**Food Modification versus Oral Liquid Nutrition Supplementation**

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**Abstract**

Oral liquid nutrition supplements (ONS) are widely used in community, residential and healthcare settings. ONS are intended for individuals whose nutrient requirements cannot be achieved by conventional diet or food modification, or for the management of distinctive nutrient needs resulting from specific diseases and/or conditions. ONS appear to be most effective in patients with a body mass index of $\leq 20$. Studies are needed to evaluate the clinical and functional efficacy of food-based versus ONS nutrition interventions.

The conditions of energy undernutrition and protein-energy undernutrition remain devastating global problems, and are especially prevalent in older adults who are hospitalized or residing in long-term care (LTC) facilities. Many older adults are admitted undernourished or become undernourished during institutionalization. Lack of attention to nutrient intakes contributes to deterioration of nutritional status. Although a number of trials have been published over the past $3\frac{1}{2}$ decades, there remains no consensus on the best method to enhance oral dietary intakes of older adults to help them achieve meeting their energy, protein and other nutrient requirements, and thereby improve body weight and body composition, physical and cognitive function, and clinical outcomes. Strategies to complement habitual dietary intakes include interventions using foods, such as manipulating the energy density of recipes, enhancing the flavor of food items served, adding snacks between meals or providing meals in community settings, and interventions using oral liquid nutrition supplements (ONS) before, during or after meals.


**Enhancing Foods and Meals**

Modification of foods and beverages to increase the energy or nutrient density (kcal or nutrient per gram weight of food) occurs by adding, substituting or enhancing energy- and/or protein-rich ingredients of food items served in the menu. Very few randomized controlled trials have been conducted to investigate the effects of increasing energy and protein density by recipe enhancement on clinical or functional outcomes in adults at nutrition risk. Manipulating recipes by adding fats such as cream or butter and carbohydrates such as glucose polymers have been used to enhance the energy density of meals served in a few care settings. In a case-control design, LTC residents who received energy-dense meals consumed about 30% more kilocalories per kilogram and were able to maintain their activities of daily living (ADL) after 15 weeks of meal enhancement [1]. In 35 older patients in a hospital rehabilitation ward, increasing the energy density of the meals served for 14 days increased caloric intakes by 25% [2]. In a randomized cross-over trial utilizing enhancement of the energy and nutrient density of the regularly served home-delivered lunch meal, both the lunch meal and 24-hour intakes improved for calories and key micronutrients in 45 older adult clients of a home health agency [3].

As reduced sensitivity to the taste and smell of foods with aging may impair the ability to appreciate the palatability of foods, flavor enhancement of foods has also been used to promote greater dietary intakes. Flavor enhancement of the protein-rich food items in a LTC menu was achieved by adding more chicken, beef, turkey or lemon butter flavor. Enhancement increased caloric intakes and resulted in a weight gain of 1.1 kg after 17 weeks [4]. In a residential home setting, flavor enhancement of energy-dense food items for 3 weeks improved immune function and grip strength in 39 older adults [5].

**Providing Between-Meal Snacks**

Adding between-meal snacks such as milk shakes, puddings, snack bars and cookies increased the energy intakes of LTC residents by 30% of total calories [6]. Notably, providing fruit and dairy-based snacks two times daily for 17 weeks to community-residing older adults improved serum levels for 25-hydroxyvitamin D, pyridoxal-5-phosphate, cobalamin and ascorbic acid [7].

In another study, investigators used the SNAQ screening tool to identify undernourished patients and trigger provision of between-meal snacks that provided an additional 600 kcal and 12 g protein/day to those patients who were classified as moderately or severely undernourished. Screening triggered significantly more referrals to a registered dietitian (76% of undernour-
ished patients vs. 46%) and shortened the interval to dietetic consultation from an average 5.8 to 2.6 days (p < 0.001). Between-meal snacks reduced length of stay in those patients with low handgrip strength (11.5 vs. 14 days) [8].

A pilot study of the Seniors Farmers’ Market Nutrition Program, funded by the US Department of Agriculture, was conducted in which a basket of locally grown fresh fruits and vegetables was provided every 2 weeks to homebound older adult participants of home-delivered meal programs in Seattle, Wash. After 5 months of deliveries, the intervention group (n = 100) were consuming 1.3 more servings of fruits and vegetables per day compared to the control group (n = 52, p < 0.001) [9].

Providing Meals

In the US, about 3 million older adults receive congregate and home-delivered meals under Title IIIC of the Older Americans Act (OAA), which is administered by the US Department of Health and Human Services under the Administration on Aging. An evaluation of the OAA Nutrition Programs conducted in 1993–1995, using a nationally representative sample of meals participants, showed that the home-delivered meal comprises 30–50% of participants’ total daily food and nutrient intakes. Use of the OAA meal programs resulted in dietary intakes that exceeded one third of the 1989 recommended daily allowances; congregate meals participants had significantly increased intakes for 16 nutrients and home-delivered meal participants had significantly increased intakes for 12 nutrients compared to age- and gender-matched non-participants [10]. In southwestern Ontario, Canada, nutrition risk was reassessed after 18 months of meal participation. A telephone administered follow-up of 263 meals participants, who had been categorized as high risk at baseline using the SCREEN questionnaire (SCREEN score ≤45), showed a significant decrease in nutrition risk [11].

To investigate the impact of adding a home-delivered breakfast meal to the home-delivered lunch meals, breakfast meals were provided in a case (n = 167) control (n = 214) intervention 5 days/week to OAA Nutrition Programs in 5 states in the US. The breakfast group consumed an average of 300 kcal and 14 g protein more per day (p < 0.001) and had significantly greater intakes of folate, calcium, magnesium, potassium, iron and zinc [12].

Despite the successes of food-based interventions (table 1) in a variety of community, residential and healthcare settings, inadequate funding for food-based interventions, inadequacies in the utilization and availability of registered dietitians, and lack of continuity of care at discharge limiting enrollment of at-risk individuals into food-based programs (such as congregate or home-delivered meals), contribute to the widespread use of ONS in all settings.
Availability of Oral Nutrition Supplements

The number and variety of products marketed as ONS, the number and types of claims for these products, and the types of ingredients used has increased significantly since the 1970s when the first ONS became commercially available [13]. Most ONS are intended for those individuals who have altered dietary requirements that cannot be achieved by conventional diet or food modification, or for management of distinctive nutrient needs resulting from a specific disease or condition that impairs ability to ingest, digest, absorb or metabolize nutrients. It is most notable that there appear to be no published randomized trials comparing food modification to oral nutrition supplementation that is isocaloric or of equal nutrient composition, and thus, no systematic reviews with meta-analysis are available comparing these two oral nutrition intervention entities equally.

Oral Nutrition Supplements versus Dietary Intervention

A meta-analysis using the Cochrane method was conducted investigating the efficacy of dietary advice (i.e., nutrition counseling) compared to either: no advice, provision of ONS, or advice plus ONS [14]. Twenty-four randomized trials were reviewed that included dietary advice provided by a dietitian or other healthcare professional to adults who had chronic disease or were categorized as being at nutrition risk. The number of usable studies was small for all outcomes. No significant difference in mortality was observed comparing dietary advice to no advice. In comparing advice with provision of an ONS, greater energy intakes were observed and greater weight gain after 3 months of ONS. No differences were observed in length of hospital stay or mortality. In comparing dietary advice to advice plus ONS, no differences in energy intakes (1 study), weight change (3 studies) or mortality (5 studies) were observed, but a small favorable difference in hand grip strength was found with advice plus ONS. Although the authors concluded that there is a lack of evidence supporting providing dietary advice, these data are confounded

Table 1. Strategies to improve the adequacy of dietary intakes using food

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<tr>
<td>Nutrition education and counseling</td>
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<td>Feeding assistance</td>
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<td>Improving dining environment atmosphere</td>
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<td>Flavor enhancement of menu items</td>
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<td>Enhancing the energy and/or nutrient density of food items</td>
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<td>Congregate meals</td>
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<td>Home-delivered meals</td>
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<td>Snacks between meals</td>
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82
in that not all dietary advice was provided by a registered dietitian and there is a bias in comparing a cognitive intervention (dietary advice) to a physical intervention (ONS).

A randomized trial was conducted in 4 LTC facilities to compare provision of 3 between-meal snacks per day to an 225-gram 300-kcal ONS provided 3 times daily for 6 weeks [6]. Residents who were at nutrition risk based on a 2.5- to 3-kg weight loss over the prior 6 months were enrolled. No compensation in habitual caloric intakes was observed with snacks or ONS. Average energy intakes increased by 26–30% in the snack group and 46–50% in the ONS group. It is not clear from the data whether the kilocalorie and nutrient contents of the snacks provided were comparable to the nutrient contents of the ONS.

**Oral Nutrition Supplements in Chronic Health Conditions**

**Hip Fracture**

In a systematic review and meta-analysis of randomized controlled trials of nutrition support after hip fracture, 8 of 21 trials used ONS in 448 participants [15]. No significant effects on length of hospital stay or mortality were observed. When the data were pooled to combine the outcomes of complications and mortality into one outcome variable, ONS appeared to reduce the number of patients with the combined clinical outcome by 48% (RR 0.52, 95% CI 0.32–0.84). In an update of this review, 4 newer randomized trials showed a 52% reduced risk of complications of hip fracture with ONS (OR 0.48, 95% CI 0.24–0.96).

**Pressure Ulcer**

A pilot study was conducted with 9 adults (55–84 years old; BMI 17.9–27.2) who were admitted for surgical treatment of chronic skin ulcers. ONS were provided 1–4 times daily to meet a caloric intake goal of 25 kcal/kg. ONS provided 35% of total energy intakes and appeared to help with wound healing with a 90% rate of skin graft acceptance at 10 days postoperatively. Subjects also received a daily multivitamin and 500-mg vitamin C supplement [16]. A larger study of ONS with 672 older adults who were at increased risk of developing pressure ulcers showed ONS reduced risk by 43% (95% CI 1.03–2.38) [17]. However, a comprehensive search on clinical outcomes from ONS in adults with pressure ulcers resulted in only 5 of 15 studies that were useable for meta-analysis [18]. Of the 5, four (n = 1,224) compared ONS to routine care in adults at risk of pressure ulcers. Only intervention with a high-protein ONS showed a significant reduction in the incidence of pressure ulcers (OR 0.75, 95% CI 0.62–0.89). The authors estimated that 19.25 patients would have to receive ONS to prevent one pressure ulcer.
Oral Nutrition Supplements in Chronic Disease States

**Diabetes Mellitus**

A systematic review in which ONS were used with adult patients with type I or II diabetes mellitus resulted in 16 of 23 studies for meta-analysis [19]. In one short-term randomized controlled trial, ONS resulted in lower postprandial glucose and insulin levels and glucose area under the curve compared to routine care. In addition, using a diabetic-specific formula (i.e., higher in fat, fructose and fiber) versus isocaloric food-based afternoon snacks lowered postprandial glucose. Using a diabetes-specific formula compared to a standard formula also improved glycemic control as 6 randomized controlled trials showed significantly less rise in postprandial glucose level by 1.03 mmol/l, 2 trials showed significantly lower peak blood glucose concentration by 1.59 mmol/l, and 4 trials showed significantly lower glucose area under the curve.

**Chronic Renal Disease**

A systematic review of ONS in chronic renal disease resulted in 18 studies (n = 541), but insufficient comparable data to perform meta-analysis on clinical or functional outcomes [20]. In assessing the 14 studies that compared renal disease-specific ONS to routine care, it appeared that disease-specific ONS increased energy and protein intakes as well as the serum albumin concentration.

**Stroke**

In a 15-country randomized trial of acute stroke patients who were not dysphasic, usual hospital diet (n = 2,007) versus usual diet plus ONS (n = 2,016) showed no difference in the frequency of in-hospital complications (defined as pneumonia and urinary tract infections), length of hospital stay or mortality [21]. However, only 8% of patients in both groups were categorized as undernourished (by observation) and dietary data were not collected to evaluate actual consumption.

**Cancer**

In a meta-analysis of 3 randomized controlled trials of ONS provided to patients with cancer who were undergoing radiation therapy [22], the findings showed an average increase in energy intakes of 381 kcal/day as compared to caloric intakes from standard hospital meal services.

Oral Nutrition Supplements in General Hospitalized Patients

Several comprehensive meta-analyses have been conducted to summarize and evaluate the published evidence on outcomes of ONS in hospitalized patients with various conditions and disease states. In a review of the
literature published from 1970 through 1996, 20 clinical trials were evaluated in which ONS was used in 1,495 hospitalized patients [23]. Although less than one third of the authors reported reliable methodology, supplementation appeared to increase body weight with a pooled weighted mean difference of 2.06% (95% CI 1.63–2.49%) and reduce mortality by 37% (OR 0.61, 95% CI 0.45–0.82). These findings were supported by a prospective randomized trial in which the oral intakes of 381 patients (aged 61–79 years) were supplemented daily with a 180-kcal ONS that was distributed during daily medication rounds. Treatment group subjects consumed significantly more calories (1,409 ± 448 vs. 1,090 ± 417 kcal), had a 1% weight gain compared to a 1% weight loss in the control group, and had a significantly lower mortality rate (14.7 vs. 35%).

Another systematic review of 55 randomized or quasi-randomized trials using ONS in adults aged ≥65 years old (n = 9,187) showed significantly greater energy and protein intakes with ONS [24]. Nineteen of the 55 trials showed decreased in-hospital complications (i.e., infections, incomplete wound healing, pressure sores or exacerbation of disease) with an OR of 0.72 (95% CI 0.53–0.97). Reduced mortality was observed in 25 trials (OR 0.86, 95% CI 0.74–1.00), which was most pronounced in adults who were aged ≥75 years.

A review of 49 randomized or quasi-randomized trials included a total of 4,790 adults aged ≥65 years old, with 40% residing in the community and 60% in acute or chronic care settings [25]. The minimum ONS intervention was 10 days. Twenty-nine studies reported increased total daily energy and protein intakes with ONS; however the variety of dietary assessment methods used did not allow meta-analysis of dietary data. Data from 34 trials showed a benefit from supplementation for percentage weight change with a pooled mean difference in weight change of 2.3% (95% CI 1.9–2.7) and data from 14 trials showed a benefit for mid-upper arm circumference with a pooled weighted mean difference of 1.2% (95% CI 0.4–2.0). Data from 10 studies showed no benefit from supplementation for length of hospital stay with a pooled weighted mean difference of –1.98 days (95% CI 5.20–1.24). Thirty-two trials showed that the relative risk for mortality was significantly reduced by 60% in supplemented subjects (RR 0.40, 95% CI 0.59–0.92). However, reduced risk may have been specific to subjects who were categorized as undernourished (n = 1,825), with a relative risk of 0.72 (96% CI 0.55–0.94).

**Oral Nutrition Supplements in Assisted Living and Long-Term Care**

A randomized double-blind placebo-controlled trial was conducted with 68 adults (≥65 years old, BMI ≤25) living in homes for the elderly or sheltered
Silver

housing [26]. They consumed ONS twice a day between meals for 6 months. The supplement group had a significantly greater total energy intake and a 2.5% greater weight gain (p = 0.031), but no difference in body composition and physical function. Importantly, no compensation was observed in the amount of caloric intakes from regular meals.

Oral nutrition supplementation is the most often prescribed approach to prevent or attenuate unintentional weight loss in LTC. Studies show that consumption of ONS is high when residents are offered choices that meet taste preferences and when they receive adequate assistance to promote consumption [27, 28]. However, LTC residents receive ONS less than one third of the time that they are prescribed and nursing home staff spends only 5% of the time that is needed for adequate encouragement of oral supplement intakes. Hence, LTC residents consume more calories when provided with snack foods and beverages between meals [29] and family members rate providing multiple between-meal snacks throughout the day as a more preferable nutrition intervention [30]. Nevertheless, ONS do not appear to interfere with food and beverage intakes in LTC and energy intakes have been increased as much as 50% [6].

**Conclusion**

The conditions of adult marasmus (energy undernutrition) and adult kwashiorkor (protein-energy undernutrition) often remain unrecognized and untreated. Yet, undernutrition contributes to a poor prognosis for many acute and chronic conditions and disease states. The most common cause of undernutrition, inadequate dietary intake, is preventable. Despite the successes of food-based strategies, inadequate funding for food-based interventions and food-based research promotes the widespread use of oral nutrition supplements – even in conditions such as hip fracture, pressure ulcers and stroke where the scientific and clinical efficacy is weak. As oral nutrition supplements are considerably more expensive than foods, national and global efforts should be made to fund, design, implement and evaluate the clinical and functional efficacy of food-based nutrition interventions. To make an equitable assessment of the overall efficacy of food-based strategies versus oral nutrition supplementation, adequately powered randomized controlled trials must be conducted where the dietary treatments being contrasted are homogeneous with regard to nutrient contents and the administration regimen. Further, registered dietitians – as the best trained healthcare professionals for nutrition intervention – should be more rapidly and wholly utilized in all care settings for identification and treatment of inadequate dietary intakes [31].
Food Modification versus Oral Liquid Nutrition Supplementation

References

Dr. Hoffer: I want to make some remarks and get your reactions to them. First, the use of meta-analysis in general, I understand the need for some way of summarizing or gaining an understanding from large numbers of studies. Meta-analysis, of course, has many potential difficulties because it condenses and its principle is that there should be no heterogeneity between the different experiments and it was designed for testing drugs. The two issues I see as potential problems, but I don’t know the resolutions, because we do need something in the nature of meta-analysis, are that the types of therapy used vary tremendously and, returning to some comments about the grey zone, one needs to distinguish between providing nutrition to people who are malnourished and providing nutrition to people who don’t need the nutrition. This is comparable to carrying out a large, controlled trial of blood pressure-lowering therapy for people whose blood pressure is normal.

Following from that, my suggestion, in terms of science and promoting the concept of the so-called nutritional paradigm, is that in future controlled trials we should only treat those people who have the disease, knowing full well that others would benefit through prevention of the development of malnutrition. People who are not in on this or don’t comprehend it, like certain individuals in committees in Germany, they just won’t get it unless there are dramatic examples. Big pharma knows this full well. Look at those pivotal trials for lowering blood pressure and lipids, they are the great exemplars of the pharmaceutical model of medicine. They were for people who had cholesterol levels of >6 and diastolic blood pressure of >105 mm Hg. I think that one has to be sophisticated or canny about it, and do studies that even you don’t think need to be done because you are convinced. I think they must be done and must give dramatic results, because then the physicians and opinion leaders will click in, see it and shift to incorporate new ones. That is a suggestion, and I wonder what you and others think.

Dr. Silver: We all agree on the limits of meta-analyses. There are differences in the timeliness of the interventions included in meta-analyses, the duration of interventions, the delivery regimens, the targeted populations, measuring whether there was compliance or adherence, and differences in study design. So, there is a lot of opportunity for heterogeneity in meta-analyses and by no means do I suggest that is not true.
I also think that one of the key problems in clinical nutrition research is inadequate funding. Without adequate funding, it is very difficult to design randomized controlled trials, which are really very costly, and that is one of the things that I alluded to in my study which was randomized, controlled and cross-over designed. But, it was limited to 4 weeks and to looking at intakes in a 24-hour period because, even in a fairly well-funded study, we are still, at least in the US, very limited in terms of applied nutrition research and what we can do with the funding that we have.

I think that meta-analyses are a tool, and Dr. Elia is far more an expert than myself, but I think that they are meant to try to pull together a number of studies that may seem somewhat disparate but are in some ways trying to measure similar outcomes. So, we try to draw some inferences from that kind of data. I do think that there are some really good hints from the meta-analyses which have shown that these kind of outcomes, increased energy intake, increased weight gain, increased strength and decreased mortality, have been more significantly observed in older people who, because of age, may be more frail, and people of a low BMI. These are the older adults who are most likely to be at nutrition risk. We don't have agreed definitions, measurement instruments or outcomes. As I tried to point out in the oral nutrition supplementation literature, the outcome of complications; frankly, the word 'complications' doesn't really mean a whole lot to me, it is a very vague, loose term. I could pretty much decide which complication I think it should be and that is the one I will speak in favor of. There are some lessons to be learned and, because of our funding limitations, we don't have the kind of pharmaceutical money to do phase-one trials. I do think that we have to look at what evidence we have if we are trying to make an argument for types of interventions or reimbursement.

**Dr. León Sanz:** I fundamentally agree with you but I think that we need to include not just malnourished patients in those studies. I think that we could establish a comparison with metabolic syndrome, for instance, and we could use drugs to treat these patients before they actually fulfill the criteria for diabetes. Even in the drug area, we also treat patients at risk, not only patients with a formal diagnosis.

**Dr. Elia:** I agree with what Dr. Silver and Dr. Hoffer have said. I would like to reinforce some of the points. Meta-analysis can be used and abused. There is particular concern when meta-analysis is being done by technicians who know how the process of meta-analysis is done but have no clinical knowledge. Problems have arisen again and again. One of them is this categorization of heterogeneity and how that is mixed with other studies. Some meta-analyses have attempted to separate the so-called normally nourished from non-normally nourished people with completely different conclusions. This kind of problem may even arise within the study. In the Food trial, which is the largest trial ever in nutritional support, involving about 4,000 subjects, 92% of the patients were normally nourished. One has to take that into consideration. I would like to make one final point about heterogeneity, which is sort of said to be bad. In some situations, I would argue that it can be very useful. There is heterogeneity between studies and it is said that there should not be meta-analysis because you are looking at different populations, but sometimes you can find a covariate that beautifully explains that heterogeneity. This is the power of meta-regression which, I think, is not used sufficiently and can actually throw up new insights and new hypotheses as a result of looking into the causes of heterogeneity in a quantitative way, using meta-analytic techniques that are available on some software products.

**Dr. Silver:** Going back to the food-based intervention issue, I would like to raise a challenge to Nestlé because there is a big opportunity here in terms of food-based intervention and the concept of food modifications and enhancing energy and nutrient density. In our study the population was older Jewish adults and even though we were limited to using Kosher foods, which are much more expensive than regular foods.
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from a grocery store, the actual cost of the meal was only increased by USD 0.81. That is very low, considering the types of food we had to use. With the number of food products that Nestlé has available, Stouffer's packaged foods, the soups, the Lean Cuisines, the chef-made entrees, the Hot Pockets, Croissant Pockets, even the candy bars and cookies, and the Lean Pockets for obese older adults with malnutrition, there is a great opportunity there to be involved in food modification and food-based intervention. If you can look at it in terms of what Wyeth did when they created Centrum Silver, the concept that older adults have different nutrient needs, those needs could also be met by foods. But there might be a need for a line of food products that is specific to the nutrient needs of older adults.

Dr. Kondrup: I agree totally with you that this is an area that will see a lot of development in the future. About 97% of the money spent in hospitals on patient nutrition is actually on food. Artificial nutrition is really a small thing and I think that we could gain a lot of political influence and sympathy for our cause by working more seriously with the food part of it. I agree totally with you and would like to point out that this food thing is not just the technology offered. In our experience, when we label a patient as being at risk, he is eating too little and therefore should eat more. In about 50% of these cases, patients eat adequately because we tell them they are at risk. They have lost their incentive to eat, have lost appetite, but once prompted, a large number of them can eat adequately when they are given this label. For those who are not capable of eating adequately, we have the problem of early satiety, which is also a big challenge. Above all of this deductive natural side, we also have the narrative side of it, and we must remember that we are serving a meal to the patients, not just technology and energy. I think that there is a whole area of social sciences, sociology or whatever that we have to learn about to make this work with the food component.

Dr. Bistrian: I have comments for Dr. Hoffer and Dr. Elia, agreeing with some and disagreeing with others. For Dr. Hoffer, to disagree, some of the most convincing evidence for the role of nutritional support in the critically ill has occurred in non-malnourished patients, whether they be head trauma, burns or multiple trauma, that is the most convincing evidence we have. Those are people who are not malnourished and the earlier it is started, the more effective it is. Just doing it in malnourished patients is going to lose some of our most effective therapy. For oral nutritional supplements, probably the strongest evidence was in hip fracture, and mostly in very thin patients. To show that, without obvious malnutrition diagnoses, it was a tremendous benefit. In fact, in hip fractures, the number in several studies was so large that it was not necessary to combine them in a meta-analysis. They were three randomized trials all of sufficient size to justify the adoption, so to put them into a meta-analysis puts them in the problems that meta-analyses have.

There was a very important study on meta-analyses. They studied seven different conditions for which there had been meta-analyses conducted, in which large randomized trials were conducted subsequently that had para-analyses to show they could be definitive. The agreement between the meta-analyses done prior and the randomized trial, one third of the time you would have rejected a therapy that would have been effective, one third of the time you would have accepted a therapy that was not effective, and only one third of the time would the meta-analyses have predicted the right answer. So, these argue that even very well-conducted meta-analyses are better than experts saying what their expert opinion is, but it is a great distance from a randomized clinical trial.

Dr. Hoffer: I agree with what you have said, Dr. Bistrian, but I have a strong intuition that the critical care situation is different for the patient outside the ICU. I am talking about in-hospital because that is my experience. For that kind of patient, I
Food Modification versus Oral Liquid Nutrition Supplementation

suspect, it will be necessary to just find the sickest and clear-cut cases and treat only those who should be treated.

Dr. Bistrian: Because they are so heterogeneous. The beauty of dealing with one disease in the critically ill is that it’s one disease and we take away a huge amount of heterogeneity. If you look at the role of nutrition support outside the ICU, where patients have many diseases, there the homogenous nature is the malnutrition. So, if you are studying something homogenous in those, it is malnutrition. In the critical care unit, it’s the disease process that is the homogeneity and enables you to find outcomes with relatively small numbers.

Dr. Silver: I think it is also important to remember that our meta-analysis process starts with a comprehensive review of the literature, with 2,000 or 3,000 studies being collected that are supposedly looking at similar interventions and outcomes. Then, through a very careful process, it really boils down to 15–30 studies that are actually used in that analysis. That was overwhelmingly the case in the studies that I reviewed in the meta-analyses that I included in the presentation. They went through very strict criteria to weed out the studies that really were addressing the outcomes as best as we have defined them.

Dr. Hoffer: There are two meta-analyses where the same literature was used on whether albumin works. The first meta-analysis of a vast number of studies said that albumin increased mortality. The second meta-analysis done with the same data, showing why the first study was defective, the studies that were included and those that weren’t, gave a better meta-analysis and gave exactly the opposite conclusions. We have a second group, with parenteral versus enteral nutrition; numerous studies have shown that total parenteral nutrition is worse than enteral nutrition. However, the most recent meta-analysis, done in intensive care medicine, where they used the best third of randomized trials, only the intention-to-treat trials show the opposite, that total parenteral nutrition reduces mortality by 50%. This is the problem, these analyses have to be viewed with a great deal of caution.

Mr. Jedwab: With regard to the food idea, I am not quite sure how to interpret what you have been saying in the sense that the difference between food and classical clinical nutrition is almost comparing apples with oranges in the sense that they are almost by definition covering different benefit territories to start with. While it is true that Nestlé and our competitors have a vast range of foods and clinical nutrition, the target populations for whom these products were designed are completely different. When you talk about making a clinical trial comparing the two, and I totally understand the logic, but you render the trials of the two different products isocaloric, I assume when you mention homogenous you also mean isonitrogenous when you talk about making the micronutrients the same. Somehow by changing the rules of the game you will be comparing apples with apples rather than apples with oranges that you wanted. So, I must admit that I am not quite clear on where we are going with this.

Dr. Silver: I really don’t agree actually. I am not a food technologist or a food scientist, I am a nutrition scientist. I do think that it’s entirely possible to take foods, whether it is an individual food item, like a broccoli dish, or an entire menu, or a 7-day cycle of menus in a long-term care facility, and clearly measure the same outcomes, we can increase caloric intakes, we can increase protein intakes, we can increase vitamin and mineral intakes. We could look at the same type of outcomes because we are increasing the same things. When you get down to it, oral nutrition supplements come from foods. They are nutrients and nutrients come from foods. Of course, there is a technology to formulate and produce the product but I think the issue is that we haven’t invested the kind of funding, as limited as it is with oral nutrition supplements, we have invested even less in investigations of food-based interventions. Unless we are going to fund these types of interventions and really look at them in a scientific
and systematic way, we really can't make an argument, pro or con, if we haven't done the research.

Dr. Roessle: I am from the Nestlé Research Center and have often been involved in the design of clinical studies for nutritional outcomes. The difficulties that we have always faced, and are very different from mock trials, are that there is by definition no placebo treatment for any nutritional intervention. The benefits that we are talking about come from calories and protein in the first place. As soon as you render any intervention isocaloric or isonitrogenous with a different product you run into trouble. The second problem is that we are also looking at outcomes in nutrition where the patients are also getting drug treatments that cannot be suspend for ethical reasons during our nutritional intervention. This makes it so difficult to compare studies because a controlled treatment is not defined. So, the meta-analysis in our situation, if it shows a positive outcome, is the minimum consensus that you can get. But probably individual studies, if repeated, would get much more significant outcomes. But this is not possible for many reasons.

Dr. Kondrup: The question about who should have these specially developed foods: I think the supplements that we have now should be used in the hospital and perhaps until shortly after discharge from the hospital. Then, after that, there will be a period before the patient is capable of eating normally, and going shopping as usual. In that transition phase, it would be very useful to have some of these modified foods for the patient. So, we see the patient's journey and have to supply nutrients for the whole journey, from the ICU to full recovery.

Mrs. Anthony: Dr. Silver's challenge to Nestlé is very interesting, and this idea of the patient's journey makes great sense because, to me, enhanced foods and oral nutrition supplements don't necessarily compete. Oral nutrition supplements offer patients the option of meeting their needs and not having to worry about eating enough. It gives them one more option, but it is not their only option; they don't compete. Talking about reimbursement, what I find interesting about your proposal is that in many countries oral nutrition isn't reimbursed but patients don't want to pay for oral nutrition supplements because they see them as medicine. For example, patients may be willing to pay for an enhanced food that is more directed towards their age group. I am not sure that there will be foods for elderly diabetics, for instance, just because the economics of making these products have to hit a broad group to be economically reasonable. But it is a reasonable idea to ask if we can make a Lean Cuisine for the elderly; if we can make Hot Pockets for the elderly, etc. Yes we can; it might not be done, but it is an idea that we can't toss out and it is not necessarily for the sick elderly. When we talk about oral nutrition supplements, it is for people who are a little more ill. There are two things but they might help us a little in getting the public to think that they might have to pay a little more for a specifically designed food. It is an interesting thought and we just have to figure out how it can all be worked together.

Dr. Silver: We must remember what the patient's or client's preference is. In the study that Simmons and Schnelle [1] did on the long-term care facilities, the overwhelming preference was for food, not nutritional supplements, by both the residents and their families. I am not suggesting that there is no place for oral nutrition supplements, as you can see from the results of the meta-analyses, but I am saying that we must not forget about food.

Mrs. Anthony: I agree, but I also think that what we prefer and what actually happens are actually two different things. The challenge from dietitians is that food is better and we should work on food. I agree, but at one point we have to realize that if food isn't being accepted or isn't being taken, we need to look at other options. It also makes great sense to supplement foods and make them higher in energy and protein, but when we talk about cost, we always think food is cheaper. We never seem to take
into account the labor, extra people and the work it takes to get the food in. It doesn't always make it less cost-effective, but it is something that we need to think about because, in an institution where food is being individualized per patient, there will be extra labor costs which need to be taken into account. I am not against food; I fully support the use of food but, as dietitians, I think we are sometimes more idealistic than realistic.

Mrs. Skouroliakou: Are you talking about nutraceuticals because the young generation buys them everyday? Specifically people who are hard workers and don't like to cook. They think that, with nutraceuticals, they solve their problems. In my institution, I see these hard-working people and advise them to get nutraceuticals because it is good for them. Is that what you mean by enriched food?

Dr. Silver: That brings us into a whole different discussion. My study was a food-based intervention where we manipulated the energy and nutrient density of the meals themselves using actual food ingredients, and we showed a clear increase in caloric intakes without energy compensation. We did not look at longer term outcomes and we have not been funded to do that. Another thing that we have not been funded to do is look at the cost-effectiveness of food-based interventions. So, while we can make suggestions that it might be expensive, we actually have no data to support or not support food-based interventions.

Mrs. Le Tadic: I have a comment in reaction to the discussion on Nestlé's role with regard to providing food-based solutions. In the UK, we have put an approach together which is actually to go for food first. The solution that we give to healthcare professionals is to start by identifying those who need fortified meals to strive or to put on weight. We suggest food-based solutions first. One thing is that Nestlé doesn't have the same sort of portfolio of solutions in all the countries. In the UK, the main categories that we sell are confectionary and coffee. That put aside, we also have milk and concentrated milk which could be a basis for a solution. What we do face, and this is the reality check that Mrs. Anthony was talking about, although we go for this kind of solution, it is not necessary to say give this food systematically. The convenience of the solution competes with common sense most of the time. In a cost-driven economy, with reduced staff in nursing homes, reduced staff in hospitals, and less and less qualified staff as well, who can understand this counseling practice? It is much easier to drop something on the table. So, that is the reality check. At the end of the day, my question is not so much should there be competition between both forms but perhaps a different way of selling clinical nutrition to the patient in a more attractive fashion, instead of having to compete against solutions that, to be honest, are like banging our heads against the wall. There is no staff to take care of it. That is what I see everyday.

Dr. Silver: I don't think the purpose was to have a battle between food-based intervention and oral nutrition supplementation interventions. I think the question is where do we have evidence to show that either one works; where do we not have evidence; who should we really be providing, and what could we do more of?

Mrs. Le Tadic: But should it be a question of eating versus not eating?

Dr. Silver: I don't know if that's the question. The question is when to enhance food options and when to provide ONS.

Reference
