

## “Eat your lunch!” – controversies in the nutrition of the acutely, non-critically ill medical inpatient

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### Summary

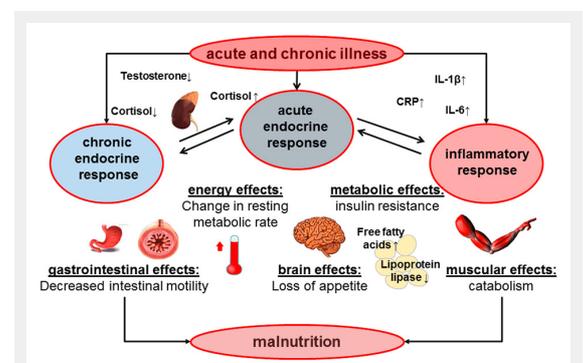
There is no doubt about the strong association of malnutrition and adverse medical outcomes including mortality, morbidity and quality of life. Particularly in the elderly and frail medical inpatient population, loss of appetite due to the acute illness further aggravates nutritional status. In fact, this relationship between acute disease and eating behaviour / nutritional status may well be bidirectional, with not only illness affecting nutritional status, but also dietary factors influencing the course of illness. Whether loss of appetite associated with acute illness is indeed a protective physiological response or a therapeutic target needing early corrective nutritional therapy is a matter of current debate and can only be resolved within a large and well-designed randomised controlled trial comparing early nutritional therapy with “appetite-guided” nutrition in this patient population. Apart from in critical care, where various large trials have recently been published, there is an important lack of high quality data from large randomised trials in unselected acutely ill medical inpatients to support the early use of nutritional therapy, to shed light on the optimal type, caloric amount and timing of nutritional therapy and to answer ultimately the question as to which patient population will in fact benefit from nutritional interventions. Currently, the EFFORT trial is enrolling patients and aims to fill these literature gaps. The aim of this review is to discuss the current evidence regarding nutritional therapy in acutely ill medical inpatients, and to recommend whether or not, based on today’s available evidence, physician should indeed encourage their malnourished patients to “...finish their lunch”.

**Key words:** nutrition; acute illness; malnutrition; inflammation

### Association and casual relationships

Acute and chronic illness is associated with loss of appetite and body weight, which increases the risk for malnutrition, particularly in the elderly and frail medical patient population [1]. This relationship between acute disease and eating behaviour / nutritional status may well be bidirectional,

not only with illness affecting nutritional status, but also dietary factors influencing the course of illness (reviewed in [2]). For example, cytokines, such as interleukin (IL)-6 and tumour-necrosis-factor (TNF)-alpha, affect the brain circuitries that control food intake, delayed gastric emptying and skeletal muscle catabolism (fig. 1) [3, 4]. From an evolutionary perspective based on the principals of Charles Darwin, it is tempting to hypothesise that loss of appetite during acute illness may well bring a natural selection advantage and increases a patient’s ability to survive. Whether loss of appetite associated with acute illness is indeed a protective physiological response or a therapeutic target needing early corrective nutritional therapy is still debated. Particularly, this is also important when asking the question “who ultimately benefits from nutritional interventions?” – malnourished patients, patients at risk of malnutrition or both? This controversy can only be resolved with a large randomised-controlled trial comparing early nutritional therapy with “appetite-guided” nutrition in this patient population.



**Figure 1**

Summary of physiopathological mechanisms occurring during acute and chronic illnesses including endocrine and inflammatory pathways leading to malnutrition.

CRP = C-reactive protein; IL = interleukin

## Malnutrition in the elderly medical inpatient population

Malnutrition is common in elderly, chronic and/or polymorbid inpatients and associated with detrimental metabolic consequences, such as catabolism and muscle wasting [1]. Malnutrition *per se* is associated with higher mortality and morbidity, increased risk for infection and an increased hospital length-of-stay (LOS) [5, 6]. Therefore, prevention of malnutrition is an important goal in patient care and probably much more effective than treating this condition in sick patients. In medical inpatients at risk for malnutrition, our current clinical approach is still to provide nutritional therapy as an alleged strategy to combat malnutrition and associated adverse outcomes. However, unlike the critical care setting, where various large trials have recently been published [7–9], as well as in surgical patients and patients living in long-term facilities [10], there is an important lack of high quality data from large randomised controlled trials (RCTs) in unselected acutely ill medical inpatients to support the early use of nutritional therapy and to shed light on which patient population ultimately benefits from nutritional interventions, i.e. only malnourished patients, patients at risk for malnutrition or both? Also the optimal type, caloric amount and timing of nutritional therapy remain largely undefined and no current guideline exists today to give physicians guidance on the best approach to the polymorbid medical inpatient.

## Evidence from randomised nutritional trials

A 2009 meta-analysis focusing on the effects of nutritional therapy in the elderly patient population and including 10,187 randomised participants in 62 trials of mostly poor study quality, found that supplementation may reduce mortality in older people who are undernourished and may lead to lower risk for complications [10]. However, no evidence of improvement in functional benefit or reduction in length of hospital stay was found with supplements [10]. Most trials, however, included outpatients, long-term facility or surgical patients. Similarly, another previous meta-analysis is confirmed the important lack of high-quality evidence to

endorse or refute nutritional support and give firm recommendations for or against nutritional therapy [11]. Again, this meta-analysis did not specifically focus on the effect of early nutritional therapy in the complex, polymorbid medical inpatient population.

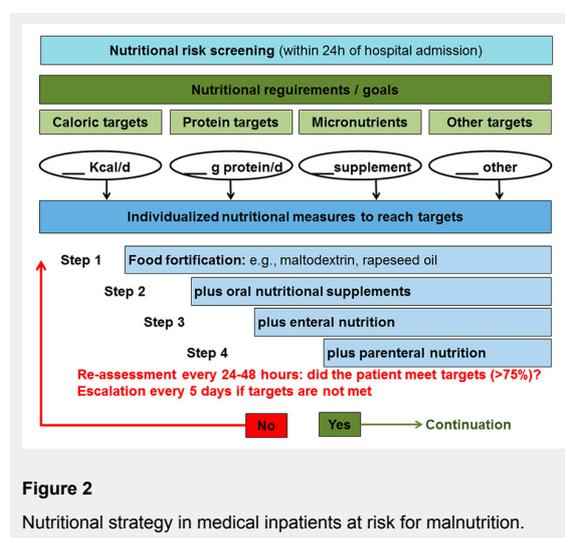
Nonetheless, for medical inpatient population, various previous trials have investigated the effects of nutritional strategies on selected patient outcomes, mainly changes in body weight and nutrition-specific quality of life. Table 1 shows a summary of most important nutritional intervention trials based on a recent Cochrane literature search [12]. However, these trials were highly heterogeneous in design, patient populations and type of interventions, lacked power to demonstrate safety and, in aggregate, produced inconclusive results.

## Current clinical approach to medical patients at risk for malnutrition

Despite the absence of high-quality RCT data, the current clinical approach in unselected medical inpatients is to provide nutritional therapy to reach nutritional requirements including caloric and protein targets, as well as micronutritional requirements (fig. 2). These considerations are mainly based on observational and preclinical studies and the non-ill physiological situation following the basic principles that a deficit in energy or protein metabolism in conjunction with disease-induced inflammation will lead to cachexia and catabolism. Whether during acute illness the same amounts of energy and proteins are needed and beneficial as in healthy patients thereby remains unclear.

In fact, some recent data from critical care suggested even harmful effects of aggressive early (over-) feeding and glutamine supplementation [7, 8, 13]. As a possible explanation for these findings, it has been emphasised that during the acute phase of illness, the body mobilises substrates from muscle and fat tissue to match the increased resting energy expenditure [14]. Exogenous calories then no longer inhibit gluconeogenesis. Excessive nutrition during the acute phase of illness can thus induce occult overfeeding. Still, recent research from Switzerland reported benefit from individually optimised energy supplementation in well-selected patients [9]. The contradictory findings from these trials may be partly explained by the differences in patient populations studied and trial design. An important consideration is, therefore, the fact that every ill patient is different, and nutritional strategies and goals need to be personalised and tailored to the individual patient's requirements [14].

Importantly, data from critical care cannot unconditionally be transferred to medical inpatients with a lower degree of disease severity. Still, the above-mentioned conflicting observations re-emphasise that nutritional therapy is a medical intervention with associated risks and costs, and call into question today's nutritional approach in medical inpatients. The current lack of strong guideline recommendations [15–28] for type, caloric amount and timing of nutritional therapy in medical inpatients is mainly explained by the paucity of high-level evidence showing such therapy's efficacy and cost benefits, and the absence of knowledge regarding which patient populations do or do not benefit.



## Current trials: EFFORT

As a result of the conflicting results and gaps in the literature, a pragmatic randomised trial is currently enrolling patients in several hospitals in Switzerland (EFFORT: Effect of Early Nutritional Therapy on Frailty, Functional Outcomes and Recovery of Undernourished Medical Inpatients Trial). The trial aims to assess the effects of early nutritional therapy in regard to effectiveness, safety and costs when applied to the heterogenous, polymorbid medical inpatient population. EFFORT will not only answer the question about overall benefit or harm, but by using a physiopathological mechanistic approach, it also will explore and provide conclusive answers about whether, why, how, and in which patient populations nutritional therapy does and does not work.

Most current nutritional research has focused on selected medical diseases (i.e. pancreatitis). As a consequence, these “clean” results may not be generalisable to “real-life” unselected medical inpatients with multiple comorbidities and illnesses. Comparative effectiveness research aims at improving quality, effectiveness and efficiency of health care and at helping patients and healthcare professionals make informed decisions [29]. To achieve these goals, research must address the patient population that actually consumes the most health care, specifically polymorbid, frail, elderly patients with complex combinations of medical diagnoses. Although this patient population accounts for the majority of costs, it is also the least studied population [30]. To correct this disparity, it has become evident that clinical trials should include large, representative populations, to enable examination of treatment effects within key subpopulations, and to allow robust head-to-head comparison of interventions [29]. Owing to its pragmatic design, EFFORT will close this important gap and because of its

large sample size (i.e., 2,000–3,000 patients target sample size) important subgroup analyses will be performed to understand which patients do or do not benefit from therapy. This is an important first step for a more “personalized nutritional care”.

## Outlook and future direction

Malnutrition is a major issue in hospital care. Whether, how and why early nutritional therapy affects outcomes of unselected, elderly, frail medical inpatients remains largely unclear today. In the absence of strong evidence for or against nutritional therapy in the medical inpatient population, the following considerations may help to guide physicians’ approach to malnutrition while awaiting more definite trial results (fig. 2): (1.) screening for malnutrition using a validated tool (such as NRS 2002) is recommended [31]; (2.) In patients at risk, a careful assessment of the nutritional situation is recommended to estimate nutritional targets (caloric, protein, micronutrient) and to find modifiable factors (e.g., poor dental status, different food preferences); (3.) If nutritional targets cannot be reached, a team approach including dieticians, nurses and physicians is warranted to optimise nutritional intake in patients; (4.) nutritional therapy should be as physiological as possible starting with between-meal snacking, food enrichment and oral supplements. Enteral and parenteral nutrition should only be used as *ultimo ratio* when other measures fail. Hopefully EFFORT will provide more definite answers and will tell us whether such an approach holds its promise and reverses the adverse effects of malnutrition in this frail patient population.

**Table 1:** Important interventional studies evaluating nutritional therapy in medical inpatients.

First author, Year	Patient type	No.	Study intervention	Control treatment	Outcomes evaluated	Main effect of study Intervention	Limitations	Ref
Starke J, 2011	Malnourished general medical inpatients	132	Individual nutritional support (oral)	Standard nutritional care <sup>1</sup>	Caloric intake, weight, vitamin levels, QoL, complications, readmission, mortality (6m)	Higher caloric/protein intake, less weight loss, increase in QoL, fewer complications	Small sample, time-consuming intervention	[32]
Hickson M, 2004	Malnourished medical patients, >65 y	592	Nutritional counselling (by healthcare assistants)	Standard nutritional care <sup>2</sup>	Weight/BMI, Barthel's index, infection, LOS, in-hospital mortality	Less antibiotic use, otherwise no effect	Short training for healthcare assistants (15 h)	[33]
Norman K, 2008	Malnourished inpatients, with GI disease	101	Dietary counselling with ONS over 3-month period	Dietary counselling without ONS	BMI, muscle strength, readmission, QoL	Improved hand grip strength and PF, fewer readmissions, better QoL	High dropout rate, two intervention groups	[34]
Rüfenacht U, 2010	Malnourished general medical inpatients	36	Intensive nutritional counselling with ONS	ONS only	Anthropometrics, energy and protein intake, QoL questionnaire	Higher caloric/protein intake, QoL improvement after hospitalisation	Small sample, two intervention groups	[35]
Gariballa S, 2006	Malnourished inpatients >65 y	445	400 ml ONS/d (995 kcal)	400 ml placebo/d (60 kcal)	Barthel, readmissions, LOS, mortality	Fewer readmissions, otherwise no effect	Low adherence	[36]
Johansen N, 2004	Malnourished inpatients	212	Individualised nutritional therapy	Standard nutritional care <sup>2</sup>	Caloric intake, LOS, complications, mortality, QoL	Higher caloric/protein intake associated with shorter LOS	Small sample	[37]

BMI = body mass index; d = day(s); GI = gastrointestinal; h = hours(s); LOS = length of stay; m = month(s); ONS = oral nutrition supplement; PF = peak flow; QoL = quality of life;  
<sup>1</sup> Including the prescription of oral nutritional supplements and nutritional therapy prescribed by the physician according to the routine ward management; <sup>2</sup> Not further specified

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Figures (large format)

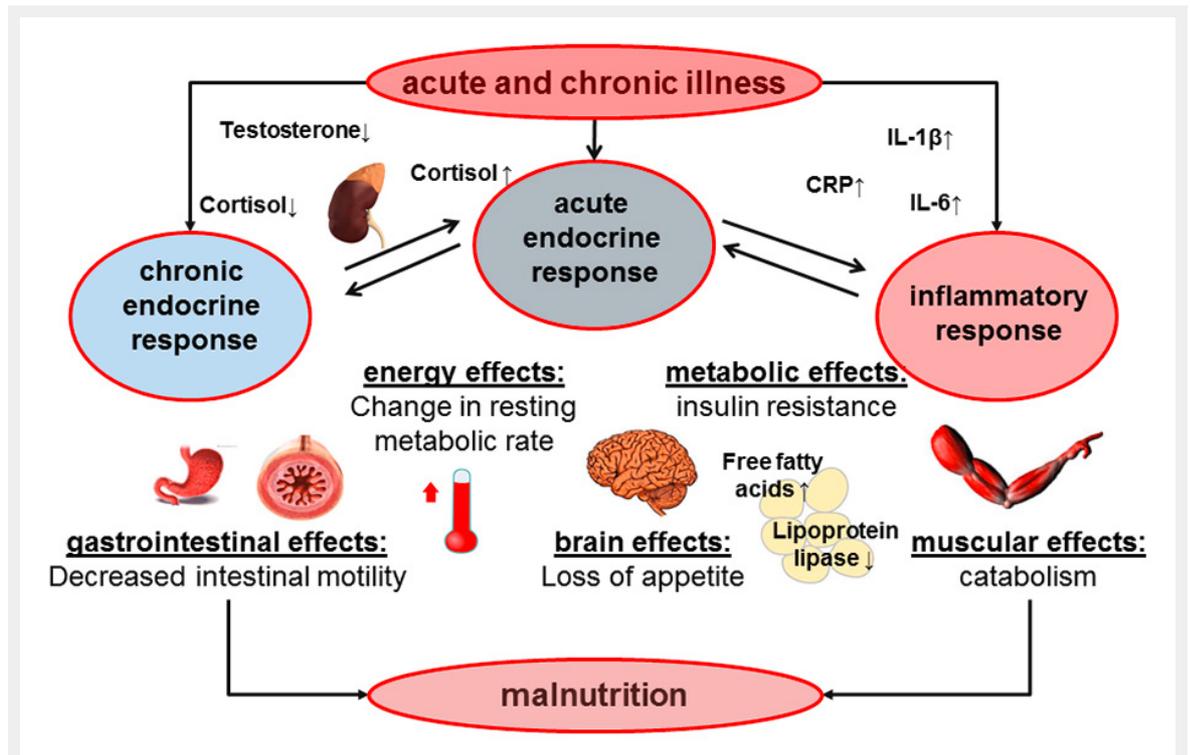
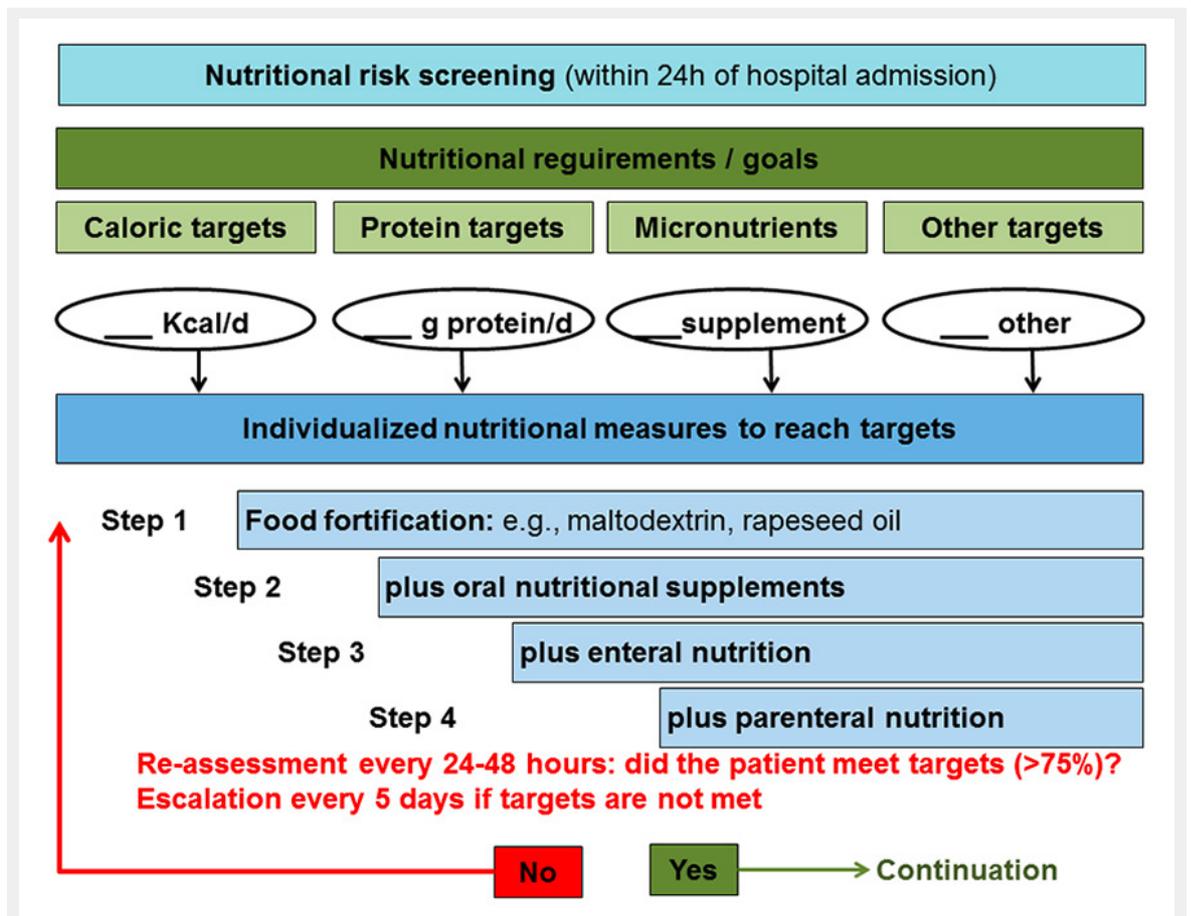


Figure 1

Summary of physiopathological mechanisms occurring during acute and chronic illnesses including endocrine and inflammatory pathways leading to malnutrition.

CRP = C-reactive protein; IL = interleukin



**Figure 2**  
 Nutritional strategy in medical inpatients at risk for malnutrition.