Accepted June 2013

REVIEW

Energy expenditure in different patient populations on intensive care: One size does *not* fit all

C. M. Mooij, C.J. Beurskens, N.P. Juffermans

Laboratory of Experimental Intensive Care and Anaesthesiology and the Department of Intensive Care, Academic Medical Center, University of Amsterdam, the Netherlands

Correspondence

C. Beurskens – e-mail: c.j.beurskens@amc.uva.nl

Keywords - **Energy expenditure, oxygen consumption, calorimetry, Intensive Care Unit**

Abstract

Objective: Adequate nutrition has an impact on outcome in critically ill patients. This descriptive literature search investigates whether there are differences in energy expenditure (EE) between specific subgroups of critically ill patients, including patients with sepsis, trauma, burns and cerebrovascular accidents. Also, we summarised specific factors which may influence EE, such as the use of sedation, body temperature and severity of illness.

Design: A descriptive review of studies which have measured EE or oxygen consumption with indirect calorimetry in critically ill patients. Studies were retrieved by a systematic search of the Medline database, using search terms referring to the measurement (energy expenditure), the patient population in general (critically ill patients), and to the four specific subgroups (sepsis, trauma, burns, stroke).

Results: EE in patients with sepsis, trauma and burns was increased (sepsis 102-198%; trauma 110-168%; burns 137-182%; stroke 149% for men and 120% for women) compared with reference values of EE in healthy individuals. Burn patients had the highest EE levels. There was no difference in EE between sepsis and trauma patients. Patients with a cerebrovascular accident had the lowest EE. Half of these patients had an EE that did not exceed EE levels in healthy adults. Use of sedation lowered EE whereas fever increased EE. Uncertainty persists whether treatment of stroke patients with hypothermia decreases EE. According to most studies, higher disease severity scores are associated with higher EE, but one study found that severity of illness is negatively correlated with EE in sepsis.

Conclusions: Data for this review were limited, precluding definite conclusions. However, it is clear EE differs among critically ill patient populations. The use of a 'one size fits all' formula to estimate caloric need in the critically ill may not be appropriate in the design of studies on caloric need nor in patient care.

Introduction

In critically ill patients, meeting caloric demand by adequate nutrition is related to better outcome.[1] Therefore, adequately responding to the nutritional demands of patients admitted to the intensive care unit (ICU) should be a daily goal in patient care. However, the optimal amount of calories that should be prescribed to critically ill patients has been a matter of debate.[1]

It is thought that the consumption of calories, termed energy expenditure (EE), is increased in critically ill patients compared with the general hospital population, due to high metabolic demands during various inflammatory conditions.[2] A disbalance between high demands and limited energy supply may contribute to organ failure and adverse outcome in ICU patients.[3,4] In this view, underfeeding could be detrimental. An alternative hypothesis relating to the optimal amount of calories holds that this hypermetabolic state might be harmful and that hypocaloric nutrition reduces hypermetabolism,[5] thereby improving outcome.[6] In both strategies, measuring or estimating energy demands of patients are crucial in determining the optimal amount of feeding.

The EE can be measured in several ways, including indirect calorimetry. Alternatively, the Harris-Benedict equation is used, which calculates the amount of calories needed in ICU patients and estimates an individual's basal metabolic rate, multiplied by an activity factor.[7] A shortcoming of this formula is the controversy about what exactly this activity factor should be.[8-10] Also, the formula does not distinguish between specific ICU patient populations. Comparing caloric targets based on the calculated caloric need with use of this formula[6,11] may therefore lead to inadequate conclusions in ICU patients.

Given the relation between caloric supply and outcome, it seems paramount to be aware of possible EE differences between different subgroups. This paper summarises data from all available studies which have directly measured EE in four specific subgroups of ICU patients: sepsis, trauma, burns and cerebrovascular accident (CVA).

Methods

The Medline database was used to identify medical subject's headings (MeSH) and select search terms. In addition to MeSH terms, free text words were used. Search terms referred to the measurement: energy expenditure *(calorimetry, indirect [MeSH]; energy metabolism [MeSH]; energy metabolism; energy expenditure; indirect calorimetry*), to the patient population in general: critically ill patients *(critical illness [MeSH]; intensive care unit [MeSH]; critical care [MeSH]; intensive care [MeSH]; critical care; intensive care unit; critical illness; ICU patients*) and to the four specific subgroups: *(septic shock [MeSH]; bacteremia [MeSH]; sepsis [MeSH]; sepsis; pyemia; septicemia; blood poisoning; severe sepsis; bacteremia; septic shock*); *(wounds and injuries [MeSH]; trauma; wounds and injuries; severe trauma*); *(burn, chemical [MeSH]; burn [MeSH]; burn; chemical burns; electric burns; burn wounds*); *(brain ischemia [MeSH]; cerebral infarction[MeSH]; subarachnoid hemorrhage [MeSH]; intracranial hemorrhage [MeSH]; stroke [MeSH]; stroke; cerebrovascular apoplexy; CVA; cerebrovascular accident; brain infarction; cerebral ischemia; intracranial hemorrhage; subarachnoid hemorrhage; SAH).* Search results were limited to adults. Studies were selected when data on EE (kcal/day) or oxygen consumption (VO_2) (ml/(min.m^2)) were provided. If not otherwise mentioned, measured EE refers to resting EE. When EE or VO_2 of individual patients were given, mean and SD were calculated. Kilojoules were converted by using the equation 1 kcal = 4184 kJ. When only EE/ kg body weight was given, EE was calculated by multiplying by the mean body weight of the patient group. In that case, no SD could be calculated.

To facilitate comparisons of metabolism between groups, all measurements of EE in the subgroups of critically ill patients were compared with a reference value of EE or VO^2 as measured in healthy adult men and women[12] and expressed as a percentage of that reference value. If the male/female (M/F) proportion of a study group was given, EE was corrected for the M/F ratio, by multiplying the number of male patients with the reference value of a healthy male and the number of female patients with the reference value of a healthy female, divided by the total number of patients. If no M/F ratio was given, an M/F ratio of 3/1 was used, because this ratio corresponded best with the M/F ratios in the studies of EE in sepsis, trauma and burns groups where this ratio was given. The normal VO^2 range is 110-160 ml/(min.m^2). The effect of several clinical conditions was investigated, including body temperature, use of sedation and disease severity. Severity of illness was estimated using either the Acute Physiology and Chronic Health Evaluation (APACHE) II or III score,[24,25] Injury Severity Score (ISS)[26,27] or the percentage of body surface area (%BSA) that was burned for burn patients only.

Results

The Medline search yielded 361 studies. Of these, 338 were not suitable because data on measured EE or VO_2 were not given for the specific patient subgroups under study, leaving 23 studies with data on EE or VO_2 in patients with sepsis (n=10), sepsis and trauma (n=3), trauma (n=3), trauma and burns (n=1), burns (n=3) and CVA (n=3). In total, EE measurements in 448 patients were included.

Comparison of EE and/or VO_2 between different patient groups

In patients suffering from sepsis (*table 1*), all studies except one[13] found an increase in measured EE with values ranging from 102-198% compared with the reference value. Three out of the six VO_2 measurements were high, but within the normal range. The other VO_2 measurements slightly exceeded the normal range.

In the trauma group (*table 2*), all studies reported high EE measurements, ranging from 110-68% compared with the reference value. Of the VO_2 measurements, one study reported values within the normal range (153.6 ml/(min.m^2)),[14] other studies reported VO^2 values higher than 160 ml/(min.m^2).

In the patient population suffering from burns (*table 3*), EE measurements ranged from 137-182% of the reference values. Two studies reporting VO_2 measurements exceeded the normal range, with values of 131 and 209% compared with the upper limit of the normal range of oxygen consumption of 160 ml/(min.m^2).[15,16]

In stroke patients (*table 4*), increased levels of EE of 149% of the reference value for men and 120% for women were found in one study.[17] However, the two other studies[18,19] found no increased EE levels compared with the reference value. In this patient group, no VO_2 measurements were available.

Clinical conditions influencing EE

The use of sedative medication generally lowers EE.[20,21] However, one study showed a positive correlation between sedative dose and EE.[22] Different types of sedative medication did not result in differences in EE levels when measurements were corrected for body temperature.[21]

An increase in EE caused by fever was found in sedated head-injured patients[21] and in septic patients.[23] Conversely, induced hypothermia to 33 °C resulted in a significantly lower EE in stroke patients.[18] However, not all studies report such a decrease, as Badjatia *et al.* found no significant differences in EE between the hypothermic (33.5-35.5 °C) and the normothermic (36.5-37.0 °C) stroke patients.[17] In this study, shivering as a result of treatment with hypothermia was clearly shown to increase EE.[17]

The severity of illness may influence EE. EE was related to either the APACHE II or III for sepsis,[24,25] ISS for trauma[26,27] or %BSA for burn patients (*table 5*). Not all studies mentioned severity scores. In general, however, patients with higher severity scores were more hypermetabolic, which was most distinct in patients with burns.[8,16] An association between severity of illness and EE was also noted in septic trauma patients.[22] One study, however, reported a negative correlation between APACHE III scores and resting EE in sepsis.[23]

Discussion

EE measurements were highest in burn patients, with all studies reporting substantially higher values than reference

Table 1. Caloric demand in critically ill patients with sepsis

References	Number of patients	Male/F	EE (kcal/ day)	% of reference EE	VO_2 (ml/(min.m^2))
Frankenfield et al.[22]	20	17/3	3395 ± 634	198%	-
Koea et al.[29]	4	3/1	2196 ± 440	132%	-
Rusavy et al.[30]	20	Unknown	2116 (No SD)	127%	-
Liggett et al.[9]*	18	Unknown	1982 ± 97	119%	-
Clark et al.[31]	11	Unknown	1950 ± 175	117%	-
Kiiski et al.[32]	21	16/5	1960 ± 486	117%	-
Uehara et al.[33]	12	8/4	1859 ± 485	114%	-
Basile-Filho et al.[13]	15	11/4	1699 ± 271	102%	-
Schaffartzik et al.[34]	30	Unknown	-	-	173 ± 30
Fernandes et al.[35]	10	10/0	-	-	168.9 ± 63.1
	5	5/0	-	-	144.0 ± 30.5
Hanique et al.[36]	14	9/5	-	-	163 ± 19
Natalini et al.[37]	10	Unknown	-	-	157 ± 35
Zauner et al.[23]	14	8/6	-	-	135 ±26
Total	**204**			**102-198 %**	

Data are mean ± SD; M/F = proportion male/ female; *In Liggett et al., EE was measured using a pulmonary artery catheter.

Table 2. Caloric demand in critically ill patients with trauma

References	Number of patients	M/F	EE (kcal/ day)	% of reference EE	VO_2 (ml/(min.m^2))
Frankenfield et al.[22]	13	10/3	2754 ± 401	168%	-
Bruder et al.[21]	24	19/5	2496 ± 574	148%	203 ± 55
Stucky et al.[38]	21	Unknown	2263 ± 599	136%	-
Kiiski et al.[32]	25	17/8	2071 ± 430	126%	-
Uehara et al.[33]	12	9/3	1953 ± 416	117%	-
Raurich et al.[10]*	Total: 26				
	20	15/5	1900 ± 394	114%	-
	20	15/5	1840 ± 311	110%	-
Huschak et al.[14]	15	14/1	-	-	165.9 ± 21.2
	18	13/5	-	-	153.6 ± 30.4
Total	**154**			**110-168 %**	

Data are mean ± SD; M/F = proportion male/ female; *In Raurich et al., 40 EE measurements are reported for 26 patients in total. One group of measurements was compared with 20 surgical patients, the other to 20 medical patients.

Table 3. Caloric demand in critically ill patients with burns

References	Number of patients	M/F	EE (kcal/ day)	% of reference EE	VO_2 (ml/(min.m^2))
Gore et al.[15]	6	Unknown	3030	182%	209 ± 27
Khorram-Sefat et al.[8]	27	27/0	2878 ± 407	172%	-
Royall et al.[16]	22	17/3	2319 ± 553	139%	335 ± 80
Stucky et al.[38]	12	Unknown	2284 ± 508	137%	-
Total	**67**			**137-182 %**	

Data are mean ± SD; M/F = proportion male/ female.

Table 4. Caloric demand in critically ill patients with cerebrovascular accident

References	Number of patients	M/F	EE (kcal/ day)	% of reference EE
Badjatia et al.[17]	50	16/34	-	-
		Male	2647 ± 1013	149%
		Female	1622 ± 596	120%
Bardutzky et al.[18]*	10	4/6	1549	102%
Bardutzky et al.[19]*	34	20/14	1568	98%
Total	**94**			**98 – 149 %**

Data are mean ± SD; M/F = proportion male/ female; *In Bardutzky et al., total EE is given instead of resting EE.

Table 5. Energy expenditure and the illness severity scores in different patient populations

References	% of reference EE	
Sepsis patients		**APACHE II score**
Clark et al.[31]	117	24 23
Uehara et al.[33]	114	16 – 34
Basile-Filho et al.[13]	102	22.6 ± 7.2
Trauma patients		**Injury severity score**
Frankenfield et al.[22]	168	33 ± 9
Bruder et al.[21]	148	27 ± 9
Stucky et al.[38]	136	22.18 ± 16.42
Kiiski et al.[32]	126	22 ± 20
Uehara et al.[33]	117	26 – 50
Burn patients		**Injury severity score**
Stucky et al.[38]	137	29.83 ± 10.55
Burn patients		**% of BSA burned**
Gore et al.[15]	182	72 ± 9.8
Khorram-Sefat et al.[8]	172	51 ± 20
Royall et al.[16]	139	36.7 ± 18.8
Stucky et al.[38]	137	40.85 ± 36.35

Data are given in mean ± SD.

EE values. Also, EE values of burn patients were higher than EE values in most studies describing sepsis or trauma patients. A probable explanation is that burned patients are highly hypermetabolic and catabolic.[28] In both the sepsis and trauma patient populations we found increased EE values compared with the EE levels in healthy adults. Patients suffering from sepsis do not have consistently higher EE values than trauma patients. As expected, EE measurements in the CVA group were lowest, with two out of three studies (50% of the patient population) not reporting increased EE compared with healthy adults.[18,19] This may be due to the fact that in these patients an inflammatory state is not as apparent as in sepsis, trauma or burn patients. Taken together, there are profound differences in EE between specific patient populations, with burn patients having the highest EE values. A large variation was also observed within subgroups of patients, as well as a large variety between different studies.

The use of sedation was generally found to decrease EE in critically ill patients, without apparent differences between types of sedative medication.[20,21] As expected, fever increases the levels of EE.[21,23] The use of induced hypothermia seems to decrease EE.[18] One study found no significant difference in EE between normothermia and hypothermia, which was attributed by the authors to the heterogeneity of the patient population.[17]

The positive correlation between body temperature and EE can be explained by thermogenesis. Of note, we found that EE was positively correlated to the severity of illness in the majority of the reviewed studies, suggesting that within a specific clinical condition, also disease severity should be taken into account when estimating the caloric need. However, it should be considered that variation was large.[8,16,22]

Given the differences in EE between patient populations as well as the variance within patient groups, we feel it would be best to measure the EE in each individual patient when assessing the amount of nutrition. When predictive equations are used instead of indirect calorimetry, factors can be added correcting for the patient's type of lesion and for clinical conditions such as the use of sedation, severity of illness and body temperature. However, various recommendations on estimating EE in patients have been made. According to some, predicting the individual EE by using an equation is not possible, because of the variation in EE in critically ill patients and the quantity of factors influencing EE.[10] Therefore, it was proposed to use the same predictive equations for all patients without adding factors. On the other hand, others hold that factors attributing to differences in energy expenditure between critically ill patients should be better understood to allow more accurate estimation of the caloric needs of individual patients.[21] In burned patients, it was recommended to use equations that do not give higher predictions of EE than 1.5-1.6 times basal EE to avoid overfeeding.[8] Taken together, there is no consensus on what the correcting factors should be. The summary of our findings points towards a patient-tailored approach, taking into account the clinical condition as well as disease severity.

Besides patient care, our findings may also have implications for future research. In studies comparing the impact of hyper- versus hypo-caloric nutrition on outcome, it should be considered that EE differs between patient populations. The use of predictive equations in such studies is inappropriate in predicting the actual EE and thus the caloric demand of individual patients. However, some of these studies claim a relation between predictive equations and outcome.[6,11] When the 'less than goal' and 'near goal' amount of calories is based on those predictions and is related to outcome, results may be confounded. Therefore, indirect calorimetry seems the best way to estimate the nutrition status of a patient and provide tailored care to possibly improve outcome.

There are several limitations to this review. The amount of data on measured EE or VO_2 is limited. Thereby, patient numbers are small. The most important limitation is that statistical analysis of the data was limited as individual patient data were not available, rendering this study a descriptive review. Also, the ratio between male and female was not always given. Most collected measurements were performed during the first week. Thereby, variations in EE during the course of illness were not detected.[23] As individual energy expenditure can fluctuate significantly from day to day,[22] this may influence the reliability of the comparison of EE measurements in the current study. However, EE is largely stable in the course of the first week.[18,19,23]

As we did not perform consecutive measurements, conclusions of this study only pertain to the first week following admission. Another limitation is that several factors such as age, body weight, types of nutrition, presence of shock, administration of medications such as insulin or inotropics and the use of mechanical ventilation were not considered. Patients and circumstances were quite heterogeneous and EE measurements were not corrected for that. However, we corrected for sex, which importantly determines EE.[7] There is a great need for collecting more data to improve the limited knowledge, before adapting this in daily ICU care. Future research should ideally include the influence of mechanical ventilation and inotropic drugs on EE values.

Nonetheless, this study attempts to give an indication of differences in EE between four distinct groups of patients. Despite the limitations of this study, results may have implications for estimating energy expenditure in clinical practice and for research goals.

Conclusion

Energy expenditure differs between and within patient populations. The use of sedatives, body temperature and severity of illness have an impact on EE values. The use of the same formula to calculate caloric need for each patient may not be appropriate.

References

1. Stapleton, RD, Jones N, Heyland DK. Feeding critically ill patients: what is the optimal amount of energy? Crit Care Med. 2007;35(Suppl 9):S535-40.
2. Tappy, L, Chiolero R. Substrate utilization in sepsis and multiple organ failure. Crit Care Med. 2007;35(9 Suppl):S531-4.
3. Villet S, Chiolero RL, Bollmann MD, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. Clin Nutr. 2005;24:502-9.
4. Rubinson L, Diette GB, Song X, et al. Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. Crit Care Med. 2004;32:350-7.
5. Patino JF, de Pimiento SE, Vergara A, et al. Hypocaloric support in the critically ill. World J Surg. 1999;23:553-9.
6. Krishnan JA, Parce PB, Martinez A, et al. Caloric intake in medical ICU patients: consistency of care with guidelines and relationship to clinical outcomes. Chest. 2003;124:297-305.
7. Harris JA, Benedict FG. A biometric study of basal metabolism in man. Carnegie Institution of Washington publication, Washington, Carnegie Institution of Washington 1919;no. 279:266.
8. Khorram-Sefat R, Behrendt W, Heiden A, et al. Long-term measurements of energy expenditure in severe burn injury. World J Surg. 1999;23:115-22.
9. Liggett SB, Renfro AD. Energy expenditures of mechanically ventilated nonsurgical patients. Chest. 1990;98:682-6.
10. Raurich JM, Ibanez J, Marse P, et al. Resting energy expenditure during mechanical ventilation and its relationship with the type of lesion. JPEN J Parenter Enteral Nutr. 2007;31:58-62.
11. Arabi YM, Haddad SH, Tamim HM, et al. Near-target caloric intake in critically ill medical-surgical patients is associated with adverse outcomes. JPEN J Parenter Enteral Nutr. 2007. 34:280-8.
12. Mifflin MD, St Jeor ST, Hill LA, et al. A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr. 1990;51:241-7.
13. Basile-Filho A, Auxiliadora Martins M, Marson F, et al. An easy way to estimate energy expenditure from hemodynamic data in septic patients. Acta Cir Bras. 2008;23(Suppl 1):112-7.
14. Huschak G, Zur Nieden K, Hoell T, et al. Olive oil based nutrition in multiple trauma patients:a pilot study. Intensive Care Med. 2005;31:1202-8.
15. Gore DC, Ferrando A, Barnett J, et al. Influence of glucose kinetics on plasma lactate concentration and energy expenditure in severely burned patients. J Trauma. 2000;49:673-8.
16. Royall D, Fairholm L, Peters WJ, et al. Continuous measurement of energy expenditure in ventilated burn patients: an analysis. Crit Care Med. 1994;22:399-406.
17. Badjatia N, Strongilis E, Gordon E, et al. Metabolic impact of shivering during therapeutic temperature modulation: the Bedside Shivering Assessment Scale. Stroke. 2008;39:3242-7.
18. Bardutzky J, Georgiadis D, Kollmar R, et al. Energy expenditure in ischemic stroke patients treated with moderate hypothermia. Intensive Care Med. 2004;30:151-4.
19. Bardutzky J, Georgiadis D, Kollmar R, et al. Energy demand in patients with stroke who are sedated and receiving mechanical ventilation. J Neurosurg. 2004;100:266-71.
20. Terao Y, Miura K, Saito M, et al. Quantitative analysis of the relationship between sedation and resting energy expenditure in postoperative patients. Crit Care Med. 2003;31:830-3.

21. Bruder N, Raynal M, Pellissier D, et al. Influence of body temperature, with or without sedation, on energy expenditure in severe head-injured patients. Crit Care Med. 1998;26:568-72.

22. Frankenfield DC, Wiles CE, Bagley S, et al. Relationships between resting and total energy expenditure in injured and septic patients. Crit Care Med. 1994;22:1796-804.

23. Zauner C, Schuster BI, Schneeweiss B. Similar metabolic responses to standardized total parenteral nutrition of septic and nonseptic critically ill patients. Am J Clin Nutr. 2001;74:265-70.

24. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13:818-29.

25. Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest. 1991;100:1619-36.

26. Copes WS, Champion HR, Sacco WJ, et al. The Injury Severity Score revisited. J Trauma. 1988;28:69-77.

27. Baker SP, O'Neill B, Haddon W, et al. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma. 1974;14:187-96.

28. Cunningham JJ, Hegarty MT, Meara PA, et al. Measured and predicted calorie requirements of adults during recovery from severe burn trauma. Am J Clin Nutr. 1989;49:404-8.

29. Koea JB, Wolfe RR, Shaw JH. Total energy expenditure during total parenteral nutrition: ambulatory patients at home versus patients with sepsis in surgical intensive care. Surgery. 1995;118:54-62.

30. Rusavy Z, Sramek V, Lacigova S, et al. Influence of insulin on glucose metabolism and energy expenditure in septic patients. Crit Care. 2004;8:R213-20.

31. Clark MA, Plank LD, Connolly AB, et al. Effect of a chimeric antibody to tumor necrosis factor-alpha on cytokine and physiologic responses in patients with severe sepsis--a randomized, clinical trial. Crit Care Med. 1998;26:1650-9.

32. Kiiski R, Takala J. Hypermetabolism and efficiency of CO2 removal in acute respiratory failure. Chest. 1994;105:1198-203.

33. Uehara M, Plank LD, Hill GL. Components of energy expenditure in patients with severe sepsis and major trauma: a basis for clinical care. Crit Care Med. 1999;27:1295-302.

34. Schaffartzik W, Sanft C, Schaefer JH, et al. Different dosages of dobutamine in septic shock patients: determining oxygen consumption with a metabolic monitor integrated in a ventilator. Intensive Care Med. 2000;26:1740-6.

35. Fernandes CJ Jr, Akamine N, De Marco FV, et al. Red blood cell transfusion does not increase oxygen consumption in critically ill septic patients. Crit Care. 2001;5:362-7.

36. Hanique G, Dugernier T, Laterre PF, et al. Significance of pathologic oxygen supply dependency in critically ill patients: comparison between measured and calculated methods. Intensive Care Med. 1994;20:12-8.

37. Natalini G, Schivalocchi V, Rosano A, et al. Norepinephrine and metaraminol in septic shock: a comparison of the hemodynamic effects. Intensive Care Med. 2005;31:634-7.

38. Stucky CC, Moncure M, Hise M, et al. How accurate are resting energy expenditure prediction equations in obese trauma and burn patients? JPEN J Parenter Enteral Nutr. 2008;32:420-6.