, namely the
RQ of the ventilated hood system was 0.89±0.04, while the estimated RQ of the Fitmate is 0.85.

Furthermore, the Fitmate obtains raw data of every single breath whereas the ventilated hood uses a mixing chamber, thereby allowing for a variable flow of air through the system with an interval of 30 seconds whereas it is still uncertain whether the ventilated hood eliminates the outliers. On first sight, this results in much more “noise” when using the Fitmate than the Ventilated hood. However when the Fitmate data were averaged according to that done by the Ventilated hood, “noise” was comparable.

<table>
<thead>
<tr>
<th>Supine position (sitting, lying)</th>
<th>Fitmate</th>
<th>Ventilated hood system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw data</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Mobile</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Costly</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Eliminates outliers</td>
<td>++</td>
<td>?</td>
</tr>
<tr>
<td>Alteration in breathing pattern</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Table 6: advantages and disadvantages of the Fitmate in comparison to a ventilated hood system
- bad
+ good
++ very good
? unknown

In conclusion, both the Fitmate and the ventilated hood system have their practical limitations, which need to be considered when using the devices in certain conditions and circumstances.

**Day-to-day reproducibility of the Fitmate in healthy subjects**
We measured day-to-day reproducibility during two days in 6 healthy subjects to determine if the Fitmate provided reproducible results over the days.

In the present study, we found a variance coefficient in REE of 18.7% between both days and $R^2 = 0.34$ and $r=0.58$, with an interday difference in REE of –91 kcal/day. Our data are not in line with a previous study done by Cosmed using the Douglas bag method to evaluate the reliability and validity of the Fitmate. The day-to-day reproducibility in the study done by Cosmed was $r=0.94$ [58]. Previous studies also reported day-to-day reproducibility using the ventilated hood, with a variance coefficient in REE ranging from 2% to 10% [59-63]. In the current study no day-to-day reproducibility was measured in the ventilated hood system (SensorMedics Vmax 29n), used in our study. Potential explanations for the high variance between both days are i.e. a change in activity level and the duration of the post absorptive state.

In conclusion, the reproducibility of the Fitmate is lower than observed in previous studies evaluating the Fitmate and a ventilated hood system. Whereas the day-to-day reproducibility of the ventilated hood system used in our study is unknown. The limitation of this aim is the small size of the subject group measured, when measured on individual level, there is a high difference in REE found between both days (see figure 4).

**Validity of the Fitmate by comparing the REE data obtained by Fitmate with those from the ventilated hood system, as reference method, and general prediction equations in healthy subjects**
The purpose of this aim is to determine the validity of the Fitmate by comparing the data obtained with those of the ventilated hood system, as the “gold standard”. The same conditions were used for both systems. After lying in a supine position for 30 minutes, REE was measured by the ventilated hood system as well as by the
Fitmate. At random half of the subjects started with the Fitmate and the other half started with the ventilated hood system. In addition, the data from the Fitmate were compared with those obtained from the prediction equations of Harris & Benedict and FAO/WHO/UNU.

The present study shows that lower values were found for REE when measured by Fitmate as compared to the ventilated hood system and the prediction equations Harris & Benedict and FAO/WHO/UNU (average: 203, 90 and 59 kcal/day), whereas the ventilated hood system overestimated the prediction equations of Harris & Benedict and FAO/WHO/UNU (average: 113 and 145 kcal/day). As shown in table 6, the Harris & Benedict equation has the lowest bias(%), and thus gives the most accurate values when compared to the ventilated hood system. In our data the Harris & Benedict equation gave the best prediction of REE when compared to the ventilated hood system, when looked at the % of accurate prediction, 57% of the subjects were well predicted by the equations of Harris & Benedict and FAO/WHO/UNU, and 43% of the subjects were accurate predicted by the Fitmate (see table 6).

Furthermore there were comparable results found between the O$_2$ obtained by the Fitmate and the ventilated hood system, and the REE obtained by the Fitmate and the ventilated hood system, indicating that the CO$_2$ does not influences the REE.

A normal healthy person will lose 1kg of body fat when energy intake is reduced by 7000kcal. When the Fitmate is used a person will eat 200 kcal/day less than required. This means that this person will lose 1kg of body fat every 5 week, which can lead to malnutrition, especially in clinical settings.

Potential explanations for a lower REE with the Fitmate are undetected air leaks around the mouthpiece. This will result in a lower value of VCO$_2$, because the VCO$_2$ will escape in the air, which will lead to a lower REE. Subjects were carefully instructed to correctly use the Fitmate and were checked for air leaks from the mouthpiece prior to each REE measurement. Although the ventilated hood is less intrusive than the Fitmate with regard to the subject’s breathing pattern, some subject can feel claustrophobic due to the entire head being enclosed in the plastic canopy. Such apprehension could lead to excess ventilation and increased resting energy expenditure.

In conclusion, the Fitmate underestimates the REE when compared to the ventilated hood system and the prediction equations of Harris & Benedict and FAO/WHO/UNU. The ventilated hood system overestimated equations of Harris & Benedict and FAO/WHO/UNU.

Determination whether the Fitmate is able to pick up differences in energy expenditure after intake of a protein rich supplement in healthy subjects

Because there is little information available about DIT we studied if the Fitmate was able to pick up differences in energy expenditure after intake of a protein rich supplement in healthy subjects. Most other studies examining DIT have used small numbers of subjects, which likely contributes to the controversy as shown in table 1, because Weststrate [18] noted that the high intraindividual variation in the measurement of DIT allows for small power in studies with sample size of <10 subjects. In this study we also used a small number of subjects (See page 26 for results). Factors that can affect DIT include palatability, consumption frequency, exercise, and meal timing [64]. This may explain the range in DIT from 2.0 to 7.8%. In the present study, only the high protein drink (see appendix 4) was consumed, no exercise was allowed 3 to 4 hours before testing. The subject tolerated the high protein drink fairly well. The 3 hour measurement period used in the present study represents the comfort limit of subjects, especially for COPD patients, and was chosen to avoid sleeping or excessive fidgeting, but a more prolonged measurement as shown in literature [25, 35-38] may be required to increase validity.
In conclusion, the Fitmate can be used to pick up differences in energy expenditure after intake of a protein rich meal but there is a wide scatter as shown in figure 12 and 13. Therefore the Fitmate cannot be used to measure individual DIT but it can be used for research studies with a higher number of subjects. Also, a measurement period > 3 hours is needed to accurately estimate DIT.

**General conclusion**

In conclusion, as shown in table 6 the Fitmate is applicable in the assessment of resting energy expenditure and diet induced thermogenesis, but it needs to be taken in account that both the Fitmate and the ventilated hood system have their limitations. The Fitmate underestimates REE in comparison with the ventilated hood system and the prediction equations of Harris & Benedict and FAO/WHO/UNU. The ventilated hood overestimates the REE when compared to the prediction equations of Harris & Benedict and FAO/WHO/UNU. Unfortunately it was not possible to test the applicability of the Fitmate in outpatients with COPD.

More research is needed about the reproducibility and accuracy of the ventilated hood system used in our data, so we can be sure that the ventilated hood system may be used as the "gold standard".
6.0 References


30. Stock M. R.N., Obesity and leanness: basic aspects. 1982(7-10).


7.0. Appendix 1: Manuel Fitmate

Calibration:
Flowmeter: This function allows you to calibrate the flowmeter device, correcting the errors caused by environmental changes that may affect the turbine, repeated use, obsolescence, etc.

The Fitmate is supplied already calibrated by COSMED. Accuracy and precision are granted over a long period of use. Additional calibration can be performed.
1. Connect the syringe to the reader through the silicon tube and the conic adapter
2. Select 4.utility/1.calibration from the main menu
3. Select 2.calibration to perform a new test
4. Start moving the piston of syringe back and forth and perform 10 strokes (way and return)

Note: If calibration is for an REE test, it is advisable to slowly move the piston (3-4 times manoeuvres per minute) in order to simulate the ventilation of a subject in rest.

O₂ analyzer check: This function allows you to verify the efficiency of the O₂ analyzer and, eventually, to program the replacement.
1. Select 4.utility/2.O₂ analyzer check

The colour of the tank and the note below indicate the analyzer efficiency. The colour change depending on the status of the analyzer:
- Green indicates normal efficiency
- Yellow warns user that the analyzer needs to be replaced soon
- Red indicates that analyzer is about to exhaust.
- No colour indicates that the analyzer is exhausted.
The REE measurement

- If you just recently exercised, ate a large meal, or were not in a restful state during the test, the REE results higher than the actual and you may want to repeat the test (ideal is fasting state for at least 10 hours).
- Measure subject height and weight accurate to 0.1 cm/kg or inch/lb.
- Make the subject sit or lay on a comfortable chair or bed. Let the subject sit or lay in this supine position for 30 minutes.
- Connect all cables. Connect the device to the computer. Start the computer and start the Fitmate program.
- On Fitmate screen, select 1.new and enter all the needed information (birthday, height, weight etc.)
- Then select 1.Resting Metabolic Rate, the analyzer calibration will now start.
- After point F. is done, place the VO₂ mask on the face and pull the elastic strings accurately in order to eliminate possible leaks. (You can use a mirror to check for air leaks).
- Ask your subject not to move or speak until the test is over.
- After measurement is done (15 minutes) the data will be automatically saved in the Fitmate device.
- After each measurement you have to save the data on the computer!!

How to receive data on the computer:

1. Open the Fitmate program on your computer.
2. Add a new person to open the download test, by clicking on the following bottom
3. Then press load and displace the test to the right → new person.
4. Press the X, go to subject manager and double click on the persons name.
5. Then go to “opened on….” → Personal Weight Management → and Resting Metabolic Rate.
6. Click on the right mouse button, save the file and open it in Excel.
8. To calculate the REE first transfer the VO₂ ml/min to VO₂ L/dag by using the following equation: 1440* VO₂ ml/min=VO₂ L/dag. Then calculate the REE in kcal/dag by using the equation of Weir [49] REE (kcal • day⁻¹) = (3.941 x VO₂ L/day) + (1.106 x 0.85 x VO₂ L/day)

For other options of the Fitmate like body composition, the personalized weight management program and the daily nutritional needs see the Fitmate wellness technology user manual.
Figure 3: Test printout of the Fitmate
Attachment 2: Operating with Fitmate

**Turn the unit on/off, press the on/off button pressed for a few seconds.**

To save energy Fitmate will automatically:

- Turn off the display, when the unit is not in use for a time interval defined by the user in settings. To reactivate the display press any button.
- Turn off the unit after 5 minutes of non-use. To turn on the unit press the on/off button for few seconds.

In case of automatic turn-off, non-confirmed date or not completed tests will be lost.

**Keyboard**

- **On/off turn**
  - Navigator tool: to scroll up a menu and/or get back to the previous field when entering data.
  - Navigator tool: to scroll down a menu and/or pass to the next field when entering data.
  - Navigator tool: to move right through the menu. To space right when entering data/or to select an entry case of multi options fields.
  - Navigator tool: to move left through the menu. To cancel the last digit when entering the data and/or to select an entry case of multi options fields.

1. To enter the number 1 or one of the symbols .,:@-+!?$&/( )
2. To enter the number 2 of the letters A B C a b c
3, 4, 5, 6, 7, 8, 9
  - Similar to button 2
0
  - To enter the number 0
X
  - Cancel
OK
  - To confirm the select entry

Attachment 3: Printer

**How to load paper in the printer compartment**

1. Remove the orange cover of the paper compartment
2. Lift up the green lever.
3. Put the paper roll in the paper compartment. Insert one end of the roll in the slit indicated by the 2 grey guides under the green lever.
4. Lift down the green lever.
5. Select 4. Utility / 5. Paper feed form the menu. The equipment will feed up the paper. If not double check whether the paper has been inserted correctly.
6. Lose the orange cover, paying attention that the paper leans off.

**Test printout**

1. Choose the test to print from a test session.
2. Select 2. Print or 2. Print all to print out the test or the whole test session.

If the paper is missing, of the printer head is lifted up, an acoustic and graphic signal warns the user and the Fitmate aborts to print.
8.0. Appendix 2: Dual-energy X-ray Absorptiometry (DEXA)

*Purpose:* Dual energy x-ray absorptiometry (DEXA) measurements will be taken to determine fat-free mass, fat mass and bone mass of the whole body and of the lower and upper extremities.

*Procedure:*
A whole body scan will be obtained following an overnight fast (minimum 8 hours) in subjects wearing light clothing without any metal or plastic buttons and after removal of any jewellery or other metal objects. Positioning of the volunteer for the whole body scan will be completed as follows:

Volunteer lying on their back with the head at the right end of the table. Entire body is positioned within the scan limit border and straight on the table pad. Arms at their sides with palms down, separated from the thighs, and within the scan limit border. Heels separated by ~8 inches with legs rotated inward 25° and tape placed around the feet to maintain position.

All scans will be analyzed by a single, trained investigator at UAMS. Data will be stored on a single computer. A three compartment model, consisting of bone, fat, and lean tissue mass, will be used for the analysis, with lean tissue assumed to be all muscle.

*Figure 4: The DEXA (Hologic Delphi W)*
9.0. Appendix 3: Ventilated Hood system

*Purpose:* The ventilated hood Vmax 29n system, designed to be used as a mobile nutritional assessment instrument, will be taken to determine resting energy expenditure.

*Procedure:* The patient has to be in a fasting state, and make sure that patient has avoided stimulants such as caffeine, tobacco, or medication prior to test. Before starting the test the patient has to rest in a supine position for at least 30 minutes.

After filling in subject’s demographics, flow volume calibration needs to be done. Now the test can begin. Place the canopy over the head of the patient and make sure there are no air leaks. The canopy measurement technique allows for the head of the patient to be covered with a transparent plastic canopy. A constant flow of air goes through the canopy and to the metabolic cart with the exact value of this flow calibrated by the instrument. All expired air is collected into this constant flow so that calculations of oxygen consumption and carbon dioxide production can be completed. The Vmax 29N uses the modified Weir equation to calculate the REE using the VO\(_2\) and VCO\(_2\).

Weir [49] \[\text{REE (kcal \cdot day}^{-1}) = ([\text{VO}_2 \times 3.796] + [\text{VCO}_2 \times 1.214]) \times 4000\]

Make sure that the patient remains in a resting state but awake during the entire test, and the patient should refrain from voluntary skeletal muscle activity throughout the test.

When the patient attains the formatted steady state conditions for minute ventilation, HR, VO\(_2\) and RQ, a green box will be displayed in the lower right corner of the screen labeled “steady state”. Suggested testing time includes at least five minutes of steady state data. If the patient has not reached steady state within fifteen minutes, it is unlikely that a steady state will be achieved for this test. Alternate testing methods or retesting should be considered.