Credible Evidence in Nutrition Health Economics Outcomes Research: The Effects of Oral Nutritional Supplementation on Hospital Outcomes

Tomas J. Philipson, PhD (with Julia Thornton Snider, PhD, Darius N. Lakdawalla, PhD, Benoit Stryckman, MA, and Dana P. Goldman, PhD)

Malnutrition is a serious problem among hospitalized patients. A growing body of evidence suggests that malnourished patients face a heightened risk of poor outcomes, including increased length of stay,[1-3] higher rates of complications[2,4] and readmission,[5,6] and greater risk of mortality.[2,7-9]

Several studies have found that oral nutritional supplements (ONS) reduce the likelihood of these adverse outcomes.[10-14] In general, however, the studies published to date are limited in various ways—modest sample sizes or narrowly selected patient populations, or the possibility of selection biases or a study environment that does not convincingly reflect real-world conditions.

Randomized controlled trials (RCTs) usually are considered the "gold standard" of evidence, but they have limitations, such as unrealistic pricing, artificially high adherence, small unrepresentative samples, and short follow-up times. Observational studies, on the other hand, better reflect real-world adherence and pricing of therapies and alternative treatments; may follow enormous patient populations, thus allowing sufficient sample sizes for the study of subpopulations; and allow researchers to measure long-term outcomes by following patients for extensive periods.

In an increasingly cost-pressured environment, economic assessments will determine a therapy's value. Given the limitations of RCTs, the availability of credible observational studies will become crucial. A study's credibility, in turn, will depend on its appropriate design.

A crucial factor in the design of any study is to avoid selection bias. RCTs do this by randomizing patients to treatments. However, an observational study will likely have a direct correlation between the patients who receive a treatment and the severity of illness, with a resulting systematic dissimilarity between patients and

controls. Health economists use a device called an instrumental variable to sever the relationship between the sickness of the patient and the treatment decision, creating what is called a "natural experiment."

The authors conducted a retrospective data analysis on the effect of ONS in the real-world hospital setting. The study sought to compare the actual cost of treatment (including supplies, labor, and equipment depreciation), the length of stay, and the 30-day readmission rate of patients receiving ONS to those same outcome variables in patients who were not given ONS.[15]

Samples were drawn from the Premier Perspectives® database and covered the years 2000–2010. Of the nearly 44 million adult inpatient episodes recorded there, the overall rate of using ONS was 1.6%. In most cases, patients given ONS were 11 years older and considerably sicker than the typical inpatient, making selection bias a concern.

To reduce the likelihood of bias, the study was restricted to a matched sample, which allowed comparison of each patient who received ONS with a similar patient who did not receive ONS. Factors used to create the matched sample included (but were not limited to) age, gender, marital status, race, hospital admission history, insurance type, admission source (eg, emergency department, physician referral), and size and type of hospital (eg, urban, teaching).

Hospitals' differing propensities to use ONS were calculated from information contained in the database. This served as the instrumental variable, allowing removal of the effects of patients' individual characteristics from the analysis and employing a natural experiment to identify the effect of ONS on outcomes. Instrumental variable analysis was employed to specifically address potential bias due to nonrandomized treatment selection, which was not possible to address with propensity matching alone.

The study showed that using ONS improved patient outcomes along all three measured dimensions—cost, length of hospital stay, and the 30-day readmission rate. It was found that the use of ONS leads to a 21.6% decrease in the cost of each episode (Fig 1). Given a cost per episode of $88.26 (fully burdened to include all relevant capital and labor expenses), each dollar spent on ONS generates more than $52 in savings from reduced episode cost.
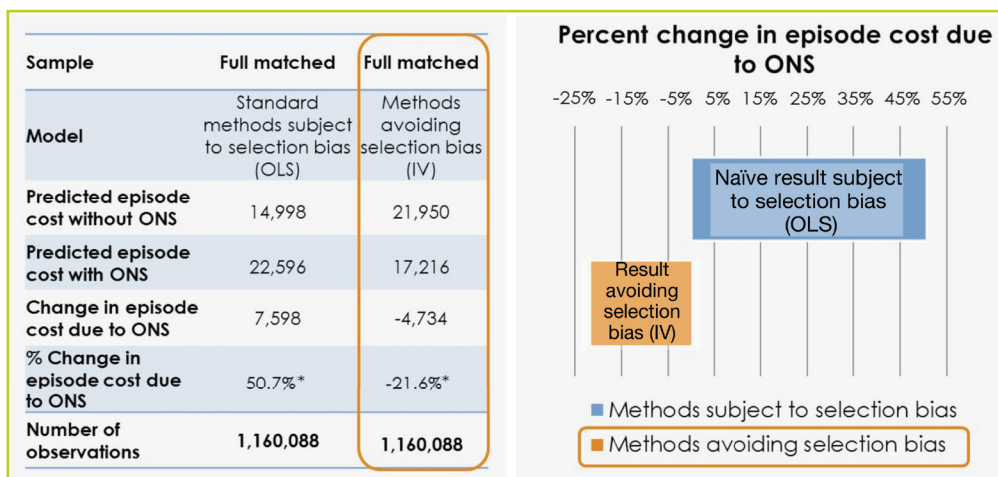
Sample	Full matched	Full matched
Model	Standard methods subject to selection bias (OLS)	Methods avoiding selection bias (IV)
Predicted episode cost without ONS	14,998	21,950
Predicted episode cost with ONS	22,596	17,216
Change in episode cost due to ONS	7,598	-4,734
% Change in episode cost due to ONS	50.7%*	-21.6%*
Number of observations	1,160,088	1,160,088

Fig 1. Change in episode cost due to ONS. Costs were measured in 2010 United States dollars and predicted using Duan's smearing estimator. Regressions include group fixed effects for the following groups: 1 day–3 months, 3 months–1 year, 1 year–2 years, 2 years–3 years, 3+ years. In addition to use of ONS, regression covariates include age, age squared, sex, married indicator, race dummies, Charlson severity index components, history of admission in previous 6 months, payer dummies (Medicare, Medicaid, managed), year dummies, quarter dummies, admission source dummies (emergency department, physician referral, transfer), number of beds in hospital, urban location, teaching hospital, and dummies for the four US Census regions. In statistics and economics, particularly in regression analysis, a dummy variable (also known as an indicator variable) is one that takes the values 0 or 1 to indicate the absence or presence of some categorical effect that may shift the outcome. The instrument employed is the percent of patients in a given hospital in a given quarter receiving any ONS.[15]

*$P<0.01$

IV=instrumental variables, OLS=ordinary least squares, ONS=oral nutritional supplements

ONS use also leads to a 21% decrease in length of hospital stay (Fig 2) and lowers 30-day readmission rates by nearly 7%, even under conservative assumptions (Fig 3). Calculating the readmission effect required restricting the sample to episodes with follow-up to overcome the issue that the data does not make a distinction between loss of follow-up due to improved health or death.

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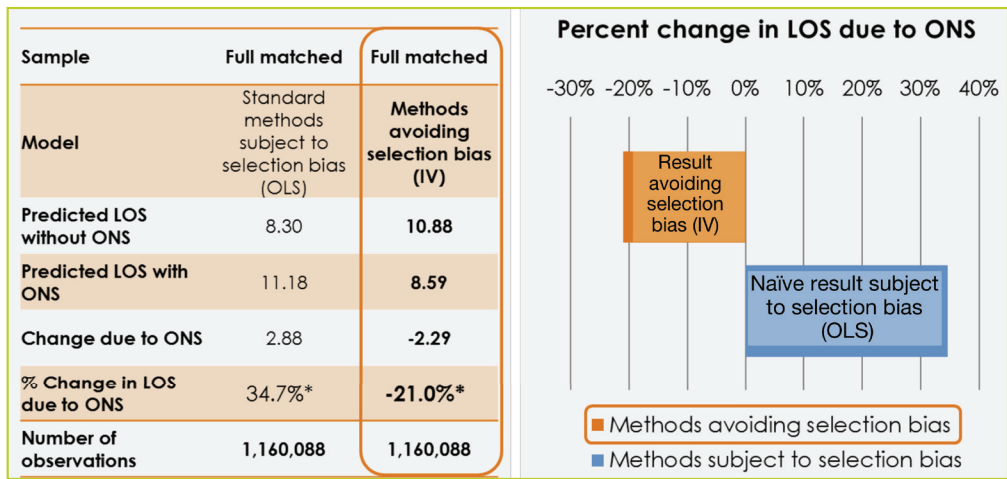
Sample	Full matched	Full matched
Model	Standard methods subject to selection bias (OLS)	**Methods avoiding selection bias (IV)**
Predicted LOS without ONS	8.30	10.88
Predicted LOS with ONS	11.18	8.59
Change due to ONS	2.88	-2.29
% Change in LOS due to ONS	34.7%*	-21.0%*
Number of observations	1,160,088	1,160,088

Percent change in LOS due to ONS

Result avoiding selection bias (IV)

Naïve result subject to selection bias (OLS)

■ Methods avoiding selection bias
■ Methods subject to selection bias

Fig 2. Change in length of hospital stay due to ONS. Costs were measured in 2010 United States dollars and predicted using Duan's smearing estimator. Regressions include group fixed effects for the following groups: 1 day–3 months, 3 months–1 year, 1 year–2 years, 2 years–3 years, 3+ years. In addition to use of ONS, regression covariates include age, age squared, sex, married indicator, race dummies, Charlson severity index components, history of admission in previous 6 months, payer dummies (Medicare, Medicaid, managed), year dummies, quarter dummies, admission source dummies (emergency department, physician referral, transfer), number of beds in hospital, urban location, teaching hospital, and dummies for the four US Census regions. In statistics and economics, particularly in regression analysis, a dummy variable (also known as an indicator variable) is one that takes the values 0 or 1 to indicate the absence or presence of some categorical effect that may shift the outcome. The instrument employed is the percent of patients in a given hospital in a given quarter receiving any ONS.[15]

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Sample	At least 1 follow-up	At least 1 follow-up
Model	Standard methods subject to selection bias (OLS)	Methods avoiding selection bias (OLS)
Predicted probability of readmission without ONS	0.334	0.343
Predicted probability of readmission without ONS	0.331	0.320
Change due to ONS use	- 0.003*	- 0.023*
% Change due to ONS use	- 0.9%	- 6.7%
Number of observations	**862,960**	**862,960**

Fig 3. Change in 30-day readmission rates due to ONS use. Costs were measured in 2010 United States dollars and predicted using Duan's smearing estimator. Regressions include group fixed effects for the following groups: 1 day–3 months, 3 months–1 year, 1 year–2 years, 2 years–3 years, 3+ years. In addition to use of ONS, regression covariates include age, age squared, sex, married indicator, race dummies, Charlson severity index components, history of admission in previous 6 months, payer dummies (Medicare, Medicaid, managed), year dummies, quarter dummies, admission source dummies (emergency department, physician referral, transfer), number of beds in hospital, urban location, teaching hospital, and dummies for the four US Census regions. In statistics and economics, particularly in regression analysis, a dummy variable (also known as an indicator variable) is one that takes the values 0 or 1 to indicate the absence or presence of some categorical effect that may shift the outcome. The instrument employed is the percent of patients in a given hospital in a given quarter receiving any ONS.[15]

*$P < 0.01$

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In the full-matched sample, each dollar spent on ONS generates at least $2.56 in savings from avoided readmissions. Findings imply that the modest cost of using ONS is offset by savings from readmissions alone.

Groups of patients with shorter durations of follow-up usually were older, had more comorbidities, stayed longer in hospital, and generally were sicker than patients with longer follow-up. Using the duration of follow-up as a proxy for underlying health status, it was found that ONS most benefits the sickest patients.

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The study contributes to the literature by addressing current gaps in the evidence. Previous observational studies were limited in their ability to account for possible bias because of nonrandom selection into ONS treatment. By using propensity score matching and instrumental variables, the issue of potential bias was addressed. In earlier studies, small patient populations had limited the generalizability of the findings. A pool of 44 million adult inpatient episodes gives this most recent study the generalizability and relevance that earlier studies often lacked.

Still not determined is the effect of ONS on preventing readmissions completely. The current data did not distinguish between readmissions that were avoided because of the recovery of the patients and those that may have resulted from the patients' death. A further avenue for study is the impact of ONS on patient outcomes following hospital stay. Data do not follow patients after release from the hospital, so the study only captures the impact of ONS while patients remain in the hospital setting.

Understanding how therapies work in the real world requires the application of technically appropriate methods to real-world data. RCTs are useful for showing clinical efficacy, but they cannot demonstrate a therapy's effects under real-world conditions. Understanding real-world effects requires real-world (observational) data. It is possible to apply econometric techniques to address the problem of selection bias in observational data. The study described here is offered as a case in point to show how applying these methods can elicit greater understanding of an important question that affects patient care in an age increasingly concerned with the costs of that care.

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