Review

Best Practice Methods to Apply to Measurement of Resting Metabolic Rate in Adults: A Systematic Review

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ABSTRACT

Several factors may alter apparent resting metabolic rate (RMR) during measurement with indirect calorimetry. Likewise, numerous indirect calorimetry measurement protocols have been developed over the years, and the methodology employed could influence test results. As part of a larger project to determine the role of indirect calorimetry in clinical practice, a systematic review of the literature was undertaken to determine the ideal subject condition and test methodology for obtaining reliable measurement of RMR with indirect calorimetry. Food, ethanol, caffeine, and nicotine affect RMR for a variable number of hours after consumption; therefore, intake of these items must be controlled before measurement. Activities of daily living increase metabolic rate, but a short rest (≤20 minutes) before testing is sufficient for the effect to dissipate. Moderate or vigorous physical activity has a longer carryover effect and therefore must be controlled in the hours before a measurement of RMR is attempted. Limited data were found regarding ideal ambient conditions for RMR testing. Measurement duration of 10 minutes with the first 5 minutes deleted and the remaining 5 minutes having a coefficient of variation <10% gave accurate readings of RMR. Individuals preparing for RMR measurement via indirect calorimetry should refrain from eating, consuming ethanol and nicotine, smoking, and engaging in physical activity for varying times before measurement. The test site should be physically comfortable and the individual should have 10 to 20 minutes to rest before measurement commences. A 10-minute test duration with the first 5 minutes discarded and the remaining 5 minutes having a coefficient of variation of <10% will give an accurate measure of RMR.

J Am Diet Assoc. 2006;106:881-903.

The determination of energy need is important in clinical dietetics practice and is a basic component of nutritional assessment because the balance between energy intake and expenditure has important health implications. Energy expenditure can be estimated or measured. Estimation errors can be significant for some individuals (1). Measurement should be more accurate than prediction, but only if the measurement is conducted properly. The American Dietetic Association has recognized the need to evaluate the methods and procedures for measuring energy expenditure using indirect calorimetry to determine the most accurate way to measure an individual's resting metabolic rate (RMR). This review describes the processes to be followed by individuals being measured (to ensure a resting state) and those to be applied by the operator conducting the RMR test (to ensure accurate measurement of the resting state).

METHODS

Question Formulation

Eighteen indirect calorimetry measurement methods were evaluated, grouped into 10 questions, and evaluated on their application to healthy older adults with and without obesity, acute care patients, and critically ill patients. Ethnicity of individuals within each study was also appraised when available. The questions pertained to conditions required of the test subject to achieve a resting state and to the conditions under which an accurate test of RMR can be obtained.

1. What period of fasting is required to avoid error in the RMR measurement resulting from the thermic effect of feeding (TEF) and alcohol?

*A complete list of Evidence Analysis Working Group Members appears in the Appendix.

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0002-8223/06/10606-0005$32.00/0
doi: 10.1016/j.jada.2006.02.009

2. Does nicotine or caffeine cause error in RMR measurement?
3. How long a rest period is needed before initiating an RMR measurement?
4. What period of restriction on physical activity is necessary before RMR measurement?
5. Are certain body positions associated with increased metabolic rate?
6. What environmental characteristics should be controlled to ensure accurate RMR measurement?
7. What is the difference in RMR when different types of gas collection devices are used?
8. What is the acceptable variation in oxygen consumption (VO_2) and carbon dioxide production (VCO_2) over what time interval to reflect steady state measurement conditions for accurate RMR, and how many measurements are needed?
9. What differences in RMR are seen when measuring the same individual at various times of the day or on different days?
10. How should respiratory quotient (RQ) be applied to the interpretation of RMR measurement?

Evidence Analysis Team

A panel of experts, recognized for their contributions in the study of energy expenditure in various settings of health and disease, were recruited to answer pertinent questions regarding the use of indirect calorimetry. These experts were teamed with evidence analysts, registered dietitians with rigorous training in the evidence analysis process (for a complete list of participants, see the Appendix).

The evidence analysts searched the literature and abstracted pertinent articles. The expert panel guided the evidence analysis process by clarifying the primary questions to be addressed, evaluating the annotated lists of included and excluded articles, and developing a scientifically sound conclusion statement with a grade describing the strength and amount of evidence on which the conclusion was based. For Question 4, panelists included research with physical activities representing recommended adult fitness programs but not with competitive trained athletics. Expert panel members and the evidence analysts reviewed each conclusion statement and grade to arrive at a consensus.

Literature Search and Data Collection

An independent researcher completed numerous electronic searches of the 1980-2003 literature regarding metabolic rate and indirect calorimetry (Figure 1). These searches were supplemented with hand searches of more recent literature. Only English language and human subject studies were considered. The National Library of Medicine's PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature 1981-2003), and EMBASE-Excerpta Medica databases were used. Most primary research designs (randomized clinical trials, cohort, cross-sectional, and repeated measures) were accepted. When limited or no primary research literature was available, consensus statements or narrative reviews were accepted. Objective inclusion and exclusion criteria described previously (1) were used to evaluate abstracts and articles were obtained when abstracts had missing information or were unclear.

Name	Description	No. of references
Search 1	Calorimetry [MeSH][ab]	1,520
Search 2	Calorimetry, indirect [MeSH]	1,277
Search 3	Resting metabolic rate [MeSH] or energy metabolism [MeSH]	13,721
Search 4	Calorimetry [MeSH] and energy metabolism [MeSH]	1,020
Search 5	Resting energy expenditure [tw][c]	87
Search 6	Indirect calorimetry [tw] and "energy metabolism" [tw]	1,050
Search 7	Calorimetry [MeSH] and basal metabolic rate [tw] or basal metabolism [MeSH]	1,276
Search 8	Calorimetry, indirect/standards [MeSH] or calorimetry, indirect/methods [MeSH]	95
Search 9	Combined Searches 1 or 2 or 3 or 4 or 5 or 6 or 7 with technique construct (see Figure 2)	Varied dependent on search permutations

[a]MeSH=Medical Subject Heading. Indexed in the National Library of Medicine. Available at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=mesh.
[b]Although "calorimetry" includes room calorimeters and the body suit calorimeters, this term was included to ensure search strategies would tag publications before the 1991 National Library of Medicine acceptance of "calorimetry, indirect" as a search term.
[c]tw=Text word. Represents text word as a search topic.

Figure 1. Search strategy summary for electronic search of literature regarding metabolic rate and indirect calorimetry. Limitations placed on all searches were publication date (January 1, 1980 to March 1, 2003, with the exception of Search 9, where date was extended to March 2004), language (English), population (adults aged ≥19 y), and subjects (human).

Evidence Appraisal

Accepted articles were carefully read and analyzed according to the American Dietetic Association's (ADA's) evidence analysis process (2). Each article was thoroughly abstracted and given a quality rating based on 10 research design areas (2) (Figures 2 and 3). In addition to ADA's analysis process, seven valid and reliable indirect calorimetry measurement techniques had to be described to achieve the highest quality rating. Findings were summarized, the strength of the evidence graded, and a draft conclusion statement written. Each conclusion statement was refined in a consensus process by the expert panel and a final evidence grade was assigned using ADA's evidence analysis process (2). The expert panel placed higher emphasis on individual differences than group means because group means tend to obscure large, clinically important individual differences.

RESULTS

Ninety-four articles were found that met the acceptance criteria and covered topics related to the questions posed

Research design areas evaluated before assigning a quality rating:

- Clear research question
- Absence of bias in subject selection
- Comparable groups after randomization
- Description of withdrawal method
- Absence of subject, clinical, and/or investigator indirect calorimetry measurement bias
- Interventions clearly described
- Outcomes stated, with valid and reliable measurement (see below)
- Appropriate statistical treatment
- Conclusions supported by results
- Funding bias unlikely

Valid and reliable indirect calorimetry protocol measurement techniques

- Machine calibration
- Twenty- to 30-minute rest before measurement if traveling to a measurement center
- Discuss procedures before single measurements (subject training)
- Steady state (predetermined group mean covariance, elimination of erratic measurements, and/or ongoing acceptable monitoring)
- Measurement length
- Exercise restrictions in healthy adults the day before measurements or description of sedentary lifestyle in healthy adults or identifying movement restrictions in critically ill patients
- Fasting

Definitions of grades for conclusion statements

Grade I: Good—The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of serious doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large sample sizes to have adequate statistical power.

Grade II: Fair—The evidence consists of results from studies of strong design answering the question addressed, but there is uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of doubts about generalizability, limited number of studies, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the questions addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: Limited—The evidence consists of results from a limited number of studies of weak design for answering the questions addressed. Evidence from studies of strong design is either unavailable because no studies of strong design have been done or because the studies that have been done are inconclusive due to lack of generalizability, bias, design flaws, or inadequate sample sizes.

Grade IV: Expert Opinion Only—The support of the conclusion consists solely of the statement of informed medical commentators based on their clinical experience, unsubstantiated by the results of any research studies, or only has the support of narrative reviews.

Grade V: No Data Exist—No studies were located that address the question at hand.

Figure 2. Research design quality rating checklist for literature regarding metabolic rate and indirect calorimetry.

in the current review. The questions posed and the evidence to answer those questions follow.

Question 1

What period of fasting is required to avoid error in the RMR measurement resulting from the TEF or alcohol? A minimum fast of 5 hours after meals or snacks (Grade II) and 4 hours after small meals is recommended if longer fast is clinically inappropriate (Grade II). A minimum of 2 hours abstention from alcohol is needed (Grade III).

The increase in metabolic rate associated with the digestion, absorption, and metabolism of dietary nutrients is referred to as the TEF. The typical pattern is that of a rapid rise to peak levels followed by a gradual return to baseline RMR.

TEF Peak. The peak in TEF occurs between 60 and 180 minutes in most individuals (3-17), with people with obesity and older people tending to peak later than nonobese and younger people. When TEF was measured in subjects with obesity for 3 hours after a 315- to 720-kcal meal, group mean TEF peaked at 60 to 90 minutes (5,12,15). In a 4-hour study using a 910-kcal test meal (14), TEF peaked at 114±14 minutes in nonobese women and 138±12 minutes in women with obesity (results not significant). Reed (10) confirmed the earlier peak in TEF in nonobese subjects, and also found the peak to be higher than in subjects with obesity.

Limited studies of TEF in elderly subjects have been published. In 103 older adults (aged 67 to 79 years) the TEF peak occurred at 90 minutes, whereas 56 young adults (aged 21 to 29 years) peaked at 60 minutes (14).

TEF Total. Total TEF is approximately 7% to 9% of energy consumed after meals of 400 to 1,200 kcal (6,7,17-19) in nonobese and obese subjects (Table 1). Studies in which metabolic rate is measured for 6 hours after consumption of moderate to large meals reveal that 57% of the TEF has been expended at 3 hours, 77% at 4 hours, and 91% at 5 hours (10). When a single measurement of RMR after a 4-hour fast was compared with RMR measured after a 12-hour fast, the 4-hour measure was 74 to 139 kcal/day (mean 99 kcal) higher (20).

Alcohol Ingestion. As with food, alcohol can also increase metabolic rate (see Table 1) (19,21,22). Based on limited available studies, individual RMR increases of 1.1% to 13.6% have been reported over 95 minutes after ingestion of alcohol in healthy men (22) and mean RMR increases of 9% have been recorded 90 to 100 minutes postingestion in women (21). In contrast, RMR was elevated 26% in middle-aged (mean age 42 years) alcoholics with overnight abstinence and decreased to levels similar to nonalcoholic controls after a 14-day abstention from alcohol (18). No studies reflecting binge drinking conditions were appraised.

Question 2

Does nicotine or caffeine ingestion cause error in RMR measurement? The minimum time to abstain from nicotine is 2 hours (Grade II) and caffeine 4 hours (Grade II) before RMR.

Nicotine Peak. The initial thermic effect of nicotine peaks at 10 to 60 minutes after exposure (3,23-25) and subse-

Resting metabolic rate measurement method search terms (Medical Subject Heading [MeSH] or text word [tw] search)	No. of final accepted original studies[a]	Research design class[b]	Quality rating frequency[c]	Population Characteristics Represented[d]					
				Healthy	Obese	Older adult	Acutely ill	Critically ill	Ethnicity
Thermic effect of feedings (Fasting [tw] or diet-induced thermogenesis [tw] or energy intake/metabolism [tw] or energy intake/physiology [tw])	24	Repeat measures crossover (n=23); nonrandom (n=1)	10 + 14 ∅	✓	✓	✓			
Alcohol (Ethanol [tw])	3	RCT[e] (n=2); nonrandom (n=1)	3 ∅	✓	✓				
Smoking (Nicotine [tw])	7	Repeat measures crossover (n=7); cohort (n=1)	7 ∅	✓					✓
Coffee consumption (Caffeine [tw])	8	RCT with placebo (n=2); nonrandom (n=1); repeat measures crossover (n=3); before/after (n=1)	1 + 7 ∅	✓	✓	✓			✓
Rest before measure (Rest [tw])	6	Repeat measure crossover (n=3); nonrandom (n=1); reliability (n=1); observational (n=1)	1 + 2 ∅ 3 −	✓	✓	✓		✓	✓
Rest length after daily activity or physical exercise (physical fitness [tw]) or exercise [tw] or running [tw] or resistance exercise [tw] or bicycling [tw])	10	Repeat measures crossover (n=8); before/after (n=1); meta-analysis (n=1)	1 + 9 ∅	✓	✓	✓			
Lighting (Light [tw])	0	Not available							
Noise distractions (Noise [tw])	0	Not available							
Humidity (Humidity [tw])	0	Not available							
Room temperature (body temperature [tw] or shivering [tw])	1	Repeat measures crossover (n=1)	1 +	✓					
Body position (posture [tw] or supine [tw] or sitting [tw])	2	Repeat measures crossover (n=2)	2 +	✓	✓		✓		
Gas collection device (ventilated hood [tw] or nose clip [tw] or mouth piece [tw] or face mask [tw])	5	Repeat measures crossover (n=5); time series (n=1); nonrandom (n=1)	1 + 3 ∅ 1 −	✓		✓			
Steady state (steady state [tw])	6	Cohort (n=5); nonrandom (n=1)	4 + 2 ∅	✓	✓	✓		✓	✓
Measurement interval (used broad search strategy)	6	Cohort	4 + 2 ∅						✓
No. of measures/24 h (used broad search strategy)	9	Cohort	3 + 5 ∅ 1 −	✓	✓	✓		✓	✓
Respiratory quotient (oxygen consumption [MeSH] or oxygen/analysis [MeSH] or respiration [MeSH] or respiratory quotient [MeSH])	36	RCT (n=4); nonrandom (n=4); cohort (n=9); cross-sectional (n=4); repeat measures crossover (n=9); meta-analysis (n=1); case-control (n=1); case study (n=1); observational (n=3)	8 + 26 ∅ 2 −	✓	✓	✓	✓	✓	✓

(continued)

Figure 3. Resting metabolic rate measurement method search terms and accepted study description, for literature regarding metabolic rate and indirect calorimetry.

Resting metabolic rate measurement method search terms (Medical Subject Heading [MeSH] or text word [tw] search)	No. of final accepted original studies[a]	Research design class[b]	Quality rating frequency[c]	Population Characteristics Represented[d]					
				Healthy	Obese	Older adult	Acutely ill	Critically ill	Ethnicity
Intraindividual variation (circadian rhythms [tw] or individual variation [tw])	13	RCT (n=1); nonrandom (n=2); repeat measures crossover (n=8); cohort (n=1); observational (n=1)	1 + 12 ∅	✓	✓	✓	✓	✓	
Hormones (hormone [tw] or menstruation [tw])	8	Repeat measures crossover (n=2); concurrent comparison groups (n=2); before/after (n=1); meta-analysis (n=1)	8 ∅	✓	✓	✓			✓

[a]The entire number of original (or primary) research studies and meta-analyses for the overall conclusion statement and related subconclusion statements. Accepted studies also included related analyses, measures, or preliminary results that were needed to develop consensus on the overall conclusion statement. Review studies and consensus statements that may have been used to identify additional research or guide conclusion statement writings are not presented (2).
[b]For the resting metabolic rate methods of measurement interval, number of measures, and steady state, studies focusing on repeated indirect calorimetry measures within a day were considered an exposure being monitored within a small cohort group. When there were two comparisons (by group or technique), the study design was repeat measures crossover. Research design was assigned based on the portion of evidence appraised measurement technique, and in some cases did not match the research design of the entire study.
[c]Quality ratings were assigned using the 10 research design areas evaluated (outlined in reference 2); −=limited research rigor, ∅=not exceptionally strong and may risk bias, and +=strong study for the questions asked.
[d]A check in the ethnicity column indicates that one or more ethnicities (African American, Asian and Pacific Islander, American Indian, Alaskan Native, and Hispanic) were represented or studies measuring individuals residing in developed countries (eg, Japan, Taiwan, and China).
[e]RCT=randomized controlled trial.

Figure 3. Continued

quent exposure can lead to additional peaks. Although RMR elevations occur within 10 minutes (8,25) with the first exposure, they are of short duration and RMR returns close to baseline 2 hours later.

Nicotine Total. Because many nicotine users report weight gain after they stop smoking, it has been suspected that nicotine might increase RMR. In men, individual thermic effect of nicotine ranges from −0.4% to +12.6% over 120 minutes (23). Group mean thermic effects range from 3.7% to 6.9% over 75 to 135 minutes (Table 2) (3,8,23-27) and 3% to 3.5% with placebo effects removed (8,26). In women group mean thermic effect of nicotine was 5.7% over 160 minutes after placebo effects were removed (3). After a 2-week smoking cessation in African-American and white adults with prior moderately high to high daily nicotine exposure, group mean RMR decreases were not statistically different from baseline measures and represented a mean decrease of 63 and 54 kcal/day, respectively (28).

Caffeine Peak and Total. In general, a thermic response to caffeine can be measured between 30 and 150 minutes after ingestion (29-31). In healthy men, caffeine ingestion of 200 to 350 mg (equivalent to about 8 to 10 oz brewed coffee) resulted in group mean RMR increases of 7% to 11% or 9 to 16 kcal between 30 minutes to 3 hours after ingestion (Table 2) (29,30). At 30 minutes after caffeine ingestion, individual RMR changes ranged from −0.7% to +24.8% in lean and obese Japanese women (31) and over 90 minutes, group mean increases of 7.8% to 15.4% were seen in white women (32). One study (33) offered a larger dose of caffeine in repeated smaller servings (ie, approximately 1,250 to 1,300 mg per 24 hours) and measured the thermic effect of caffeine over 24 hours in a respiratory chamber. After controlling for physical activity and TEF, the thermic effect of caffeine, on average, was 98 to 174 kcal/day in lean women and women with obesity.

There is no direct evidence to determine when metabolic rate returns to true resting levels following caffeine consumption. The increase in metabolic rate was sustained at 3 hours (30), but one study reported that after overnight abstinence from caffeine, RMR had returned to baseline levels (33). This suggests that a maximum of 12 hours of abstinence will eliminate the thermic effect of caffeine, but that 3 hours of abstinence comes close to baseline RMR.

Question 3

How long a rest period is needed before initiating an RMR measurement? A minimum rest of 10 to 20 minutes is suggested (Grade III).

RMR may be erroneously increased due to physical activity engaged in before the RMR measurement. Low levels of physical activity related to activities of daily living have minimal influence on RMR measurement, provided that a suitable rest period follows the activity. Group mean RMR measurements taken in 10 young (mean age 25.1 years, no standard deviation provided) and 30 older (aged 69±7 years) adults after rising from bed, dressing, traveling by automobile, and walking approximately 50 meters to a test center were statistically similar to when they slept overnight at the center (34,35). In another study of older adults (mean age 66.1±1.4

Table 1. Thermic effects of food (TEF) and alcohol in healthy adults, expressed as percent of energy intake and mean cumulative energy above resting metabolic rate (RMR)[a]

Primary author, y	Subject age range (y), number, and sex[b]	Weight class, NHLBI BMI[c] category or % body fat or % ideal body weight[b]	Study design class (study quality)[d]	Calorimetry method criteria met	Missing technique	Test meal energy intake and % macronutrient composition	TEF and Alcohol Outcomes: % energy intake	TEF and Alcohol Outcomes: Mean RMR increases, energy/post-ingestion measurement interval (min)
TEF							←— *mean±standard deviation*	—→
Bissoli L, 1999 (17)	Vegetarian diet 25-43 Mediterranean diet 25-35	Lean BMI=19-23 BMI=20-25	Repeat measure crossover, Ø	No	Calibration, activity	515 kcal *Pasta meal* (80% carbohydrate, 10% protein, 8% fat)	12±7.2 10±6.8	Not available
Kinabo JL, 1990 (7)	18-40 16 females	Lean BMI=18-22	Repeat measure crossover, +	Yes		600 or 1,200 kcal *Standard food meal* (24% carbohydrate, 11% protein, 65% fat) (70% carbohydrate, 11% protein, 19% fat)	9.0±0.6 7.0±0.3 9.0±0.5 7.0±0.4	54±2/360 85±6/360 54±3/180 90±7/180
Kinabo JL, 1990 (6)	Low-carbohydrate, high-fat diet 18-29 10 females High-carbohydrate, low-fat diet 19-34 8 females	Underweight-lean BMI=16-23 BMI=18-22	Nonrandom, +	Yes		Two 600-kcal meals, 3 h apart *Standard food meal* (24% carbohydrate, 11% protein, 65% fat) (70% carbohydrate, 11% protein, 19% fat)	6.8±0.3 7.5±0.6	81±4/360 91±6/360
Levine JA, 2000 (18)	30-54 individuals with alcoholism 20 males, 15 females Controls 20 males, 15 females	Lean BMI=17-29	Repeat measure crossover, +	Yes		478 kcal *Standard food meal* (55% carbohydrate, 12% protein, 33% fat)	Not available	Alcoholism 25±3/150 Control 26±5/150
Raben A, 2003 (19)	21-26 10 males, 9 females	Lean BMI=19-24	Repeat measure crossover, Ø	No	Calibration, steady state, training	600 kcal *Danish food meal* High protein: (37% carbohydrate, 32% protein, 31% fat) High carbohydrate: (65% carbohydrate, 12% protein, 24% fat) High fat: (24% carbohydrate, 12% protein, 64% fat)	8.3* 7.1* 7.1*	Not available

(continued)

Table 1. Thermic effects of food (TEF) and alcohol in healthy adults, expressed as percent of energy intake and mean cumulative energy above resting metabolic rate (RMR)[a] (continued)

							TEF and Alcohol Outcomes	
Primary author, y	**Subject age range (y), number, and sex[b]**	**Weight class, NHLBI BMI[c] category or % body fat or % ideal body weight[b]**	**Study design class (study quality)[d]**	**Calorimetry method criteria met**	**Missing technique**	**Test meal energy intake and % macronutrient composition**	**% energy intake**	**Mean RMR increases, energy/post-ingestion measurement interval (min)**
Reed GW, 1996 (10)	18-65 54 males, 77 females	Underweight-obese % body fat=8.7-51.3	Meta-analysis, Ø	No	Steady state, training, activity	650-1,394 kcal *Standard food meal* (20%-69% carbohydrate, 15% protein, 24%-65% fat)	Not available	Not available
Alcohol								
Klesges RC, 1994 (21)	21-35 16 females	Nonobese and obese; 3-10 drinks/d; 13 smokers	Randomized controlled trial, Ø	No	Calibration, rest, training activity	251 kcal *23 g ethanol*	Not available	10/100[ef]
Raben A, 2003 (19)	21-26 10 males, 9 females	Lean BMI=19-24	Repeat measure crossover, Ø	No	Calibration, steady state, training	600 kcal *Danish food meal* High alcohol: 49% carbohydrate, 12% protein, 24% fat, 23% ethanol *20 g ethanol*	9.0*	Not available
Weststrate JA, 1990 (22)	22-41 22 males	Lean-obese BMI 18-36	Randomized controlled trial, Ø	No	Rest, steady state	140 kcal *20 g ethanol*	Not available	Dose-dependent increases[f]

[a]Expert Panel members (see the Appendix) agreed by consensus to report TEFs using two methodologies and accepting a third statistical modeling as supportive data. The first approach was expressed as a *percentage rate* with RMR increases above premeal RMR over time per kilocalories eaten. Second, a postprandial meal effect was quantified using area under the time curve (AUC) analysis. This statistical model evaluates the nonlinear relationship between food-induced thermogenesis and energy expenditure over time. A meta-analysis using a three parameter, nonlinear integral evaluation was accepted and allows for a cumulative best estimate using two parameters of postprandial RMR meal (size and composition) and individual characteristics (fat-free mass and body fat percent) with an adjustment for methodological quality (ie, noise) as a third parameter.
[b]When not provided, range was established from mean±standard deviation or standard error of the mean.
[c]NHLBI BMI=National Heart, Lung, and Blood Institute body mass index.
[d]Study design quality definitions (2): −=limited research rigor; Ø=not exceptionally strong and may risk bias; and +=strong study for the questions asked.
[e]Thermic effect of alcohol did not use AUC analysis but was the difference between the average energy expenditure over time minus baseline RMR for the same period.
[f]Derived from mean RMR increases above baseline/minute in 10-min increments provided in original study.
*$P<0.05$ for meal or alcohol effect.

Table 2. The effects of nicotine and caffeine on resting metabolic rate (RMR) (expressed as RMR percent and energy increases above baseline over a time interval)[a]

Primary author, y	Subject age range (y), number, and sex[b]	Weight class (NHLBI BMI[c] category or % body fat or % ideal body weight) and subject characteristics	Study class	Study quality[d]	Calorimetry method criteria met	Missing techniques	Test dose exposure level and source[e]	Mean RMR Increases above Baseline/Postingestion Measurement Interval: % Interval (min)	Mean RMR Increases above Baseline/Postingestion Measurement Interval: kcal± standard deviation/interval (min)
Nicotine									
Audrain JE, 1991 (3)	18-32 15 females	Lean 15-85th percentile for weight; ≥20 cigarettes/d all smokers	Repeat measures crossover (smoking only group)	Ø	No	Calibration, rest, exercise	Moderately high 5 cigarettes total 2 cigarettes; 1 additional cigarette every h for 3 h (brands varied but no ultra low-tar and nicotine cigarettes allowed)	7.0/185* Placebo 1.3/185	Not available
Collins LC, 1996 (23)	18-65 16 males	Lean-overweight 14.5-24.5 body fat % 10 smokers, 6 nonsmokers	Repeat measures crossover	Ø	No	Calibration, exercise	Moderately high 6 cigarettes total; 2 cigarettes; 1 additional cigarette every 30 min for 2 h (1.74 or 0.8 mg nicotine/cigarette)	6.9/120* 5.2/120*	Not available
Jessen AB, 2003 (24)	18-45 12 males	Lean BMI=18.5-25 ≥15 cigarettes/d in 6 smokers, 6 nonsmokers	Repeat measures crossover (smoking only)	Ø	No	Training, steady state, exercise, fasting	Moderately high or moderate 2 nicotine chewing gum sticks total (2 or 1 mg nicotine/stick)	Moderately high 4.9/150* Moderate 3.7/150*	Not available
Klesges RC, 1991 (25)	18-35 20 females	Lean 15-85th percentile for weight; ≥20 cigarettes/d all smokers	Repeat measures crossover	Ø	No	Calibration, rest, training, activity, fasting	Moderately high or moderate 2 sticks of nicotine chewing gum or 2 cigarettes total (2 mg nicotine/stick; nicotine/cigarette unknown)	Moderately/high nicotine gum 18.5/10* Moderate cigarettes 11.5/10*	1.7/10 1.1/10

(continued)

Table 2. The effects of nicotine and caffeine on resting metabolic rate (RMR) (expressed as RMR percent and energy increases above baseline over a time interval)[a] (continued)

Primary author, y	Subject age range (y), number, and sex[b]	Weight class (NHLBI BMI[c] category or % body fat or % ideal body weight) and subject characteristics	Study class	Study quality[d]	Calorimetry method criteria met	Missing techniques	Test dose exposure level and source[e]	Mean RMR Increases above Baseline/Postingestion Measurement Interval: % Interval (min)	Mean RMR Increases above Baseline/Postingestion Measurement Interval: kcal± standard deviation/interval (min)
Perkins KA, 1995 (26)	18-30 38 males	Within 20% ideal body weight; 15-40 cigarettes/d all smokers	Repeat measures crossover within treatment groups (moderate dose and placebo)	Ø	No	Calibration, training	Moderately high 4 nasal spray doses (15 μg nicotine/kg)	5.7/80* Placebo 2.2/80	Not available
Perkins KA, 1990 (8)	18-30 20 males	Within 20% ideal body weight; 10 smokers 15-40 cigarettes/d in 10 smokers, 10 nonsmokers	Double-blind, repeat measures within treatment group (moderate dose and placebo)	Ø	No	Calibration, training	Moderately high 6 nasal spray dose (15 μg nicotine/kg)	6.5/120* (smokers and nonsmokers) Placebo 1-4/120 (smokers and nonsmokers)	Not available
Perkins KA, 1989 (27)	18-30 18 males	Within 20% ideal body weight 15-40 cigarettes/d all smokers	Double-blind, repeat measures crossover within treatment group (low and moderate dose, and placebo)	Ø	No	Calibration, training	Moderately high or moderate 4 moderate or low nasal-spray doses (15 or 7.5 μg nicotine/kg)	*See 1995 results* Low* 6/75 Placebo 3/75	Not available
Caffeine									
Arcerio PJ, 2000 (32)	21-31 10 females, 50-67 10 females	15.8-34.1 % body fat % body fat=24.5-40.1	Repeat measures crossover	Ø	No	Calibration, steady state	1 pill (5 mg/kg fat-free mass (based on group mean kg fat-free mass, ~240 mg caffeine)	15.4/90*7.8/90*	16/90 9/90
Collins LC, 1994 (29)	18-65 16 males	Lean-overweight % body fat=14.5-24.5 10 smoked regularly for at least 1 y, 6 nonsmokers	Repeat measures crossover	Ø	No	Calibration activity	1 tablet (200 mg/dose)	Abstinence smokers 4.8/150* Nonsmokers 6.7/150*	Not available
Koot P, 1995 (30)	No age given 12 males	Lean BMI=19.3-24.5	Repeat measures crossover	Ø	No	Steady state	6-8 oz coffee (200 mg/dose)	Not available	12.9±8.8/180*

(continued)

Table 2. The effects of nicotine and caffeine on resting metabolic rate (RMR) (expressed as RMR percent and energy increases above baseline over a time interval)[a] (continued)

Primary author, y	Subject age range (y), number, and sex[b]	Weight class (NHLBI BMI[c] category or % body fat or % ideal body weight) and subject characteristics	Study class	Study quality[d]	Calorimetry method criteria met	Missing techniques	Test dose exposure level and source[e]	Mean RMR Increases above Baseline/Postingestion Measurement Interval	
								% Interval (min)	kcal± standard deviation/interval (min)
Yoshida T, 1994 (31)	24-27 10 females 41-44 136 females	Lean BMI=19-21 Obese BMI=29-32	Nonrandomized controlled trial	Ø	No	Calibration, training, steady state, activity	Saline with caffeine (4 mg/kg ideal body weight; based on group mean ideal body weight, ~240 mg caffeine)	Not available	Not available

[a]Effect of stimulus compounds ingested was expressed as a *percentage rate* with RMR increases above preingestion (ie, baseline) RMR over time. Accepted studies did not quantify RMR effects using nonlinear area under time curve methodology.
[b]When range not provided, range established from mean±standard deviation or standard error of the mean.
[c]NHLBI BMI=National Heart, Lung, and Blood Institute body mass index.
[d]Study design quality definitions: −=limited research rigor; Ø=not exceptionally strong and may risk bias; and +=strong study for the questions asked (2).
[e]Nicotine exposure from cigarettes or chewing gum dose levels were defined (low=<1 mg nicotine, moderate=≥1 mg to <3 mg nicotine, moderately high=≥3 mg to <11 mg nicotine, and high=≥11 mg nicotine). When nicotine content/cigarette was unknown, an estimate of 0.9 mg nicotine/cigarette was used to aid comparisons. Similarly, when doses were based on weight or fat-free mass, mean weight (kilograms) was used to estimate exposure. Dose levels of 15 μg/kg body weight were interpreted as 1 mg nicotine/cigarette exposure per dose.
*$P<0.05$ for main effect of nicotine or caffeine from baseline RMR.

years), the outpatient RMR was approximately 7% greater than inpatient ($P<0.01$), equivalent to approximately 103 kcal/day (36).

In healthy adults, a minimum rest period of 10 to 20 minutes is stated as an adequate testing condition (36-38), although shorter times were not measured. In 12 elderly patients with chronic obstructive pulmonary disease who were transported to the test site in wheelchairs and allowed a 7-minute rest, RMR was <70 kcal/day different from that obtained after a 20-minute rest (38).

Two narrative reviews are frequently cited to justify a 30-minute rest period for critical care patients (39,40). In a primary study, activities requiring patient repositioning led to a 5.8%±4.3% increase in RMR during a 30-minute block (41). Shorter times were not reported. Further studies are needed to determine the minutes of rest required after intensive care unit activities to avoid influencing RMR.

Question 4

What period of restriction on physical activity is necessary before RMR measurement? A minimum abstention from moderate aerobic or anaerobic exercise for 2 hours before test (Grade II), and for vigorous resistance exercise abstention of at least 14 hours is needed (Grade III).

Energy expenditure increases with physical activity in proportion to the amount of work performed. Following activity, energy expenditure returns toward baseline resting levels, but the recovery time varies as a function of the type, intensity, and duration of the activity, and the physical fitness level of the individual. Thus, it is important to allow ample recovery time following physical activity to obtain an accurate measure of RMR.

After walking or jogging on a treadmill at low to moderate intensity for 20 to 30 minutes, metabolic rate returns to baseline RMR in 30 to 90 minutes (42-44). One study of trained and untrained individuals demonstrated that metabolic rate returned to resting levels within 60 minutes following 30 minutes of cycling at a higher intensity (70% of aerobic capacity) (45). The time to return to baseline RMR was more rapid in trained individuals (40±15 minutes) compared with untrained individuals (50±14 minutes) (45). In a different study, the recovery time after a 15-minute high-intensity (70% maximum oxygen consumption) and low-intensity (35% maximum oxygen consumption) exercise using a smaller mass of muscle (arms and shoulders rather than legs) was examined (46). Recovery time was 14±6.5 minutes for high-intensity exercise and 5.7±4.9 minutes for low-intensity exercise. Extending low-intensity exercise time to 30 minutes did not change recovery time (5.5±4.4 minutes) (46).

Performing resistance exercise also elevates metabolic rate following cessation of exercise. Young women who performed a weight circuit at high intensity for 45 minutes had an average increase in metabolic rate of about 100 kcal/day above RMR measured 90 minutes after exercise (47). Young men who performed a circuit weight training sequence at moderate or high intensity for 27 or 100 minutes had an average increase above RMR of about 250 and 360 kcal/day, respectively, measured at 90 minutes after completing the exercise (42,48). Even 14.5 hours after a workout, metabolic rate was still around 100 kcal above baseline RMR (48). Forty-eight hours after 12 older (aged 59 to 77 years) men completed single-leg knee extensions and bench press lifts (at 75% of each individual's three repetitions max), a 3% average increase (57 kcal/day) above RMR was recorded ($P<0.001$) (49).

Question 5

Are certain body positions associated with increased metabolic rate? Ensure each individual is physically comfortable with the measurement position during the test and repeated measures are in the same position (Grade V).

Certain postures require increased muscle tone and may influence the measurement of RMR. In 24 adults with a weight range of 48 to 109 kg, group mean RMR measured while sitting upright motionless was 70 kcal higher than supine RMR (3.7±6.3% increase) (50). There are no studies of RMR in the semirecumbent position.

One narrative review recommends supine measures of RMR in critically ill patients (39). One study measured patients (17 men and five women) before and after an elective thoracotomy. Postoperative mean RMR increases measured in the supine position were higher by 96 kcal/day than RMR measured at a 30° head-of-bed elevation ($P<0.01$) (51).

Question 6

What environmental characteristics should be controlled to ensure accurate RMR measurement? Allow a room temperature of 20°C to 25°C (68°F to 77°F) (Grade III).

Humidity, Noise, and Environment. No primary research studies addressed the effects of ambient noise and lighting on RMR in healthy adults. Two narrative reviews suggest that the room should be quiet and lighting mild when measuring RMR for patients in critical care settings (39,52). These conditions logically extend to other settings.

Ambient Temperature. RMR is affected to variable degrees by moderate cold exposure or ambient room temperatures outside a comfortable zone (22°C to 25°C or 72°F to 75°F). In a study of 10 women and 10 men (aged 19 to 36 years and body mass index [calculated as kg/m^2] 17 to 32), the individual change in RMR after 3 hours of exposure to moderate cold (15°C or 59°F) compared with RMR at typical ambient temperature ranged from a decrease of 4% to an increase of 30% in winter and from a decrease of 12% to an increase of 24% in summer (53). At temperatures within the usual zone of comfort for human beings, no changes in RMR based on adjustment to ambient temperature are observed.

Question 7

What is the difference in RMR when different types of gas collection devices are used? Use rigorous adherence to prevent air leaks (Grade III).

Further studies comparing modern gas collection devices are needed in healthy and clinical populations (Grade V).

Several types of gas collection devices are available for indirect calorimetry, including rigid canopies, facemasks, and mouthpieces with nose clips. In indirect calorimetry

Table 3. Indirect calorimetry measurement length, expressed in number and time interval with or without steady state criteria

								Indirect Calorimetry (IC) Measurement Length				
Primary author, y	**Subject age range (y), number, and sex[a]**	**Weight class, NHLBI BMI[b] category or % body fat or % ideal body weight (IBW)**	**Study design classes**	**Study quality[c]**	**Calorimetry method criteria met**	**Missing techniques**	**Gas collection device**	**Initial acclimation (min)[d]**	**Measures, n, and defined time interval (min)**	**Defined steady-state interval (min)**	**Steady-state criteria**	**Total IC measure interval recommended (min)**
Healthy adults												
Gasic S, 1997 (58)	22-48 8 males, 16 females	Lean-overweight BMI=19-27	Prospective cohort	+	No	Activity[e]	Canopy	10	2-Undefined; range: up to 30		Oxygen uptake, carbon dioxide production equilibration	Up to 30
Horner NK, 2001 (59)	50-79 102 females	Lean-obese postmenopausal	Prospective cohort	+	Yes		Canopy	5	1-30-45 1-30-45	5 10	<5% CV <10% CV	23%-26% achieved 82%-84% achieved
Isbell TR, 1991 (54)	No age data given 20 females	Lean-overweight 25th-70th weight percentile	Prospective cohort	+	Yes		Canopy Mouthpiece w/nose clip Face mask	5	1-50		Not applicable	1-20-min canopy (ICC[g]=0.75), 40-min face mask (ICC=0.79), and ≤10-min nose clip/mouthpiece (ICC=0.75)
Leff ML, 1987 (60)	22-47 2 males, 12 females	Underweight-lean BMI=17-28	Prospective cohort	Ø	No	Activity	Face mask	Training effect noted	8-60		Respiratory volume stabilized	1-60 (r=0.846)
Rehabilitation center												
Delinkanaki-Skaribas, 2001 (61)	56-87 35 males	Lean-obese BMI=16-39; long-term rehabilitation	Nonconcurrent cohort data-base	Ø	Yes		Face mask	0	1-20		None	1-20 (analyze 12 min)
Schols AM, 1992 (38)	60-72 12, sex unknown	Chronic obstructive pulmonary disease rehabilitation patients	Nonrandomized trial with concurrent controls	−	Yes		Ventilated hood	5-7	1-30		None	No difference between 1, 5, 10, 15, 25, and 30 (P>0.05)
Stable acute-care, critical illness or trauma, or subacute care												
Cunningham KF, 1994 (62)	No age reported, 47 No sex reported	Intubated adults in ICU[h]	Prospective cohort	Ø	Yes		Ventilated hood	Not specified	1-Undefined; range 18-44	5	<5% CV	1-5 <5% steady state varied by <5% from entire measure time interval in 42/47; −2.6±60 kcal/d
Frankenfield DC, 1996 (63)	33-73 20 males, 14 females	76%-164% ideal body weight; mechanically ventilated in ICU	Retrospective cohort	+	Yes		From ventilator	Not specified	1-Undefined; range: 5-27 1-Undefined; range: 30-40	5 30	≤5% CV ≤10% CV	1-5 ≤5% steady state=1-30 ≤10% steady state

(continued)

Table 3. Indirect calorimetry measurement length, expressed in number and time interval with or without steady state criteria (continued)

								Indirect Calorimetry (IC) Measurement Length				
Primary author, y	Subject age range (y), number, and sex[a]	Weight class, NHLBI BMI[b] category or % body fat or % ideal body weight (IBW)	Study design classes	Study quality[c]	Calorimetry method criteria met	Missing techniques	Gas collection device	Initial acclimation (min)[d]	Measures, n, and defined time interval (min)	Defined steady-state interval (min)	Steady-state criteria	Total IC measure interval recommended (min)
Fredrix EWHM, 1990 (34)	20-60 9 males, 6 females, 1 drop-out	95%-121% IBW; stable hospitalized	Prospective cohort	Ø	No	Training, steady state	Ventilated hood	0	2-30		Not applicable	High reliability (r=0.98, P<0.001) in 2 AM measures
McClave SA, 2003 (64)	16-84 13 males, 9 females	Mechanically ventilated in short-term acute care unit	Prospective cohort	+	Yes		Not applicable	Not specified	1-24 h		≤10% CV ≤15% CV ≤20% CV	1-5 ≤10%; steady state attained in 16/22; correlated to 24-h total energy expenditure (r=0.943)
Petros S, 2001 (65)	41-79 28 males, 18 females	Mechanically ventilated or spontaneously breathing	Prospective cohort	+	Yes		Ventilated hood	5	1-Undefined; range: 5-24, 29-32	5 30	≤5% CV	1-5 ≤5% correlates with 1-30 (r=0.972-0.994)
Stokes MA, 1992 (66)	17-85 21 males, 19 females	Elective surgery patients or nutritionally depleted	Prospective cohort	Ø	No	Steady state, test length	Ventilated hood	Acclimatization to the gas collection device results in lower 2nd measure	2-Undefined		Not applicable	2nd measure is more accurate in 34 of 40 patients[i]
vanLanschot JJ, 1988 (67)	15-83 40 males, 10 females	Surgical ICU; mechanically ventilated; ≥6 h post-anesthesia	Prospective cohort	Ø	Yes		Not applicable	*See steady-state criteria*	1-24 h		Artifacts suppressed by IC	2-15
vanLanschot JJ, 1986 (68)	15-83 19 males, 6 females	Surgical ICU; 7 heavily sedated	Prospective cohort	Ø	No	Calibration	Ventilated hood	*See steady-state criteria*	1-24 h		Artifacts suppressed by IC	1-5 (r=0.90), 1-10 (r=0.92) 2-5 (r=0.95)

[a]When not provided, range established from mean±standard deviation or standard error of the mean.
[b]NHLBI BMI=National Heart, Lung, and Blood Institute body mass index.
[c]Study design quality definitions: −=limited research rigor; Ø=not exceptionally strong and may risk bias; and +=strong study for the questions asked.
[d]Initial acclimation to gas collection device is not represented in total IC measure interval.
[e]Study received a "+" quality rating although not stating exercise restriction before morning measure; exception granted based on analysts' evaluation of research study plan and implementation.
[f]CV=coefficient of variation [SD×(mean of individual replicate measures)×100].
[g]ICC=intraclass correlation coefficient.
[h]ICU=intensive care unit.
[i]Study had an intervening variable affecting IC measure because total body potassium measure was taken after the first measure, likely initiating subject anxiety. This testing sequence doesn't occur in clinical practice conditions, limiting generalizability.

Table 4. Variability of resting metabolic rate (RMR) within 24 hours, between days, and up to 5 months in healthy and ill adults

Primary author, y	Subject age range (y), number, and sex[a]	Weight class, NHLBI BMI[b] category or % body fat or % ideal body weight (IBW)	Study class	Study quality[c]	Calorimetry method criteria met	Missing techniques	Gas collection device	Measurement number and measure points	Mean Intra-Individual Variation %	Range	RMR group mean difference (D) between measures
Within 24 h											
Audrain JE, 1991 (3)	18-32 15 females	Lean 15-85th percentile	Randomized controlled trial	Ø	No	Calibration, rest	Ventilated hood	5 10 AM, 11 AM, noon, 1 PM, 2 PM	Not available		2.5% higher at 11 AM vs 10 AM and 2 PM vs 10 AM
Frankenfield DC, 1994 (69)	*Trauma:* 19-37 10 males, 3 females (33 paired measures) *Septic* 21-43 17 males, 3 females (22 paired measures)	*Trauma:* 92%-112% id eal body weight *Septic:* 91%-133% ideal body weight	Nonrandomized controlled trial	+	Yes		Ventilated hood	2 7 AM-7 PM, 7 PM-7 AM	Not available		Within 5% in both groups
Heymsfield SB, 1987 (70)	19-51 8 males, 6 females	Lean-overweight BMI=21-29	Nonrandomized controlled trial	Ø	No	Calibration, steady state, activity	Face-mask	5-8 morning, times not given	6.1%±0.6%	1.9%-17.8%	Not available
vanLanschot JJ, 1988 (67)	15-83 40 males, 10 females	Surgical intensive care unit; mechanically ventilated; ≥6 h post-anesthesia	Time series	Ø	No	Calibration, steady state, training	Ventilated hood	1 7 AM-7 AM 24 h continuous measure segmented into 8 3-h intervals	Not available		<3% *D* between 3-h intervals
Weststrate JA, 1993 (15)	24-25 12 males	Lean 14%-16% body fat	Narrative review	Ø	No	Steady state, training, activity	Ventilated hood	5 morning, every 30 min for 2.5 h	Not available		<2% *D*[d] between 5th 30-min measure vs 1st 30-min measure
Weststrate JA, 1989 (71)	20-24 10 males	Lean BMI=20-26	Repeat measures crossover	+	Yes		Ventilated hood	6 3 at 8-9 AM (different days) 3 at 2-3 PM (different days)	Not available		<3% *D*[d] between morning vs evening
Between days and up to 5 mo											
Adriaens MP, 2003 (72)	16-31 8 males, 11 females	Not available	Nonrandom group w/ repeat measures	Ø	No	Steady state	Ventilated hood	3 2 wk	3.3%±2.1%	0.4-7.2	4% *D* between 1st vs 2nd measure[d] (65 kcal/d)
Fredrix EW, 1990 (73)	56-72 22 (sex not provided)	Not available	Nonrandom group w/ repeat measures	Ø	No	Rest, steady state, training	Ventilated hood	2 within 5 mo	3.5%		<1% *D*[d] (7 kcal/d)

(continued)

Table 4. Variability of resting metabolic rate (RMR) within 24 hours, between days, and up to 5 months in healthy and ill adults (continued)

Primary author, y	Subject age range (y), number, and sex[a]	Weight class, NHLBI BMI[b] category or % body fat or % ideal body weight (IBW)	Study class	Study quality[c]	Calorimetry method criteria met	Missing techniques	Gas collection device	Measurement number and measure points	Mean Intra-Individual Variation		RMR group mean difference (D) between measures
									%	Range	
Gibbons MR, 2004 (74)	62-83 7 males, 20 females	Lean-obese BMI=19-34	Nonrandom group w/ repeat measures	Ø	No	Steady state	Ventilated hood	2 1 mo	3.6% men, 2.5% women	0.1-9.9 0.0-16.8	4% *D*[d] (men: 53 kcal/d; women: 29 kcal/d)
Gibbons MR, 2004 (74)	62-83 6 males, 13 females	Lean-obese BMI=19-34	Nonrandom group w/ repeat measures	Ø	No	Steady state	Ventilated hood	3 1 mo	3%-4%	(men: 1.1-8.5 women: 0.4-12.5)	2% D between 1st vs 3rd measure (men: 29 kcal/d; women: 25 kcal/d)
Goran MI, 1993 (75)	18-28 10 males	Underweight-lean BMI=17-24	Nonrandom group with repeat measures	Ø	No	Calibration, rest, steady state, measurement length	Face-mask	3 within 14 d	4.8%±2.8%[d]	0.7-8.0	4.5% *D*[d] (69 kcal/d)
Haugen HA, 2003 (20)	Males: 29-51 females: 25-49 10 males, 24 females	Underweight-obese BMI=17-34	Repeat measure crossover	+	Yes		Ventilated hood	2 each; morning, evening, within 14 d	4.5% morning, 2.8% evening		Not available (<80 kcal/d)
Henry CJK, 2003 (76)	19-35 19 females	Lean-obese BMI=19-40	Nonrandom group repeat measures	Ø	No	Rest, steady state	Ventilated hood	12/3 d each wk for 4 wk	4.6%±2.2%	1.7-10.4	Not available
Short KR, 1996 (46)	22-32 5 males, 5 females	Nonobese-obese, no other information available	Repeat measures	Ø	No	Steady state	Non-rebreathing valve	3 2 d	7.5%[e]		Not available
Visser M, 1995 (14)	*Young* 21-29; 56 both *Older* 67-79; 103 both	Lean BMI=~20-25 Lean-overweight BMI=~22-30	Nonrandom group repeat measures	Ø	No	Rest	Ventilated hood	2 within 1 wk	Men: 4.5%, women: 5.6% Men: 6.0%, women: 7.8%		Not available
Weststrate JA, 1993 (15)	21-45 49 males, 54 females	Nonobese and obese	Nonconcurrent database	Ø	No	Steady state, training, activity	Ventilated hood	Varies 2-12, varies ≥2 d	Men: 5.5%, women: 6.1%	0.1-16.5 0.5-13.2	Not available

[a]Range established from mean±standard deviation or standard error of the mean.
[b]NHLBI BMI=National Heart, Lung, and Blood Institute body mass index.
[c]Study design quality definitions: −=limited research rigor; Ø=not exceptionally strong and may risk bias; and +=strong study for the questions asked.
[d]Absolute measurement differences calculated using absolute value of the difference between a mean repeated RMR measure from baseline RMR divided by baseline RMR×100; kcal/d provided, if available.
[e]Intraindividual variation based on oxygen consumption intake only.

studies in which the devices were carefully monitored to ensure that no air leaks were occurring, RMR measures are comparable among these devices (38,54-56). In one study (57), however, mean RMR was 7% higher for facemask and 9% higher for mouthpiece than for canopy measurements. Recent design improvements in facemasks and mouthpieces have not been tested, so further studies are needed to determine whether these devices give RMR values equivalent to those measured with rigid canopy systems.

Question 8

What is the acceptable variation in $\dot{V}O_2$ and $\dot{V}CO_2$ to reflect steady-state measurement conditions for accurate RMR, and how many measurements are needed over what time interval? Discard the initial 5 minutes then achieve 5-minute period with ≤10% coefficient of variation (CV) for $\dot{V}O_2$ and $\dot{V}CO_2$ (Grade II). If steady state is achieved, one measure is adequate; if not, two to three nonconsecutive measures improve accuracy (Grade II).

To obtain accurate RMR measurement, attention must be given to ensure steady-state conditions, defined by the degree of variation in $\dot{V}O_2$ and $\dot{V}CO_2$ over a set time period. Steady-state conditions minimize the chance that a short-term respiratory artifact will affect the measurement (Table 3) (34,38,54,58-68).

In healthy individuals, reliable RMR measurements can be obtained with the use of a 10-minute protocol in which the first 5 minutes of data are discarded and the remaining 5 minutes of data have a CV of no more than 10% (54,59). In critically ill patients using ventilators, 5-minute measures with <5% CV are equivalent to 30-minute measures with <10% CV (62-65). Sedation has a significant positive influence on successfully achieving the steady-state criteria. RMR in such patients is within 5% of total energy expenditure over 24 hours (69). For spontaneously breathing, critically ill patients, the 10-minute steady-state protocol (deleting the first 5 minutes) produces reliable RMR with minimal patient burden.

For healthy individuals, residents of transitional care units, and critically ill patients, a single measurement (in steady state) is sufficient to describe RMR. For critically ill patients using ventilators, if steady state is not achieved with the first measure, a second measurement should be obtained and the results averaged to reflect RMR.

Question 9

What differences in RMR are seen when measuring the same individual at various times of the day or on different days? Repeated measures vary 3% to 5% over 24 hours (Grade II) and up to 10% over weeks to months (Grade II).

In healthy fasted adults and in patients receiving continuous nutrition support, repeated measures of RMR during 24 hours and up to 5 months vary (Table 4) (3,14-15,46,67,69-76). Using repeated morning fasted measures over 4 hours in 24 healthy adults (aged 19 to 51 years), individual within-subject variation was 1.8% to 17.8% (mean 6.1%±0.6%) (70). Group mean RMR variability with repeated morning measures in 34 young (aged 18 to 32 years) nonobese adults was within 2% to 3% (3,15,71).

A group of 14 healthy adults were fed continuously using an enteral feeding that provided energy at maintenance and repletion levels. Individual within-subject variation for five to eight measures at each level was 3% to 12.8% and 2% to 13.6%, respectively (70). In sedated, continuously fed intensive care unit patients, total energy expenditure measured continuously during nighttime hours was not different than that measured during the day (69). A second study examining 50 mechanically ventilated, continuously fed, surgical intensive care unit patients confirmed a <3% group mean RMR variation during eight 3-hour intervals (67).

When the measurement interval is >24 hours, the intraindividual variation is within 10% (14,15,20,46,72-76). In 19 young adults (aged 16 to 33 years) measured biweekly three times, intraindividual variation in RMR was 0.4% to 7.2% (72), and was 0.7% to 8% with measures every 3 months in 18 young men (aged 18 to 28 years) (75). In 19 young women (aged 19 to 35 years) measured at 12 points during their menstrual cycle, intraindividual variation in RMR ranged from 1.7% to 10.4% (76). One study of 27 older adults (aged 62 to 83 years) reported a range in intraindividual RMR variation of 0.1% to 9.9% for men and 0% to 16.8% for women with measures taken at monthly intervals (74). With a single exception (15), all studies controlled for mediating variables potentially affecting RMR (ie, physical activity, TEF, and lean muscle mass changes) and documented mean intraindividual variation ranges between 3.3% and 7.8% with measures taken 2 days, 1 to 2 weeks, or 5 months apart in 220 adults (aged 16 to 79 years and having a body mass index of 19 to 42) (14,46,72-74). When repeated within 2 weeks, the difference in RMR was 79.2 kcal/day (95% confidence interval 55.9-102.6) (20).

Question 10

How should RQ be applied to the interpretation of RMR measurement? RQ measures <0.70 or >1 suggest protocol violations or inaccurate gas measurement (Grade II).

RQ is the ratio of $\dot{V}CO_2$ to $\dot{V}O_2$. Under typical metabolic conditions with stable respiratory function, the range of RQ in human metabolism is approximately 0.7 to 1 (40,52,76-82). Under atypical metabolic and respiratory conditions, RQ can be <0.7 or >1 and so RQ might aid in the assessment of the validity of some indirect calorimetry measurements of RMR.

Metabolic. Prolonged fasting (Table 5) (60,83-87), recent or excessive food consumption, and ethanol consumption before RMR measurement may affect RQ. Individual RQ values ranged from 0.72 to 0.80 after 16 hours of fasting but sometimes dropped below 0.70 in fasts lasting 22 hours (range 0.65 to 0.79) (84). Other studies reported that group mean RQ remained >0.70 in fasts lasting 36 to 84 hours (0.71±0.04) (60,83,85), but based on group standard deviation, some individuals must have had RQ <0.70 (possibly as low as 0.61). Similarly, in trauma patients fasting for 48 to 60 hours, group mean RQ remained >0.70 but based on variation about the mean, some of the individual RQ values must have dropped below 0.70 (87).

Food consumption increases RQ depending on the amount and composition of the meal. A mean RQ of

Table 5. The effects of extended fasting on respiratory quotient (RQ) in healthy and ill (acute, critically ill, and trauma) adults

Primary author, y	Subject age range (y), number, and sex[a]	Weight class, NHLBI BMI[b] category or % body fat or % ideal body weight	Study class	Study quality[c]	Calorimetry method criteria met	Missing techniques	Gas collection device	Fasting length (h)	RQ group mean[d]
Healthy adults									
Johnstone AM, 2002 (83)	18-37 12 males, 12 females	Lean BMI=20-25	Repeat measures crossover	Ø	No	Calibration, rest	Ventilated hood	36	36-h 0.73±0.05
Leff ML, 1987 (60)	22-47 2 males, 12 females	BMI=17-28	Prospective cohort	Ø	No	Activity	Face-mask	Overnight plus 7 h	Overnight plus 7-h fast: Day 1: 0.75±.02 SEM *(Recalculate to SD: 0.07)* Day 2: 0.74±0.01 SEM *(Recalculate to SD: 0.04)*
Romyn JA, 1990 (84)	22-44 12 males	Lean within 10% ideal body weight; BMI=21-25	Repeat measures crossover	+	Yes		Ventilated hood	16, 22	16 h 0.77±0.01 SEM *(Recalculated to SD: 0.04)* 22 h 0.72±0.01 SEM *(Recalculated to SD: 0.04)*
Zauner C, 2000 (85)	24-32 4 males, 7 females	Lean BMI=19-26	Repeat measures crossover (time series)	Ø	No	Steady state	Ventilated hood	36, 60, 84	36-h fast: 0.74±0.04 60 h fast: 0.72±0.03 84-hour fast: 0.71±0.04
Ill adults									
Brandi LS, Oleggini M, 1997 (86)	33-80 12 males, 10 females Control 12 males, 10 females	Underweight-obese BMI=16-32 surgical patients with age, sex, and weight-matched controls	Case-control	Ø	No	Calibration, measurement length	Douglas bag	12-72	0.78±0.01 SEM *(Recalculated SD 0.04)*
Jeevanandam M, 1992 (87)	18-50	Overweight BMI=28-29 trauma patients	Nonrandomized controlled trial	+	Yes		Ventilated hood	48-60 after injury	0.73±0.09 SEM *(Recalculated SD 0.13)*

[a]Range established from mean±standard deviation (SD) or standard error of the mean (SEM) and was recalculated into standard deviations using square root n×SEM.
[b]NHLBI BMI=National Heart, Lung, and Blood Institute body mass index.
[c]Study design quality definitions: −=limited research rigor; Ø=not exceptionally strong and may risk bias; and +=strong study for the questions asked.
[d]Data expressed as mean±SD unless otherwise indicated. Some studies reported only group statistics rather than range. Thus, it was assumed that if 2 SD above or below the mean equated to an RQ <0.7 or >1, some of the individuals in the study sample had RQ values outside the 0.7 to 1 range. This assumption is based, in turn, on an assumption that the data were normally distributed.

0.86±0.11 was recorded 60 minutes after a mixed meal providing 25% of energy needs (88). In postoperative and critically ill adults (89-91), consuming adequate energy resulted in RQ values in the middle of the physiologic range.

Excess energy intake, on the other hand, more often raises the RQ above 1. When measured 10 minutes after consuming about 1,200 kcal as a high-carbohydrate or a high-fat meal, mean RQ in healthy subjects was 1±0.04 and 0.98±0.04, respectively (92). At 2.5 hours, the group mean RQ for the high-carbohydrate meal remained at 0.99±0.08 but for the high-fat meal had dropped to 0.90±0.08. In 25 nutrition support patients with glucose infusion rates in excess of 7 mg/kg/min, 19 (76%) of the RQ values were greater than 1 (93). Similarly, a group mean RQ of 1.16±0.32 was reported in 19 hemodynamically stable individuals using mechanical ventilators receiving energy at 110% above measured RMR supplied in various specialized nutrition support (91). The standard deviations of these mean values indicate that a large proportion, although not all, of the subjects exceeded RQ of 1. In another study (94) of patients with and without sepsis receiving 125% of measured RMR supplied with total parenteral nutrition, mean RQ was 0.86±0.05.

The RQ of ethanol oxidation is 0.67 (78,80,95) and so may be expected to lower RQ during a test of RMR. However, as the RQ measured in human beings is a net value of all metabolism, ethanol consumption does not decrease the RQ below 0.7 (22).

Respiratory. Respiratory changes can cause artifact change in RQ. In a case presentation (96), an air leak led to RQ values ranging from 0.32 to 1.02 in the same subject. When ventilator settings were abruptly changed in stabilized patients, RQ was >1 with hyperventilation (carbon dioxide removal) and <0.73 with hypoventilation (carbon dioxide retention) (97).

DISCUSSION

An evidence-based protocol for measurement of resting metabolic rate by indirect calorimetry is summarized in Figure 4, with separate guidelines for clinical measurements of healthy adults and for critically ill patients. Patients who are not critically ill but are cooperative and breathing room air would likely be measurable with the same guidelines developed for healthy adults.

Available data are somewhat limited regarding the minimum length of fasting and abstinence from caffeine, ethanol, nicotine, and exercise before attempting a measurement of RMR. Likewise, proper body posture and ambient conditions to ensure resting state have not been completely studied. It seems prudent and no great imposition on the client to conduct RMR measurements in a quiet, private space with temperature and humidity controlled at levels typical of most modern buildings. Light blankets should be available for clients who request them.

For measurements of RMR that require the strictest adherence to true resting state (eg, RMR research) subjects should have fasted for at least 6 hours, should have abstained from caffeine overnight, from nicotine and alcohol for at least 2 hours, from moderate physical activity for at least 2 hours, and from vigorous physical activity for possibly 14 hours. Measurement should be made with subjects in the supine or slightly elevated body posture. For research on TEF, studies should be conducted for a 6-hour period, because shorter measures do not capture the entire TEF.

In clinical situations in which time, space, and facilities may be limited, abstinence times and body postures may need to be liberalized. In situations where long fasts are not advisable, a shorter fast of 4 hours can be used, but the final meal should be small (<400 kcal). Measurement of RMR during continuous intravenous or enteral feedings that have continued for ≥24 hours will not be appreciably influenced by TEF. Abstinence from caffeine for 4 hours, from nicotine and ethanol for 2 hours, and from moderate physical activity for 2 hours may provide acceptable accuracy in RMR measures. Clients can be positioned in the sitting posture (semirecumbent might be better, but there are no data to guide this decision). RMR measures from this more relaxed protocol should not be used for research on RMR because they may be 100 kcal different from actual RMR. It is not known if the effect of the presence of more than one of these factors is additive, so even larger errors might occur. More research is needed to determine how significant the differences are in measured metabolic rate between these two levels of restriction.

The available data to determine the optimal period of rest before RMR measurement are surprisingly sparse. Methodologic reviews have suggested a 30-minute rest before measurement, but this is not supported by experimental data. In fact, the available data suggest that rest periods need only be 7 to 20 minutes long, provided the first 5 minutes of the measurement are discarded. Sleeping onsite before the test is not necessary. In critical care unit situations little data exist to guide the decision on how long to wait after activities requiring patient repositioning. Thirty minutes may be appropriate, but level of sedation, the exact nature of the activity, and the presence or absence of agitation can lengthen or shorten this time.

Likewise, prolonged periods (24 to 48 hours) of abstention from physical activity or exercise before RMR measurement are not necessary for most individuals. A 2-hour rest period following moderate, short-duration aerobic activity is sufficient to allow energy expenditure to return to resting levels. Vigorous resistance training has a more prolonged effect on metabolic rate and should be avoided for 14 hours before RMR is measured. Appropriate rest required after intense physical activity in competitive athletes was not evaluated with this effort.

There seems to be little difference in RMR measurement results based on the type of gas collection device used, provided the devices are used carefully. With all devices, it is important to observe for air leaks because leaks will result in artificially low RMR values. With the facemask, it is important to ensure that the mask fits tightly on the subject's face, and a sealant may be needed to avoid air leaks. With the mouthpiece and nose clip, the best size mouthpiece should be selected for each subject and the operator should ensure that a subject cannot breathe in or out through the nose after the clip is in position, and that there is a good lip seal around the mouthpiece. For the canopy, air leaks can occur if the

Criteria	Healthy adults	Critically ill, ventilated patients
Fasting (thermic effect of food)	Minimum fast 5 hours after meals or snacks (Grade II),[a] 4 hours after small meal if longer fast is clinically inappropriate (Grade II)	Minimum fast 5 hours after meals or bolus enteral feeding (Grade II) Allow continuous intravenous (eg, 5% dextrose), enteral, or parenteral feedings to remain constant during 24 hours before and during measure (Grade III)
Alcohol ingestion	Minimum abstention from alcohol for 2 hours (Grade III)	Not applicable
Nicotine ingestion	Minimum abstention from nicotine for 2 hours (Grade II)	Wait 2½ hours after nicotine patch is removed (Grade V)
Caffeine ingestion	Minimum abstention from caffeine for 4 hours (Grade II)	Caffeine should not be an issue
Rest periods	Rest 10-20 minutes (Grade III)	May need 30 minutes rest after procedures to achieve steady-state conditions during measure, though sedation may shorten needed rest time (Grade V)
Physical activity restriction	Minimum abstention from moderate aerobic or anaerobic exercise for 2 hours before test (Grade II), for vigorous resistance exercise abstention of at least 14 hours (Grade III)	Limited application due to illness; special restrictions do not apply (no evidence analysis question completed)
Environmental conditions	Allow a room temperature of 20°C-25°C (68°F-77°F) (Grade III) Ensure each individual is physically comfortable with measurement position during the test and repeated measures are in the same reclined position (Grade V)	Allow a room temperature of 20°C-25°C (68°F-77°F) (Grade III) Ensure each individual is physically comfortable with the measurement position during the test and that repeated measures are in the same position (Grade V)
Gas collection devices	Use rigorous adherence to prevent air leaks (Grade III) Further studies comparing modern gas collection devices are needed in healthy and clinical populations (Grade V)	Use rigorous adherence to prevent air leaks (Grade III) Further studies comparing modern gas collection devices are needed in clinical populations (Grade V)
Steady-state conditions and measurement interval	Discard initial 5 minutes. Then achieve a 5-minute period with ≤10% CV[b] for Vo_2[c] and Vco_2[d] (Grade II)	Discard initial 5 minutes of measurement. Then achieve a 5-min period with CV ≤5% for Vo_2 and Vco_2. Alternate protocol can be 25 minutes with ≤10% CV (Grade I)
No. of measures/24 hours	Achieve steady state and one measure is adequate; if not, two to three nonconsecutive measures improve accuracy (Grade II)	Achieve steady state and one measure is adequate; if not, two to three nonconsecutive measures improve accuracy (Grade II)
Repeated measures (daily to monthly variation)	Repeated measures vary 3%-5% over 24 hours (Grade II) and vary up to 10% over weeks to months (Grade II)	No evidence analysis question completed
Respiratory quotient (RQ)	RQ measures <0.70 or >1 suggest protocol violations or inaccurate gas measurement (Grade II)	RQ measures <0.70 or >1 suggest hyperventilation or inaccurate gas measurement (Grade II)

[a]Grade I=strong, consistent evidence; Grade II=somewhat weaker evidence and disagreement among authors may exist; Grade III=limited design quality; Grade IV=professional opinion only, no clinical trials; Grade V=no available studies; see Figure 2 for definitions of grades for conclusion statements.
[b]CV=coefficient of variation (standard deviation×[mean of individual replicate measures]×100).
[c]Vo_2=oxygen consumption.
[d]Vco_2=carbon dioxide production.

Figure 4. Evidence-based guidelines for measurement of resting metabolic rate with indirect calorimetry.

plastic sheet is not completely tucked in, or if the plastic sheet around the canopy is not tight fitting. For any patient who expresses a feeling of claustrophobia with the facemask or canopy in place, the mouthpiece and nose clip would be a better choice. For those who are uncomfortable with the nose clip, either the facemask or canopy could be offered.

The time needed to obtain an accurate measurement of RMR is only 5 to 10 minutes, after discarding the first 5 minutes of data, provided steady-state conditions can be obtained. Steady-state conditions have been established as a 10% CV in V_{O_2} and V_{CO_2} for healthy adults, or 5% CV in V_{O_2} and V_{CO_2} for critically ill patients (or a longer, 30-minute measure with 10% CV). When steady-state conditions are obtained, a single measurement of RMR is adequate to describe the resting caloric expenditure over 24 hours. If steady state is not obtained, two to three repeated measures would increase the accuracy of the 24-hour extrapolation. Clearly, long measurements of RMR are not needed for measurement accuracy and could place an undue time burden on subjects and operators.

Repeated measurements taken within 1 week's time in healthy, including older, adults vary only 4% to 6% or <100 kcal/day. Repeated measures up to 1 month show similar mean variation, although individual measures may vary by 1% to 10% over 1 month. Repeated RMR measures are only necessary when a significant change in clinical status has occurred (eg, unexplained change in body weight) or when clinical goals have not been achieved after appropriate nutrition interventions.

RQ can serve as a tool to detect some inaccurate measurements or RMR protocol violations. If RQ is <0.7 or >1, prolonged starvation or excessive recent energy consumption should be suspected. Both of these events represent RMR protocol violations. If metabolic reasons for an aberrant RQ do not exist, then air leaks, hypoventilation, hyperventilation, or inaccurate gas sensors should be suspected. If recalibration of the calorimeter does not result in an RMR test result with an RQ between 0.7 and 1 and similar results are obtained in a different test subject, the gas sensors should be tested with an alcohol burn test or the machine sent to the manufacturer for repair. Within the range of 0.7 to 1, typical variation in RQ is high enough that RQ cannot be used to detect protocol violations or inaccurate measurements.

Limitations

Large gaps exist in our knowledge of the times over which the ingestion of substances and the performance of rigorous physical activity will increase the apparent RMR. Therefore, whereas restricting intake and activity for long periods will likely eliminate any effect on RMR, minimum restriction times cannot be firmly established without more data. Body posture and rest period length before measurement also need more study.

Measurement methodology is assumed to apply to human subjects in general, but there is limited representation of ethnic minorities and elderly subjects in the experiments considered here. The slight differences in methodology applied to critically ill, compared with healthy adults, suggest that modifications in methodology may be needed in a few extreme clinical states, where respiratory function is impaired. Because only studies from adults were appraised, these findings may not apply to measurement of RMR in children, where particular consideration of rest and fasting times and even steady-state conditions may be different from adult subjects.

This project was funded by an educational grant to the ADA Foundation by Healthetech Corporation, Golden, CO.

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