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Anwar E Owais, Rachael Frances Bumby, John Macfie

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Review article: permissive underfeeding in short-term nutritional support

Authors: Anwar Elias Owais MBBS, MRCSEd, Research Fellow
Rachael Frances Bumby MNut, Senior Dietitian
John MacFie MD, FRCS, **FRCPEd** Professor of Surgery

Institution: The Combined Gastroenterology Research Unit
Scarborough General Hospital
Woodlands Drive
Scarborough YO12 6QL
United Kingdom

Corresponding author: Anwar Owais
Research Fellow
The Combined Gastroenterology Research Unit
Scarborough Hospital
Woodlands Drive
Scarborough, YO12 6QL
United Kingdom
Email: anwarowais@nhs.net

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ABSTRACT

Background: The importance of adequate nutritional support in selected patient groups is well established. Traditionally, the amounts of macronutrients provided have been based upon a perceived need to achieve, if not exceed, energy and protein balance. In recent years there has been increasing interest in the concept of “permissive underfeeding”.

Aim: The aim of this review was to determine whether or not there is evidence of benefit for permissive underfeeding in selected groups.

Methods: Studies were identified from Medline, Embase and PubMed databases and the Cochrane collaboration. The search was limited from January 1950 to January 2010. Further searches were made from the references of original articles. The literature search revealed 591 abstracts of relevant studies. All abstracts were initially reviewed by the primary author (AO) and those which did not fulfil the inclusion criteria were discarded. The remaining papers were requested and were reviewed independently by two authors (AO, JM). Twelve studies were included in the final analysis.

Result and conclusion: The results of this review suggest that permissive underfeeding may be associated with improved outcomes and reduced morbidity in patients requiring short term nutritional support.

INTRODUCTION

An implicit assumption in the provision of nutritional support in hospitalised patients is that adequate amounts of both energy (and protein) should be administered to offset the consequences of starvation. The dilemma is that uncertainty prevails as to what represents “adequate nutrition”. In the early days of parenteral nutrition clinicians routinely adopted what is now termed “hyperalimentation”. The rationale to hyperalimentation was simple. As repeated studies had demonstrated significant increases in energy expenditure following stress, sepsis or injury of any kind, then the assumption was made that these patients required to receive amounts of energy sufficient to meet resting demands but with an added supplement to account for the increased metabolic requirements during stress. It was not uncommon for patients to be prescribed amounts up to 40-50 kcal/kg/day. In some patients this amounted to almost 4000 kcals/day (1). However it soon became apparent that, contrary to the presumed benefits, administration of such large calorie loads was actually associated with significant morbidity and “hyperalimentation” fell into disrepute (2-4). In recent years the trend has swung towards much lower calorie intakes. It is now common practice to recommend intakes equivalent to 20-25 kcals/kg/day but the evidence base that these amounts represent “optimal nutrition” is poor.

This dilemma is further complicated by the fact that there is now some evidence that contrary to overfeeding, “permissive underfeeding” may be associated with clinical benefit. The aim of this paper was to carry out a review of hypocaloric feeding or permissive underfeeding in patients requiring nutritional support.

METHODS

Search criteria: Studies were identified from Medline, Embase and PubMed databases and the Cochrane collaboration. The search was limited from January 1950 to January 2010. The following keywords were searched: “permissive underfeeding” OR “artificial underfeeding” OR "hypocaloric nutrition" OR "hypocaloric feeding" OR "hypoenergetic feeding" OR "hypoenergetic nutrition". Further searches were made from the references of original articles.

Inclusions and exclusions: Studies were included if they compared outcomes between patients receiving two or more regimens of artificial feeding, which were different in the amount of calories. Studies were excluded where they **did not** contain a comparison group and where the comparison groups **did not** receive different amount of calories.

Data extraction: All abstracts were initially reviewed by the primary author (AO) and those which did not fulfil the inclusion criteria were discarded. The remaining papers were requested and were reviewed independently by the two authors (AO, JM). The studies were appraised using the Jadad score (5).

RESULTS

Studies included: The literature search revealed 591 abstracts of relevant studies. Figure 1 provides a breakdown of these studies. Five hundred and seventy abstracts were excluded because they were either not in English language, or not human studies or not on adults (19 years or older). Further studies were excluded if they were not related to underfeeding or they did not compare outcomes between patients receiving different amounts of parenteral and/or enteral nutrition. The remaining twenty one papers were reviewed. A further nine papers were excluded. Seven of the papers were review articles (6-12). One study had no comparison group (13). One study was excluded because there were too many variables other than caloric intake and at the end of the study, caloric intake was not significantly different between the groups (14).

Twelve studies were therefore included in the final analysis. Eight of these were randomised interventional trials (15-22). Three abstracts described prospective observational (cohort) studies (23-25) and one was a retrospective analysis (26). Table 1 summarises the methodological quality of the studies included. Table 2 summarises the outcomes reported by the included studies. A systematic review or a metanalysis was not possible, because those studies that have been published have examined heterogeneous groups of patients and used different end points.

Parenteral nutrition: All the studies investigating patients receiving total parenteral nutrition (TPN) were randomised trials (15-20, 22).

Sandstrom et al, in 1993, randomised 300 patients undergoing major surgery to receive either TPN or glucose alone (250-300 g/day). The patients receiving TPN received 105% of their requirements and the patients on glucose alone (the hypocaloric group) received 65% of their requirements. There were no differences in

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3 morbidity, based upon intention to treat analysis, between the two groups. In this
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5 study post operative semistarvation was not a limiting factor for outcome in a
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7 majority of patients. Overfeeding was found to be the most frequent cause of nutrition
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9 related morbidity. The authors concluded that permissive underfeeding was
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11 appropriate for a majority of patients after elective surgery (16).
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15 Muller et al investigated the effect of seven different nutritional regimens in
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17 20 critically ill intensive therapy unit (ITU) patients. The regimens varied in terms of
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19 calories (14, 28 and 56 kcals/kg) representing hypo, iso and hypercaloric feeding
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21 respectively. In addition, there were variations in the amounts of amino acids,
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23 carbohydrates, and long-chain and medium-chain triglycerides administered. Each
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25 regimen was administered over 12 hrs. Metabolism was measured by energy
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27 expenditure (indirect calorimetry), body temperature, nitrogen balance, and blood
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29 glucose and lactate levels. Nitrogen balance was positive in the hypercaloric group
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31 but negative in the other two groups. Neither hypercaloric nor isocaloric feeding
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33 prevented protein catabolism. Further, in both these groups they aggravated the
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35 metabolic burden as assessed by energy expenditure, thermogenesis, urea production
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37 rate and glucose and lactate levels. These authors concluded that a hypocaloric
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39 feeding regimen was preferable (18). This was an interesting study with appropriate
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41 end points designed to assess metabolic burden. However, it is debatable whether or
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43 not it is valid to extrapolate results obtained from 12 hour infusion periods to overall
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45 outcomes of nutritional support.
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53 Frankenfield et al investigated whether or not energy balance influenced
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55 nitrogen loss in trauma patients. Patients were randomised to three groups: patients in
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57 group 1, the nonprotein calorie group, received dextrose and lipid equivalent to
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59 energy expenditure. In group 2, the total calorie group, patients received dextrose,
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lipid and protein equivalent to measured energy expenditure. Group 3, the hypocaloric group, received dextrose and lipid equal to 50% of measured energy expenditure. The primary end points in this study were nitrogen balance and catabolism of myofibrillar muscle protein. Achievement of energy balance (groups 1 and 2) failed to decrease catabolic rate or nitrogen loss. The authors concluded that providing a caloric intake equivalent to energy expenditure is not necessary in the acute phase of traumatic injury. Further, hypocaloric feeding promoted endogenous lipid mobilization without adversely affecting protein metabolism (19).

Burge et al, in a double blind trial, randomised 16 obese hospitalised patients to receive either hypoenergetic TPN (14 kcals/kg) or normocaloric TPN (25 kcals/kg). Their primary end point was nitrogen balance. They found no differences in measured nitrogen balance. They concluded that permissive underfeeding can be effectively administered to hospitalised obese patients (22). However, in this study, critically ill patients and patients with diabetes mellitus were excluded and therefore, this limited the broader clinical application of this study. Three years later, a similar study was published from the same centre, but in this trial they included critically ill patients and those with diabetes mellitus. In a double blind trial, Choban et al randomised 30 obese hospitalised patients to receive either hypoenergetic TPN (13 kcals/kg) or to a control group who received 22 kcals/kg. End points were nitrogen balance and glycaemic control. Again, they found no differences in measured nitrogen balance, although improved glycaemic control was observed in obese patients with non-insulin-dependent diabetic patients, who received hypoenergetic TPN. This was reflected by a reduction in the number of days insulin was required and lower serum glucose concentrations (15). Both these studies were conducted on patients with morbid obesity which limits wider applicability of results.

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3 In a non blinded study, McCowen et al compared 40 hospitalised patients who
4 required TPN who were randomised to either a hypocaloric formula (1000 kcal/day
5 of fat free TPN, containing 70 g of protein) or a normocaloric formula (25 kcal/kg
6 containing 1.5g/kg protein and fat as part of 3-in-1 TPN solution). They evaluated the
7 frequency of hyperglycaemia, together with septic and non-septic morbidities and
8 nitrogen balance. They found no differences between the groups in terms of episodes
9 of hyperglycaemia, septic complications, length of stay or mortality. The only
10 difference between the groups was in nitrogen balance which was more negative in
11 the hypocaloric group (17). However, this measurement was only completed in 50%
12 of the patients. One of the limitations of this study was that the restricted group
13 received a fixed amount of calories regardless of their weight, and they received a
14 different formulation of TPN (fat free TPN). Nonetheless, the results of this study
15 suggest that restricting intake is not associated with increased morbidity.
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34 Schricker et al reported a study of 16 patients in which the primary aim was to
35 investigate if hypocaloric nutrition can induce anabolism in patients who receive
36 perioperative epidural analgesia. Protein anabolism was measured using radio labelled
37 leucine. They compared two randomised groups of surgical patients, one who
38 received 50% of their measured energy expenditure (as glucose only) and the other
39 who received 70% of their measured energy expenditure (50% as glucose and 20% as
40 amino acids). Epidural analgesia was used in both groups. A positive leucine balance
41 (indicating anabolism) was achieved with the 70% group. The authors concluded that
42 patients who received hypocaloric TPN can be rendered anabolic after surgery in the
43 presence of epidural analgesia (20). The relevance of this study to the debate about
44 permissive underfeeding is debatable. The primary aim of this study was to determine
45 the effect of epidural analgesia on surgical patients receiving different levels of
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hypocaloric feeding. Therefore, there was no group who received normocaloric feeding.

Enteral nutrition: The literature search revealed only two studies involving patients fed exclusively by the enteral route. One was a randomized trial and the other was a retrospective study (21, 26).

In a prospective, controlled, unblinded clinical trial, Ibrahim et al in 2002 evaluated the outcome of 150 medical ITU patients randomised to receive either early or late enteral feeding. The early feeding group received the full requirements from day one. The late feeding group received 20% of their requirements for the first 4 days and subsequently were fed to full requirements. The patients randomised to “late” enteral nutrition were, therefore, effectively underfed. These patients had significantly less episodes of ventilator associated pneumonia and Clostridium Difficile diarrhoea, shorter ITU and hospital stays, but no difference in hospital mortality (21).

Dickerson et al in 2002, in a retrospective study of 40 patients, compared septic and non-septic complications in two groups of multi-trauma obese patients who were fed either 25-30 Kcal / kg or less than 20 Kcal / kg. The hypocaloric group had reduced durations of ITU stay, less duration of ventilation and fewer days of antibiotics therapy. There were no differences between the groups in hospital stay, septic complications or mortality (26). It should be noted that in this study the number of patients in the hypocaloric group was more than double the number of patients in the normocaloric group.

Miscellaneous: Three prospective observational studies were identified, in which patients were retrospectively grouped on the basis of their caloric intake irrespective of route of feeding (enteral, parenteral or combined nutrition) (23-25).

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3 In the study by Krishnan et al, 187 patients from two medical ITUs between
4 February 1999 and October 2000 were retrospectively allocated to one of three groups
5 depending upon their caloric intake. Group 1 received <33%, Group 2 received 33-
6 65% and Group 3 received >65% of their estimated energy requirements calculated
7 using the American College of Chest Physicians (ACCP) guidelines. The group that
8 received 33-65% of their requirements achieved spontaneous ventilation the quickest.
9 There was no significant difference in the incidence of nosocomial sepsis between the
10 groups in this study. This study suggests that moderate underfeeding (33-65%) may
11 improve outcomes, but absolute starvation (<33%) is harmful (23).
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25 Robinson et al reported a similar design study from a single medical ITU
26 between February 1999 and October 2000. In this trial 138 patients were
27 retrospectively allocated to 4 groups, again relating to percentage intake received of
28 ACCP target (<25%, 25-49%, 50-74% and >74%). In the group that received <25%
29 of ACCP, which was equivalent to 6 Kcal/kg/day; there was a significant increase in
30 nosocomial bloodstream infections compared to the other groups (24). This supports
31 the first study by Krishnan et al that absolute starvation (in this study less than 25%)
32 is harmful as well.
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44 We note that the studies by Robinson and Krishnan (23-24) are from the same
45 institution over similar time periods. We cannot exclude the possibility that the patient
46 populations overlap in these two studies which weaken conclusions based upon these
47 studies.
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53 The consequences of underfeeding were investigated by Villet et al in 48
54 surgical ITU patients by measuring cumulative energy deficit or surplus calculated
55 over their entire hospital stay. Significant negative balances (energy debts) correlated
56 significantly with length of stay, non septic complications, septic complications,
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duration of antibiotics treatment and duration of mechanical ventilation. This study concluded that hypocaloric feeding and cumulative energy deficit may be a risk factor for worse clinical outcomes (25).

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DISCUSSION AND CONCLUSION

The results of this review suggest that permissive underfeeding may be associated with improved outcomes and reduced morbidity in patients requiring short term nutritional support. There is insufficient data available to draw firm conclusions as to the degree or duration of underfeeding that is associated with net benefit when weighed against the inevitable deleterious consequences of starvation. This review would suggest that at least in short term nutritional support (up to 2 weeks), that benefits in terms of reduced complications outweigh potential harm from loss of lean body mass of fat stores in patients prescribed between 50-100 % of their requirements.

We recognise certain limitations to this review. Firstly, there are relatively few published trials which have set out as their primary objective to investigate the putative role of underfeeding. Secondly, those studies that have been published have examined very heterogeneous groups of patients and used very different end points. Thirdly, some of the parenteral studies used different macronutrient compositions in the randomised groups, and some of the results (especially nitrogen balance) could be attributable to this. Fourthly, and most importantly, it is very difficult, and arguably inappropriate, to draw conclusions from studies in which underfeeding occurred by default rather than intention such as occurs in many trials of enteral nutrition.

The term permissive underfeeding was first used by Zaloga et al in 1994 (27) to describe a strategy which was based on the premise that short term dietary restriction (but not elimination) would limit pathological processes associated with overfeeding while minimally impairing organ function. A number of reviews and a limited number of prospective studies referred to in this systematic review, have investigated this strategy but the evidence in support of this hypothesis remains

tenuous. This may reflect the fact that clinicians and others responsible for nutritional support find it counter intuitive to deliberately fail to meet a patient's macronutrient requirements. The explanation for benefit for permissive underfeeding is based upon the premise that the morbidity associated with over feeding offsets any possible disadvantage from failing to maintain body composition. Further, there is increasing evidence to suggest that energy and protein requirements have been overestimated in the past such that what we term permissive underfeeding may actually represent optimal provision of nutrients (11, 28).

The aim of adjuvant nutritional support is an attempt to minimise losses of lean body mass and body fat. In the early days of nutritional support therapy clinicians witnessed the rapid wasting of patients with overwhelming sepsis and the consequences of severe starvation. Not surprisingly, the prevailing view was that patients required their measured or estimated requirements together with additional supplements to account for stress, be this surgical or septic. It was not unusual for intakes of 4000 kcals/day to be administered (1). It was commonly believed that energy intakes of 30% above resting energy expenditure were required to meet the metabolic requirements of patients. There is now overwhelming evidence to show that surgical patients rarely require more than 2000 kcals/day and often much less (29). More importantly, there is now evidence to demonstrate that the provision of nitrogen intakes above 8-10 gm N₂/kg day is not associated with any additional benefit with respect to reducing losses of lean body mass (30). Similarly, it is now well recognised that the provision of nutrients to patients following surgery or those with sepsis will not reverse the gluconeogenesis that characterises the metabolic response to trauma and sepsis. Nutritional support has no impact on rates of protein catabolism in septic patients although it can reduce net losses a little by enhancing anabolism. The aim of

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3 nutritional support therefore, at least in the critically ill is to minimise losses accepting
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5 that these cannot be entirely prevented (31-32). It is worth emphasising that this
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7 approach would not be appropriate in the convalescent patient in whom exogenous
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9 calories and nitrogen can reverse gluconeogenesis and thereby stimulate accretion of
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11 lean body mass and body fat. Permissive underfeeding therefore has no role in
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13 metabolically stable patients where growth is an objective of nutritional support.
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17 Another justification for permissive underfeeding relates to the fact that energy
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19 requirements of disease have frequently been over estimated in the past. For example,
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21 it is now well recognised that the so called hypermetabolism of trauma or burns is
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23 relatively short lived (11, 28). Accordingly, to extrapolate measurements of oxygen
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25 consumption made at the time of admission may not accurately reflect the situation a
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27 few days later. Similarly, it is now well known that infusion of nutrients itself results
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29 in increased energy expenditure as a result of a phenomenon termed dietary induced
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31 thermogenesis. Finally, it is now generally agreed that patients, particularly those on
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33 ITUs do not require supplementary energy over and above resting requirements to
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35 compensate for changes in body temperature or the effort of breathing. Indeed, the
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37 measured resting requirements of these patients are often of the order of only 1500
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39 kcals/day (11). This latter point is important because it emphasises the weakness of
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41 estimating energy requirements from prediction equations. These are calculated from
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43 multiple measurements in stable patients. Numerous studies have demonstrated that
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45 they are inclined to overestimate requirements. This over-estimation is further
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47 magnified by adding factors for stress, growth and dietary induced thermogenesis (11,
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49 28).
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58 Whilst, as this review demonstrates, there is a relative paucity of data from
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60 prospective studies on the subject of permissive underfeeding it is important to

emphasise that there is much circumstantial evidence to support the concept. Early studies which investigated outcomes of patients receiving up to 60 kcals/kg/day consistently reported problems with hyperglycaemia and weight gain caused by retention of water (33). The much cited Veteran's study which was a controlled trial of preoperative TPN in 395 patients undergoing laparotomy or noncardiac thoracotomy demonstrated a significantly higher incidence of sepsis in the patients who were aggressively fed (1000 kcals/day above resting energy expenditure) (34). Concerns about "aggressive" TPN were highlighted by a number of reviews which concluded that septic morbidity was consistently higher in patients who received TPN (and met their requirements) as compared to those that received enteral nutrition (who frequently failed to meet requirements). The common denominator in septic morbidity in patients who received TPN was hyperglycaemia.

The only study in this review which concluded that underfeeding was associated with harm is that by Villet et al. In this retrospective analysis they found that calculated energy deficits were associated with poorer outcomes. However, the deficits in this study amounted to over 50% of estimated requirements.

Clearly, the provision of no nutrients whatsoever, absolute starvation, is harmful. Similarly, the administration of excessive calories is detrimental. The results of this review confirm that permissive underfeeding in critically ill patients requiring artificial nutrition on a short term basis may be preferable to normocaloric nutrition. The optimal level of feeding is unknown but must be a balance between minimising catabolism and avoiding morbidity. We would suggest that in critically ill or severely malnourished patients that macronutrient intakes do not exceed 50% of estimated requirements for the first few days of nutritional support. Intakes can increase

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6 minimising losses to encouraging growth.
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Ethical conflicts: Nothing to declare

Personal interests: Nothing to declare

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Figure 1: Results of literature search

Author	Type of study	Number of patients	Route of feeding	Random sequence generation	Concealment of allocation	Blinding	Jadad score
Sandstrom <i>et al.</i> (16)	RCT	300	Parenteral	Computer generated	Not described	Not blinded	2/5
Muller <i>et al.</i> (18)	RCT	20	Parenteral	Not described	Not described	Not blinded	1/5
Frankenfield <i>et al.</i> (19)	RCT	30	Parenteral	Not described	Not described	Not blinded	1/5
Burge <i>et al.</i> (22)	RCT	16	Parenteral	Not described	Not described	Double blinded	2/5
Choban <i>et al.</i> (15)	RCT	30	Parenteral	Randomisation tables	Not described	Double blinded	3/5
McCowen <i>et al.</i> (17)	RCT	40	Parenteral	Not described	Not described	Not blinded	2/5
Schricker <i>et al.</i> (20)	RCT	16	Parenteral	Computer generated	Sealed envelopes	Double blinded	4/5
Ibrahim <i>et al.</i> (21)	RCT	150	Enteral	Date of admission (even or odd)	Not applicable	Not blinded	0/5
Dickerson <i>et al.</i> (26)	Prospective controlled trial	40	Enteral	Not applicable	Not applicable	Not applicable	0/5
Krishnan <i>et al.</i> (23)	PCS	187	Enteral and/or parenteral	Not applicable	Not applicable	Not applicable	0/5
Rubinson <i>et al.</i> (24)	PCS	138	Enteral and/or parenteral	Not applicable	Not applicable	Not applicable	0/5
Villet <i>et al.</i> (25)	PCS	48	Enteral and/or parenteral	Not applicable	Not applicable	Not applicable	0/5

Table 1: Methodological quality of the studies included
RCT: Randomised controlled trial, PCS: Prospective cohort study

Author	Patients	Comparison groups	End points / results	Conclusion
Sandstrom <i>et al.</i> (16)	Surgical patients	1. Normocaloric (TPN 105%) 2. Hypocaloric (Glucose 65%)	Morbidity and mortality: No difference	Hypocaloric feeding is appropriate
Muller <i>et al.</i> (18)	ITU patients	1. Hypocaloric (14 kcal/kg/day) 2. Normocaloric (28 kcal/kg/day) 3. Hypercaloric (56 kcal/kg/day)	Metabolic burden: Less in hypocaloric group Nitrogen balance: Positive in hypercaloric group Protein catabolism: Present in all groups	Hypocaloric feeding is appropriate
Frankenfield <i>et al.</i> (19)	Trauma patients	1. Nonprotein calorie group (Dextrose and lipid 100%) 2. Total calorie group (Dextrose, lipid & protein 100%) 3. Hypocaloric group (Dextrose and lipid 50%)	Nitrogen balance: No difference Protein catabolism: No difference Lipid mobilization: Hypocaloric feeding promotes endogenous lipid mobilization	Normocaloric feeding is not necessary in the acute phase of traumatic patients
Burge <i>et al.</i> (22)	Obese hospitalised patients	1. Hypocaloric (TPN 14 kcal/kg/day) 2. Normocaloric (TPN 25 kcal/kg/day)	Nitrogen balance: No difference	Hypocaloric feeding is appropriate
Choban <i>et al.</i> (15)	Obese hospitalised patients	1. Hypocaloric (TPN 13 kcal/kg/day) 2. Normocaloric (TPN 22 kcal/kg/day)	Nitrogen balance: No difference Glycaemic control: Better in insulin-dependent diabetics in the hypocaloric group	Hypocaloric feeding is appropriate
McCowen <i>et al.</i> (17)	Hospitalised patients	1. Hypocaloric (Fat free TPN 1000 kcal/day) 2. Normocaloric (Fat TPN 25 kcal/kg/day)	Nitrogen balance: Negative in both groups Glycaemic control: No difference Morbidities: No difference	Hypocaloric feeding is appropriate
Schricker <i>et al.</i> (20)	Surgical patients requiring epidural analgesia	1. Hypocaloric (70% of ER as glucose and amino acids) 2. Hypocaloric (50% of ER as glucose only)	Leucine balance (anabolism): Positive for the 70% group	Hypocaloric feeding can induce anabolism after surgery in the presence of epidural analgesia

Ibrahim <i>et al.</i> (21)	Medical ITU patients	1. Hypocaloric (20% of ER for first 4 days then 100% of ER) 2. Normocaloric (100% of ER from day 1)	Morbidity: Less with hypocaloric feeding Mortality: No difference	Hypocaloric feeding is appropriate in the early stages of critical illness
Dickerson <i>et al.</i> (26)	Trauma obese patients	1. Hypocaloric (<20 cal/kg/day) 2. Normocaloric (25-30 kcal/kg/day)	ITU stay, duration of ventilation/antibiotics: less with hypocaloric group Hospital stay, septic complications, mortality: No difference	Hypocaloric feeding is appropriate
Krishnan <i>et al.</i> (23)	Medical ITU patients	1. Group 1 (<33% of ER) 2. Group 2 (33-65% of ER) 3. Group 3 (>65% of ER)	Spontaneous ventilation: Quicker in group 2 Nosocomial sepsis: No difference	Moderate underfeeding (33-65%) may improve outcomes
Rubinson <i>et al.</i> (24)	Medical ITU patients	1. Group 1 (<25% of ER) 2. Group 2 (25-49% of ER) 3. Group 3 (50-74% of ER) 4. Group 4 (>74% of ER)	Nosocomial bloodstream infections: significant increase in group 1	Absolute starvation is harmful
Villet <i>et al.</i> (25)	Surgical ITU patients	1. No energy deficit group (+1000 to -5000 kcal/week) 2. Moderate energy deficit group (-5001 to -10000 kcal/week) 3. Severe energy deficit group (-10000 to -20000 kcal/week) 4. Extreme energy deficit group (>-20000 kcal/week)	Duration of stay, septic and non septic complications, duration of antibiotic and duration of ventilation: Negative balances correlated significantly with all end points	Hypocaloric feeding and cumulative energy deficit may be a risk factor for worse clinical outcomes

Table 2: Outcomes of the studies included
TPN: Total parenteral nutrition, ER: Energy requirements, ITU: Intensive therapeutic patient.

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Results of literature search
155x121mm (96 x 96 DPI)