

## Review

# Is the Use of Specialized Nutritional Formulations a Cost-Effective Strategy? A National Database Evaluation

Adrien Strickland, MD; Anita Brogan, PhD; Janis Krauss, RN; Robert Martindale, MD, PhD; and Gail Cresci, MS, RD/LD, CNSD

*From the Department of Surgery, Medical College of Georgia, Augusta, Georgia*

**ABSTRACT.** *Background:* We apply currently published clinical outcomes data to length of stay and hospital cost to determine the potential economic benefit associated with the use of specialized nutritional formulations in elective surgical, trauma, and medical patients. Although the use of immune-modulating formulations has repeatedly shown favorable clinical outcomes, including decreased complications (both infectious and noninfectious), length of stay (both ICU and total days), and ventilator days, the cost-effectiveness of nutritional modulation of the immune response in a US-based population has not previously been explored. *Methods:* Data for the current study were obtained from a large national database with 126 member hospitals and data from over 1 million patients. Data extracted from the database included patient type (surgical, medical, and trauma) and subservice, whether the hospital stay was “complicated” or “uncomplicated” (as determined by diagnosis-related groups and *International Classification of Diseases, Ninth Revision* coding), mean length of stay, mean cost, and incremental cost per complication experienced. The clinical outcomes measures from 3 major peer-reviewed studies were then applied to the cost data in order to determine the cost savings associated with the use of specialized nutritional formulations in

each of the patient populations. Additionally, cost data were segmented by region of the United States (New England, mid-Atlantic, South, Midwest, Southwest, and West) and by primary focus of the health care facility (academic, indigent care, large community) to enable more meaningful cost comparisons. *Results:* For the medical patient population, according to the published rate of 51% decrease in risk of infectious complications and a decreased length of hospital stay of 9.7 days, net cost savings (after accounting for the increased costs of administering immune modulating formula) is \$2066. The same calculations were done for surgical and trauma patients, with \$688 and \$308 net cost savings per patient, respectively. These figures assume a base infection rate of 5%. Expected cost savings vary markedly for deviations in base infection rate and slightly for differences in facility type or region of the country. *Conclusions:* This study demonstrates that specialized nutritional formulations are a cost-effective way for hospitals to improve clinical outcomes while reducing resource consumption and total cost. These benefits are observable in all patient types, all facility types, and all regions of the United States. (*Journal of Parenteral and Enteral Nutrition* 29:S81–S91, 2005)

The concept of specialized nutritional formulations modulating immune function has been evaluated in more than 30 well-designed, peer-reviewed, clinical trials since the early 1990s. Three meta-analyses have also been completed confirming the clinical benefits. In all but a few of these studies, a positive clinical outcome was noted in the groups receiving a variety of specific nutrients, with reported modulating influence on either immunity or inflammation. The specific nutrients alone or in combination include arginine, glutamine, ribonucleic acids and  $\omega$ -3 fatty acids, and trace nutrients.

Reduction of complications, both infectious and non-infectious, is now a prime focus in the acute care and critical care arenas. The added expense of a single intensive care unit (ICU) infection has been estimated at \$21,000.<sup>1</sup> These infectious complications are becoming

even more important with the rise in bacterial species resistant to 1 antibiotic or multiple antibiotics. The increased microbial resistance has made many antibiotics relatively ineffective in the ICU setting and, therefore, the push for prevention of infections is becoming a subject of growing interest and attention. In addition to infectious complications, the adverse impacts and cost associated with noninfectious complications are often marked. For example, Waitzberg et al<sup>2</sup> have recently demonstrated that anastomotic leaks, although frequently noninfectious, are the most costly postoperative complication in the surgical patient population.

Patients with trauma, sepsis, or undergoing major surgery exhibit depressed immune function and are at relatively high risk of developing nosocomial infections and other major morbidities. Several nutrients in specialized nutritional formulations have been shown to improve immune function and decrease infectious complications,<sup>3,4</sup> which would ultimately decrease mortality, morbidity, and resource use. Several specialized nutritional formulations are now commercially available; the profile of these immune modulating ingredi-

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Correspondence: Adrien Strickland, MD, 1120 15th Street, BI-4072, Augusta, GA 30912. Electronic mail may be sent to astricklandmd@students.mcg.edu.

TABLE I  
Details of studies used

Study	Trial feeding	Control feeding	Double-blind	Patient type/number/arm
Gianotti	Impact*	No enteral nutrition	Y	Well-nourished GI surgery 305 total = 102 control group 102 preoperative group 101 perioperative group
Braga	Impact	Standard enteral diet	Y	Malnourished GI surgery 150 total = 50 control group 50 preoperative group 50 perioperative group
Beale (meta-analysis)	Impact, Immunaid†	Varies	Varies	1,282 total = 434 medical 247 trauma 601 surgical

\*Impact, Novartis Nutrition, Minneapolis, MN.

†Immunaid, BBraun, Irvine, CA.

ents is listed and reviewed elsewhere in this supplement. Demonstrated benefits include decreasing the incidence of complications (both infectious and noninfectious), ventilator days, ICU length of stay (ICU LOS), and overall LOS.<sup>5-7</sup>

Given these clinical findings, practitioners will presumably be motivated to use immune-modulating enteral formulas in their treatment of patients. Balanced against this clinical demand will be a consideration of the economic consequences of their use. This cost-effectiveness study was undertaken to facilitate decision-making, health care policy, and revision of nutritional standards of care.

MATERIALS AND METHODS

Available clinical outcomes data from 3 published peer reviewed studies using commercially available immune-modulating formulas (Impact [Novartis Nutrition, Minneapolis, MN] and Immunaid [BBraun, Irvine, CA]) in 4 specific patient populations (well-nourished surgical, malnourished surgical, trauma,

and medical ICU). Each of these studies was intensely reviewed to ensure methodological quality, consistency of study design, and applicability of clinical outcome measures. The methodology for each of the studies used is summarized below, and a comparison of the study designs is presented in Table I. Cost data (in US dollars) were collected from the Medical College of Georgia, Augusta, GA (MCG), and University Health-System Consortium's (UHC, Chicago, IL) clinical database. A detailed methodology for each of the clinical studies can be found in other manuscripts in this *Journal of Parenteral and Enteral Nutrition* supplement and the original referenced manuscripts. The UHC methodology is given in detail below.

Clinical studies (see current supplement pages)

Well-nourished surgical patients; refer to Gianotti et al, 2002.<sup>6</sup>

Malnourished surgical patients; refer to Braga et al, 2002.<sup>7</sup>

Trauma and medical ICU patients; refer to Beale et al, 1999.<sup>5</sup>

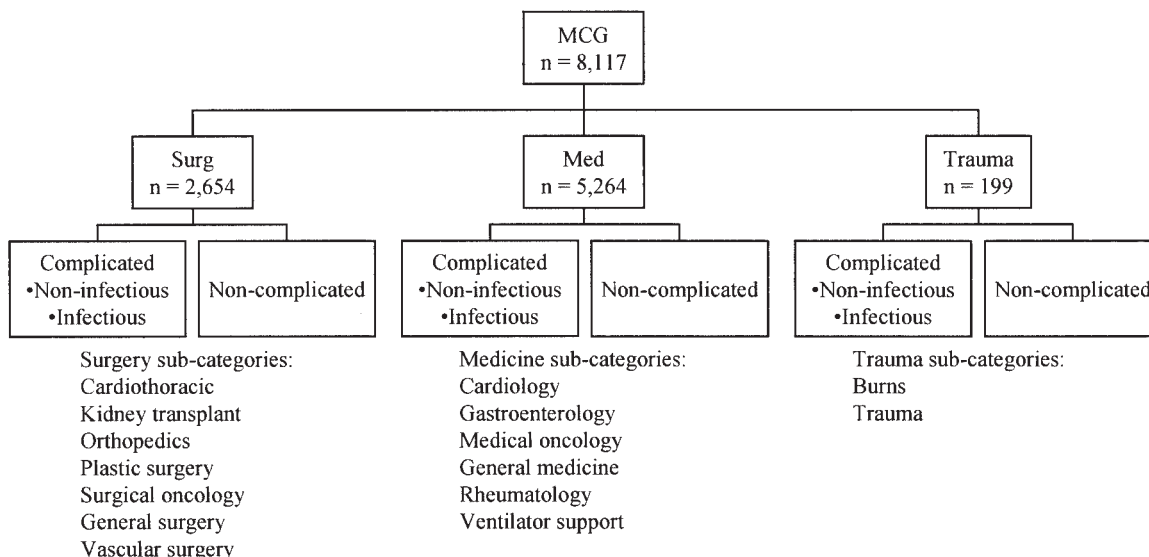


FIG. 1. Medical College of Georgia (MCG) study design and patient category-subcategory mapping.

TABLE II  
*Definition of complications: University HealthCare Consortium*

Complication	Inclusion/exclusion criteria
1. Postoperative stroke	Secondary diagnosis postoperative CVA, not assigned nervous system DRG.
2. Aspiration pneumonia	Secondary diagnosis of aspiration without primary diagnosis of seizure, consciousness-altering drug overdose, trauma, poisoning, or DRG related to trauma.
3. Postoperative pulmonary compromise	Secondary diagnosis of postoperative pulmonary compromise, without assignment to respiratory or circulatory system DRG.
4. Postoperative GI hemorrhage or ulceration following non-GI surgery	Secondary diagnosis of postoperative GI hemorrhage without assignment to digestive system or hepatobiliary system and pancreas DRG.
5. Postoperative complications relating to urinary tract	Secondary diagnosis of postoperative urinary tract problem without assignment to urinary tract or male reproductive system DRG.
6. Cellulitis or decubitus ulcer	Other diagnosis (#6 or later) of decubitus ulcer and patient <80 years old, LOS $\geq 10$ days, not assigned skin, subcutaneous tissue or breast DRG, no diagnosis of drug abuse or plegia.
7. Septicemia	Secondary diagnosis of septicemia with septicemia-related DRG with LOS $\geq 3$ days, no primary diagnosis of infection, no DRG related to infection, no diagnosis of AIDS or compromised immunity or cancer.
8. Post- or intraoperative shock due to anesthesia	Secondary diagnosis of shock due to anesthesia.
9. Reopening of surgical site	Secondary procedure of reopening a surgical site 1 day or more after principal procedure.
10. Mechanical complications due to device, implant or graft, except organ transplant	Secondary diagnosis of mechanical problems, no primary diagnosis of a complication.
11. Miscellaneous complications of procedures	Secondary diagnosis of miscellaneous complication, no primary diagnosis of a complication.
12. Shock or cardiorespiratory arrest in hospital	Secondary diagnosis of shock, no assignment to respiratory system or circulatory system DRG, no primary diagnosis of hemorrhage.
13. Postoperative complications relating to the central or peripheral nervous system	Secondary diagnosis related to postoperative central nervous system, had disc surgery procedure or procedure for carotid endarterectomy. No primary diagnosis or DRG related to trauma.
14. Postoperative acute myocardial infarction	Secondary diagnosis of postoperative acute myocardial infarction with no assignment to circulatory system DRG.
15. Postoperative cardiac abnormalities except acute myocardial infarction	Secondary diagnosis of postoperative cardiac abnormalities with age $\leq 65$ and no assignment to circulatory system DRG.
16. Postoperative infections except pneumonia and wound	Secondary diagnosis of postoperative infection with no assignment to urinary tract DRG or male or female reproductive system DRG.
17. Procedural-related perforations or lacerations	Secondary diagnosis related to procedural perforation or laceration with qualifying diagnosis of a foreign body after principal procedure. No diagnosis of cancer, infected bowel, diverticulitis, or appendicitis. No primary diagnosis of trauma or trauma DRG.
18. Postoperative coma or stupor	Secondary diagnosis of postoperative coma without diagnosis or DRG related to trauma.
19. Nosocomial pneumonia after procedure	Secondary diagnosis of postoperative pneumonia, no assignment to respiratory DRG, no indication of immune system problems or diagnosis of AIDS or cancer.
20. Postoperative physiologic and metabolic derangements	Secondary diagnosis of postoperative physiologic derangement, no assignment to trauma, connective tissue or cardiac arrhythmia DRG. No diagnosis of trauma, diabetes, acute myocardial infarction, arrhythmia, cardiac arrest, or GI hemorrhage.
21. Complications relating to anesthetic agents or other central nervous system depressants	Secondary diagnosis of poisoning by anesthetics, no leading secondary (2–4) diagnosis of psychosis or other mental disorder, no diagnosis of attempted suicide or substance abuse, no DRG related to substance abuse, poisoning or allergic reaction.
22. Venous thrombosis and pulmonary embolism	Secondary diagnosis of thrombus or pulmonary embolism, no primary diagnosis of phlebitis or thrombophlebitis and no pulmonary embolism or DVT DRG.
23. Wound infection	Secondary diagnosis of postprocedure wound infection.
24. Postprocedural hemorrhage or hematoma	Secondary diagnosis of hemorrhage or hematoma or secondary procedure related to hemorrhage after the principal procedure.
25. Other complications of procedures	Secondary diagnosis of other complication of procedure without primary diagnosis of a complication.

CVA, cerebral vascular accident; DRG, diagnosis-related group; LOS, length of stay; DVT DRG, deep vein thrombosis diagnosis-related group.

### *UHC Cost Data*

In order to generate bills for services rendered and to profile clinical and cost-effectiveness of the care provided, health care organizations gather volumes of administrative data. These data are largely retrospective and collated after a patient has been treated by a health care organization. The coded abstract from a patient's medical record after discharge is used to compile the appropriate financial information that, in turn,

feeds into the Uniformed Billing system (UB-92) set up by the Center for Medicare and Medicaid Services. In order to generate "benchmark reports," health care organizations are oftentimes forwarding their administrative data to external agencies for analysis and reporting. Participation in external databases returns aggregate data reporting parameters such as LOS, cost per case, complications, readmission within 30 days, attending physician, principal procedure physician,

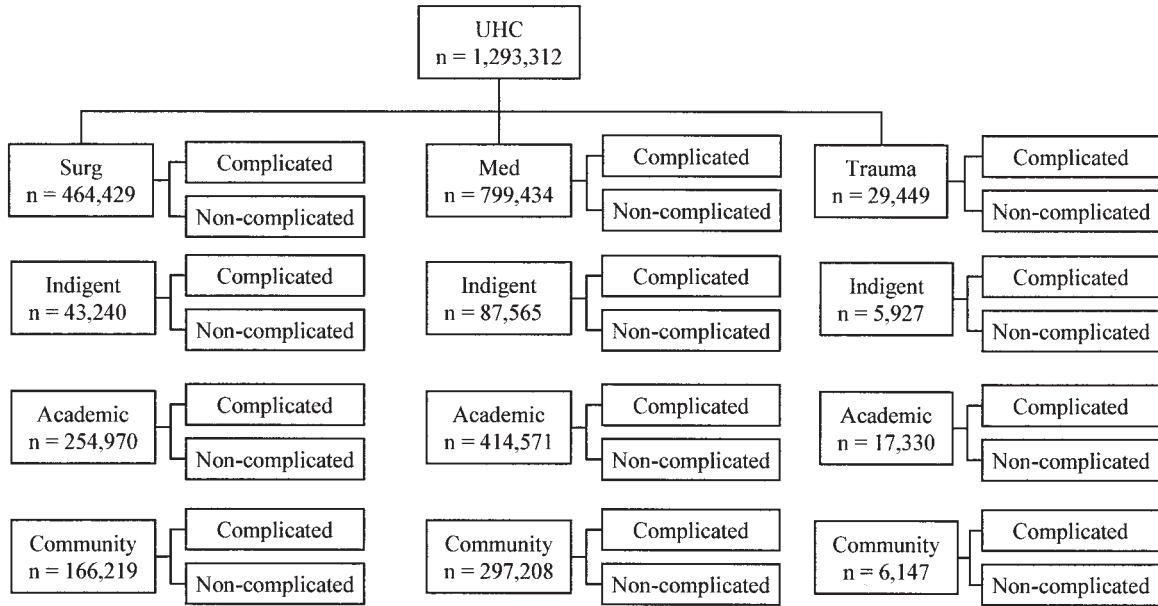


FIG. 2. University of HealthSystem Consortium (UHC) study design: facility types.

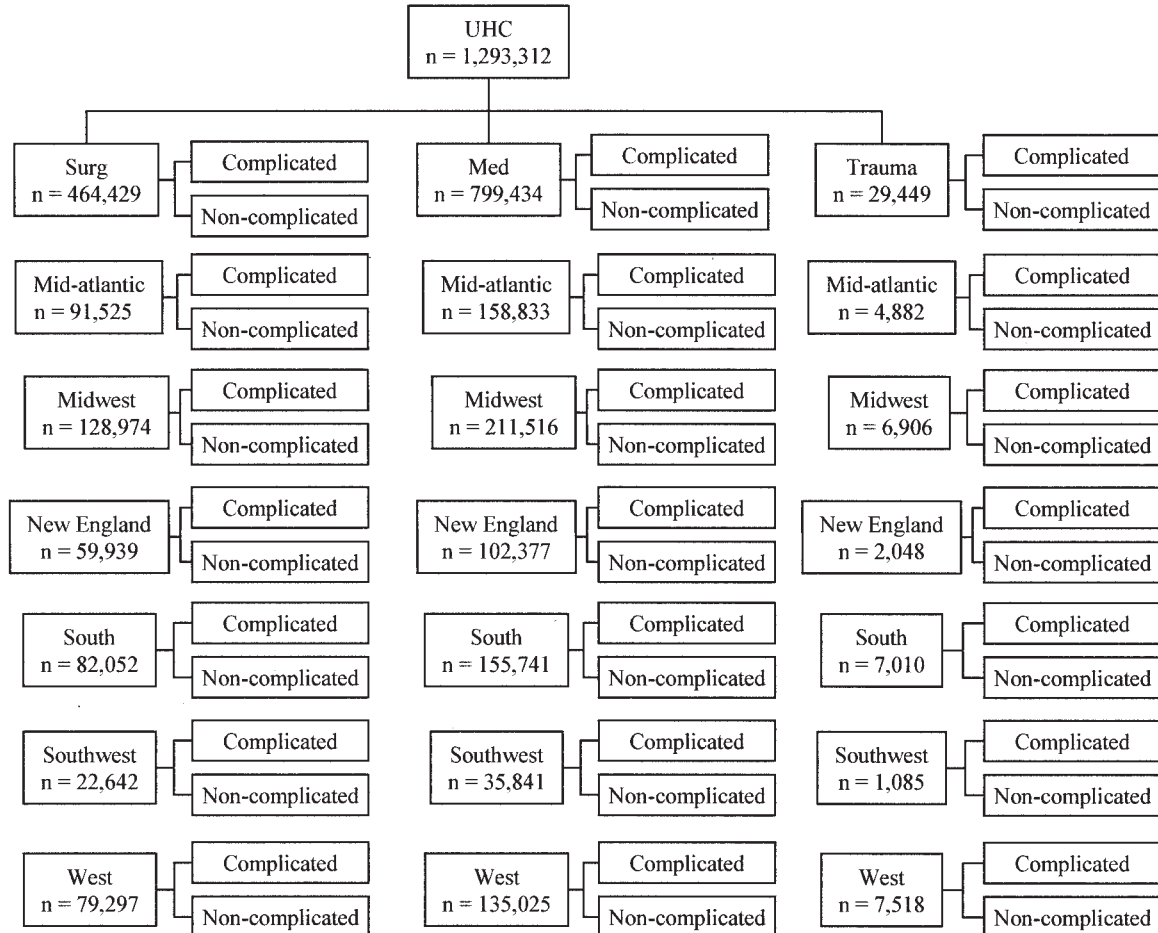


FIG. 3. University HealthSystem Consortium (UHC) study design: regions of the United States.

primary payer, admission source, and discharge disposition.

Guidelines for the external data are defined and developed by the organizations that act as repositories for this information.<sup>8</sup> Data for this study were obtained from an external database administered by the UHC. The UHC gathers data from more than 100 hospitals that participate with the majority categorized as academic medical centers.

The UHC database was queried initially for MCG-specific information only. Patients were grouped into 3 categories according to UHC product lines: surgery, medical ICU, and trauma, and then further into subcategories. For example, within the surgery category, patients were further divided into the subcategories of gastrointestinal surgery, orthopedic surgery, and plastic surgery (see Fig. 1 for more details). Within subcategories, patients were divided into 1 of 2 groups (“complicated” and “noncomplicated”), depending on whether or not they had experienced a postoperative/postadmission complication. Within the “complicated” patient group, patients were further divided into “infectious” and “noninfectious” complications. Information regarding LOS, resource consumption, complications/comorbidities, and costs were collected for all patients. The costs of complications included direct medical costs of treating postoperative complications for surgical patients and postadmission complications for medical and trauma patients. Routine postdischarge ambulatory visits after hospital discharge were included in the analysis. Postdischarge medications and indirect costs such as the patient’s loss of productivity were not taken into account. The categories of expenses analyzed included:

- Room and board, ICU, and general care units
- Physical therapy

- Respiratory therapy
- EKG/telemetry and other cardiac diagnostic services
- CT/MRI, nuclear medicine, x-ray, and other diagnostic imaging
- Laboratory
- Surgical services
- Blood
- Dialysis
- Pharmacy (including IV and antibiotic therapy)

The incremental LOS and cost (by category and as a total) of a complication (both infectious and noninfectious) within the 3 patient categories (surgical, medical ICU, and trauma) were determined. Clinical outcomes data from the 3 studies cited above were applied to the cost data, and the cost-savings associated with the aversion of specific complications was calculated. A “breakeven” complication rate was calculated for each subspecialty within the 3 patient groups. This analysis was repeated using just the patients experiencing “infectious” complications, and a breakeven infection rate was calculated for each of the 3 patient subgroups. Number needed to treat (NNT) and net savings per patient beyond the breakeven complication rates were also calculated. Detailed definitions of these terms are provided in Cost-effectiveness and Breakeven Analysis below.

Postoperative/postadmission infectious complications included septicemia, pneumonia (except aspiration pneumonia; this is recorded as separate diagnosis-related group [DRG]), cellulitis/decubitus ulcers, urinary tract infections, wound/surgical site infections, and “other infections” (excluding those specifically listed). Postoperative/postadmission noninfectious complications included aspiration pneumonia<sup>9</sup> (this is recorded as a separate DRG), hemorrhage or hematoma, GI hemorrhage or ulceration, pulmonary com-

TABLE III  
Clinical outcomes data from studies used\*

Study	Patient type/number/arm	Clinical outcomes
Gianotti	Well-nourished GI surgery	Preop: RR infection = 0.45, $p = .006$
	305 total =	RR non-inf complic = 0.83
	102 control group	LOS ↓ 2.4 d, $p = .008$
	102 preoperative group	Antibiotic days ↓ 3.2 d, $p = 0.01$
	101 perioperative group	Periop RR infection = 0.52, $p = .02$
Braga	Malnourished GI surgery	RR non-inf complic = 0.78
	150 total =	LOS ↓ 1.8 d, $p = .03$
	50 control group	Antibiotic days ↓ 2.1 d, $p = 0.03$
	50 preoperative group	Preop: RR infection = 0.67
	50 perioperative group	RR non-inf complic = 0.91
Beale (meta-analysis)	1282 total =	LOS ↓ 2.1 d, $p = 0.01$
	434 medical	Periop RR infection = 0.42
	247 trauma	RR non-inf complic = 0.55
	601 surgical	LOS ↓ 3.3 d, $p = .001$
		Medical: RR infection = 0.49
		LOS ↓ 9.7 d, $p = 0.01$
		ICU LOS ↓ 0.4 d
	Ventilator days ↓ 1.1 d	
	Trauma: RR infection = 0.74	
	LOS ↓ 3.2 d	
	ICU LOS ↓ 3.2 d	
	Ventilator days ↓ 4.0 d, $p = 0.02$	

LOS, length of stay; RR, relative risk; ICU, intensive care unit.

\*RR >1 indicates that the patients receiving the intervention are more likely to experience the complication, whereas RR <1 indicates a favorable reduction in the likelihood of complication. For example, RR = 0.39 indicates that patients receiving the intervention were 39% as likely as the control patients to develop a complication.

TABLE IV  
MCG surgery subspecialties\*

MCG Surgery subspecialty	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, well nourished, %	Breakeven complication rate, malnourished, %
Kidney transplant	22,231	10.93	0.37	1.35
Plastic surgery	17,659	15.83	0.47	1.70
Vascular surgery	14,378	10.86	0.57	2.09
General surgery	13,442	6.93	0.61	2.23
Cardiothoracic	12,631	4.18	0.65	2.38
Orthopedics	7,153	3.89	1.15	4.19
Surgical oncology	7,098	12.15	1.16	4.23

LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as "1.10%," this means that if your actual rate of complications is greater than 1.10%, it is profitable to give specialized nutritional formulations to that entire patient population.

promise, metabolic derangements, stroke, cardiac abnormality (excluding acute MI), acute MI, shock or cardiorespiratory arrest, venous thrombosis/pulmonary embolism, coma or stupor, reopening of surgical site, and procedure-related perforations or lacerations (including anastomotic leaks). UHC uses a complication profiler to first classify patients into risk pools according to DRG or *International Classification of Diseases, Ninth Revision (ICD-9)* diagnosis and procedure codes. They identify patients at risk for specific types of complications. For example, a classification of miscellaneous complications is triggered by the *ICD-9* diagnosis code 995.86, Malignant hypertension, or 999.6, ABO incompatibility reaction, or 13 other *ICD-9* codes. Twenty-five specific complications groups exist, such as aspiration pneumonia, postoperative pulmonary compromise, septicemia, and shock or cardiorespiratory arrest.<sup>10</sup> The definitions of these complications are presented in Table II, an overview of the UHC Complication profiler user's guide. The complication profiler is limited to 4 surgery- or procedure-based risk pools. The risk pools identify patients at risk for specific types of complications: 1 to 11 assigned to all surgical DRG risk pool, 12 assigned to minor surgery DRG risk pool, 13 to 17 assigned to all surgical DRG or GI endoscopy risk pool, 18 to 25 assigned to all surgical DRG, cardiac procedures or GI endoscopy risk pool.

In order to extend the applicability of the cost-savings findings, the scope of the project was expanded

after the initial query of MCG-specific metrics. First, the 125 additional UHC member hospitals were segmented into 1 of 3 facility types, depending on primary responsibility and payer mix (academic, indigent care, or community hospital), and LOS/cost data for complicated *vs* noncomplicated patient stays was collected for each of the 3 patient groupings (surgical, medical ICU, and trauma). To further extend the analysis, the UHC members were then segmented into 1 of 6 US regions (mid-Atlantic, Midwest, New England, South, Southwest, and West), and LOS/cost data for complicated *vs* noncomplicated patient stays for each of the 3 patient groupings (surgical, medical ICU, and trauma) were again analyzed. An "all UHC" benchmark of complicated and noncomplicated patient stays was also established.

In order to protect patient confidentiality, the UHC database does not allow for individual patient account-level detail for the other UHC member hospitals to be obtained. Therefore, patients in the facility type and region analyses could not be segmented into subcategories, and data were available for only the broad patient groupings (medical, surgical, trauma). Also, patients experiencing complications in the other UHC member hospitals could not be further segmented into noninfectious or infectious complication groups.

A schematic of the study design is presented in Figures 1 to 3. Note: facilities with fewer than 20 results

TABLE V  
MCG Surgery infectious complications\*

Infectious complications, MCG surgery	Incremental cost of infection, \$	Incremental LOS with infection	Breakeven infection rate, well nourished, %	Breakeven infection rate, malnourished, %
Septicemia	51,329	9.03	0.10	0.34
Postop UTI	11,084	7.43	2.03	3.16
Postop pneumonia	16,700	12.32	0.43	2.10
Cellulitis/decubitus ulcer	9,192	13.03	0.89	3.26
Postop infections (excluding pneumonia/wound)	9,066	15.03	0.91	3.31
Wound infection	7,345	15.44	1.69	4.77

UTI, urinary tract infection; LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as "0.35%," this means that if your actual rate of complications is greater than 0.35%, it is profitable to give specialized nutritional formulations to that entire patient population.

TABLE VI  
MCG Medical ICU subspecialties \*

MCG medicine subspecialty	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, %
Ventilator support	67,804	30.08	0.51
Cardiology	9,875	4.51	3.48
General medicine	8,435	7.99	4.07
Gastroenterology	7,459	7.21	4.60
Medical oncology	4,422	11.69	7.76

MCG, Medical College of Georgia; ICU, intensive care unit; LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “3.48%,” this means that if your actual rate of complications is greater than 3.48%, it is profitable to give specialized nutritional formulations to that entire patient population.

were excluded from the facility type analysis but are included in the all UHC benchmark.

*Cost-effectiveness and Breakeven Analysis*

Cost-effectiveness is defined as a formal statistical method for comparing the cost and benefits of a medical intervention in order to determine whether it is of sufficient value to adopt or reimburse. Direct costs were measured in physical units and dollars. Effectiveness was measured in averted complications (infectious and noninfectious). This study used an incremental cost-effectiveness analysis, weighing the incremental expense of immune-modulating enteral formulas (compared with the control, no enteral nutrition) against the incremental savings associated with averted complications (as determined by published reductions in relative risk [RR]). In assessing the incremental cost of providing a commercially available specialized nutritional formulations to patients, significant published data exist to indicate that preoperative immune-modulating formula (Impact Recover, Minneapolis, MN) is the most cost-effective. In fact, a preoperative (instead of perioperative) regimen may benefit

TABLE VII  
MCG medical ICU infectious complications \*

Infectious complications, MCG medicine	Incremental cost of infection, \$	Incremental LOS with infection	Breakeven infection rate, %
Postop infections (excluding pneumonia/wound)	150,651	99.37	0.23
Cellulitis/decubitus ulcer	69,337	37.54	0.50
Postop pneumonia	45,898	28.11	0.75
Wound infection	27,587	16.71	1.24

MCG, Medical College of Georgia; ICU, intensive care unit; LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “0.23%,” this means that if your actual rate of complications is greater than 0.23%, it is profitable to give specialized nutritional formulations to that entire patient population.

TABLE VIII  
MCG trauma \*

MCG trauma	Incremental cost of complication, \$	Incremental LOS with complication	Break even complication rate, %
Trauma	28,839	10.44	2.33

MCG, Medical College of Georgia; LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “2.33%,” this means that if your actual rate of complications is greater than 2.33%, it is profitable to give specialized nutritional formulations to that entire patient population.

the well-nourished patient equally and both preoperatively and postoperatively.<sup>11,12</sup> In a malnourished patient, however, both preoperative and postoperative administration of immune-enhancing substrates is required for optimal reduction in complications, and therefore a perioperative regimen is recommended.<sup>6</sup>

With these guidelines in mind, the incremental expense of supplying immune-modulating enteral formulas to various patient groups will differ. The current cost of preoperative oral regimen of immune-modulating formula in the United States is \$45 (1 L/d for 5 consecutive days). The cost of a perioperative oral regimen in the United States is \$220 (1 L/d for 5 consecutive days preoperatively plus 2000 kcal/d enterally for 7 consecutive days postoperatively). The cost of a post-admission regimen (2000 kcal/d for 7 consecutive days) for medical ICU or trauma patients is \$175.

The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. As the incremental savings in this study are dependent upon averted complications, a breakeven complication rate could be calculated for various patient categories and subcategories. The breakeven complication rate for a specific patient population is the percentage of infectious and noninfectious complications at which there is no economic benefit or expense associated with the use of specialized

TABLE IX  
MCG trauma infectious complications \*

Infectious complications	Incremental cost of infection, \$	Incremental LOS with infection	Breakeven infection rate, %
Postop pneumonia	36,574	17.73	1.84
Post-op infections (excluding pneumonia/wound)	27,011	17.23	2.49
Wound infection	15,104	9.56	4.46

MCG, Medical College of Georgia; LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “1.84%,” this means that if your actual rate of complications is greater than 1.84%, it is profitable to give specialized nutritional formulations to that entire patient population.

TABLE X  
Surgery comparison by facility type\*

Surgery facility type	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, well nourished, %	Breakeven complication rate, malnourished, %
Academic	25,013	5.94	0.33	1.20
Community	24,811	5.79	0.33	1.21
Indigent care	32,279	7.37	0.25	0.93
All UHC benchmark	25,103	5.97	0.33	1.20

LOS, length of stay; UHC, University HealthSystem Consortium.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as "1.20%," this means that if your actual rate of complications is greater than 1.20%, it is profitable to give specialized nutritional formulations to that entire patient population.

nutritional formulations for all patients in that group and can be described by the following equation:

$$\begin{aligned} &\text{Break-even complication rate} \\ &= \text{cost of regimen} / [(1 - \text{relative risk}) \\ &\quad \times (\text{incremental cost of the complication})] \end{aligned}$$

For example, if the breakeven complication rate for a given patient population is expressed as "0.35%," this means that if your actual rate of complications is >0.35%, it is profitable to give specialized nutritional formulations to that entire patient population. The savings associated with averting complications, even though few in number, are great enough to offset the additional expense associated with procuring the immune-modulating formula for the group. If, however, your actual rate of complications is <0.35%, supplying your patients with immune-modulating formula will not be profitable because not enough complications will be averted to result in cost savings greater than the incremental expense of providing the formula.

RR is defined as the likelihood that a patient receiving an intervention will experience a certain complication, relative to the control. RR >1 indicates that the patients receiving the intervention are more likely to experience the complication, whereas RR <1 indicates a favorable reduction in the likelihood of complication. For example, RR = 0.39 indicates that patients receiving the intervention were 39% as likely as the control patients to develop a complication.

It is clear that at complication rates greater than the breakeven complication rate, economic benefits abound. As the actual complication rate continues to

exceed the breakeven rate, the net savings per patient continues to increase linearly. Where infectious complications could be broken out of the overall complications specifically, a breakeven infection rate was calculated using the same methodology and formula.

NNT is defined as the number of patients that an intervention should be administered to in order to avert 1 complication and can be described by the following equation:

$$\begin{aligned} \text{NNT} &= 1 / [\text{base infection rate} \\ &\quad - (\text{relative risk} * \text{base infection rate})] \end{aligned}$$

The NNT can be calculated easily and kept as a single numerical reminder of the effectiveness of a particular therapy. NNT is commonly used because it has the crucial advantage of direct applicability to clinical practice and shows the effort that is required to achieve a particular therapeutic target. The NNT has the additional advantage that it can be applied to any beneficial outcome. The concept of NNT always refers to a comparison group (in which patients receive placebo, no treatment, or some other treatment), a particular treatment outcome, and a defined period of treatment. To be fully specified, NNT should specify the comparator (standard enteral formula or no formula in this case), the therapeutic outcome (averted infectious and noninfectious complications), and the duration of treatment that is necessary to achieve the outcome (defined above, depending on the patient's prehospital nutritional status).<sup>13</sup>

TABLE XI  
Medical ICU comparison by facility type\*

Medical ICU, facility type	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, %
Academic	78,471	12.65	0.44
Community	71,274	11.36	0.48
Indigent care	71,325	17.97	0.48
All UHC benchmark	81,035	12.62	0.42

ICU, intensive care unit; LOS, length of stay; UHC, University HealthSystem Consortium.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as "0.44%," this means that if your actual rate of complications is greater than 0.44%, it is profitable to give specialized nutritional formulations to that entire patient population.

TABLE XII  
Trauma comparison by facility type\*

Trauma, facility type	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, %
Academic	15,104	8.56	4.46
Community	21,531	7.11	3.13
Indigent care	31,139	10.28	2.16
All UHC benchmark	23,689	8.59	2.84

LOS, length of stay; UHC, University HealthSystem Consortium.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “3.13%,” this means that if your actual rate of complications is greater than 3.13%, it is profitable to give specialized nutritional formulations to that entire patient population.

## RESULTS

The clinical outcomes data utilized in the cost-effectiveness analysis are summarized in Table III. Incremental cost, LOS, breakeven complication rates, and breakeven infection rates are presented for MCG subspecialties in Tables IV to IX. The same data (less infection breakeven rates) is presented for the other UHC member hospitals, segmented by patient subgroup (surgical, medical ICU, and trauma) and facility type or region in Tables X to XV.

National Nosocomial Infections Surveillance (NNIS) data for January 1992 to June 2003<sup>14</sup> are provided as a standard of reference for comparison of breakeven complication rate and expected infection rates (Tables XVI and XVII). NNIS data were used in the calculation of NNT.

Using MCG Surgery infectious complications data, it is evident that net cost savings per patient increase rapidly above the breakeven infection rate of 0.66%. At MCG Surgery’s baseline infection rate of 3.2%, the hospital would experience \$217 net savings per patient (Fig. 4). The same is true for both medical ICU and trauma populations (baseline infection rate 1.0% and 5.5%, with net savings per patient of \$264 and \$410, respectively; Figs. 5 and 6).

## DISCUSSION

The importance of nutrition support in the hospitalized patient is no longer disputed. The benefits of

TABLE XIV  
Medical ICU comparison by facility type\*

Medical ICU, region	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, %
Mid-Atlantic	76,968	16.18	0.45
Midwest	65,419	10.94	0.53
New England	52,222	8.59	0.66
South	76,925	12.87	0.45
Southwest	107,853	13.88	0.32
West	93,008	14.72	0.37

ICU, intensive care unit; LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “0.45%,” this means that if your actual rate of complications is greater than 0.45%, it is profitable to give specialized nutritional formulations to that entire patient population.

enteral feeding over parenteral nutrition are also well accepted.<sup>15</sup> The question of the optimal enteral formula for each patient group remains controversial. The clinical data supporting the use of specialized nutritional formulations are rapidly expanding. These new data and the heterogeneity of the surgical and critically ill patient make the dogmatic statement “one formula fits all” somewhat archaic.

Despite promising clinical results, the currently marketed immune-modulating enteral formulas are considered by some to be “too expensive” for routine use. However, in light of the increasing pressure to reduce costs while still providing high-quality patient care and improving patient outcomes, the adoption of new products for routine use in specific patient populations should weigh the clinical benefits and risks against cost and resource consumption. This decision-making process should be informed by cost-effectiveness data when available.

This paper represents the third original manuscript showing the economic benefit of immune-modulating enteral formulas and is the first to use a national database of more than 1 million patients to demonstrate cost-effectiveness across a variety of patient categories, types of facilities, and regions of the United States. The 2 previous economic analyses of immune-modulating enteral formulas used gastrointestinal surgery patients in Europe. The benefit of the current

TABLE XIII  
Surgery comparison by region\*

Surgery, region	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, well nourished, %	Breakeven complication rate, malnourished, %
Mid-Atlantic	29,954	6.58	0.27	1.10
Midwest	23,267	5.51	0.35	1.29
New England	19,872	5.54	0.41	1.51
South	20,180	5.72	0.41	1.49
Southwest	30,400	7.57	0.27	0.99
West	27,921	6.08	0.29	1.07

LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as “1.10%,” this means that if your actual rate of complications is greater than 1.10%, it is profitable to give specialized nutritional formulations to that entire patient population.

TABLE XV  
Trauma comparison by facility type\*

Trauma, region	Incremental cost of complication, \$	Incremental LOS with complication	Breakeven complication rate, %
Mid-Atlantic	15,886	6.59	4.24
Midwest	16,341	7.15	4.12
New England	22,033	6.88	3.06
South	3,885	9.45	17.33
Southwest	30,886	7.81	2.18
West	34,113	11.15	1.97

LOS, length of stay.

\*The breakeven point is defined as the point at which the incremental expense exactly equals the incremental savings, and, therefore, there is no economic benefit to the intervention. For example, if the breakeven complication rate for a given patient population is expressed as "2.18%," this means that if your actual rate of complications is greater than 2.18%, it is profitable to give specialized nutritional formulations to that entire patient population.

methodology is that data are available for a broader patient base (surgical and medical ICU and trauma patients), and the cost figures reflect US trends in cost and reimbursement. Additionally, the current methodology used previously collected clinical data, which allowed for more rapid completion of the economic

TABLE XVI  
2003 NNIS Service-specific infection rates (NNT extrapolated from NNIS data)\*

Service	National Nosocomial Infection Study: infection rate, %	Number needed to treat (NNT)*
Transplant	4.53-14.52	13-45
Vascular surgery	0.91-4.42	42-203
General surgery	0.44-11.53	16-414
	(Appendectomy and colorectal surgery, respectively)	
Cardiothoracic surgery	0.3-2.48	74-506
Orthopedic surgery	0.77-3.62	51-237

NNT, number needed to treat; NNIS, National Nosocomial Infections Surveillance.

\*NNT is defined as the number of patients to whom an intervention should be administered to in order to avert 1 complication.

TABLE XVII  
2003 NNIS unit-specific infection rates (NNT extrapolated from NNIS data)

Unit/Complication	National Nosocomial Infection Study: infection rate, %	NNT
Surgery ICU		
Catheter associated UTI	6.2	30
Central line-associated bacteremia	5.2	35
Ventilator-associated pneumonia	9.9	19
Medicine ICU		
Catheter associated UTI	5.1	36
Central line-associated bacteremia	5.7	32
Ventilator-associated pneumonia	5.0	37
Trauma ICU		
Catheter associated UTI	6.4	29
Central line-associated bacteremia	7.8	24
Ventilator-associated pneumonia	15.1	13

NNT, number needed to treat; NNIS, National Nosocomial Infections Surveillance; ICU, intensive care unit; UTL, urinary tract infection.

MCG Surgery - Cost Savings per Patient

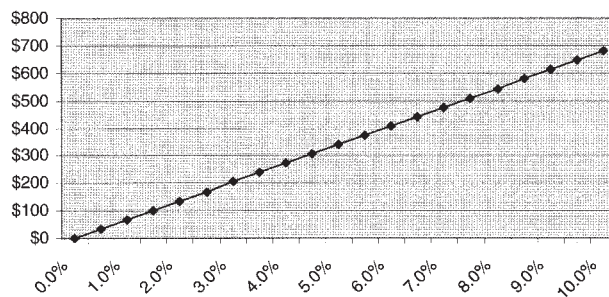


FIG. 4. At a baseline infection rate of 3.2%, \$217 net savings per patient can be realized.

analysis and averted ethical considerations of randomizing patients to a control group in which they would be at an anticipated higher risk of complications.

When developing cost estimates for health economic analyses, it is important to understand the limitations of DRG-based data.<sup>16</sup> Although they are often the most accessible, they are not necessarily the optimal cost source. DRG-based estimates, like any administrative data, must be used with caution. It is the duty of the cost developer to know as much as possible about the DRG assignments and modifiers before using DRG payments in an economic analysis. DRGs can be a valuable and convenient source for information, as in the present study, or can lead to substantial miscalcu-

MCG Medicine - Cost Savings per Patient

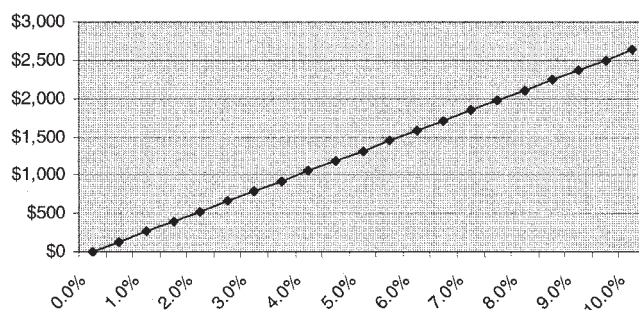


FIG. 5. At a baseline infection rate of 1.0%, \$264 net savings per patient can be realized.

MCG Trauma - Cost Savings per Patient

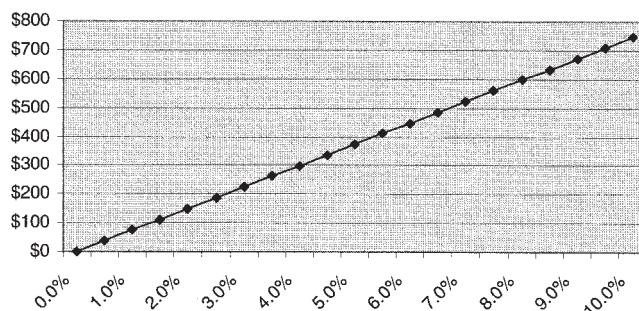


FIG. 6. At a baseline infection rate of 5.5%, \$410 net savings per patient can be realized.

lations. Their applicability should be determined for each analysis.<sup>17</sup>

The results of the present study demonstrate that administration of immune-modulating substrates pre- or perioperatively or upon admission to the hospital could be a dominant cost-reduction strategy. The significant reduction in postoperative/postadmission complications translates into significant cost savings and improved cost-effectiveness when compared with the alternative (standard enteral formulas). The cost-effectiveness of this intervention could be even greater by accounting for indirect and socioeconomic costs such as sick leave, rehabilitation, and full recovery of physical and social functioning.

#### CONCLUSIONS

In summary, despite the increased cost of acquiring specialized formulas over standard enteral formula, specialized nutritional formulations demonstrate clear cost benefits and compare favorably with other widely accepted health care strategies (such as antibiotics). Clinical findings on the effects of immunonutrition are robust, and use of the UHC database gives the study increased power and sensitivity.

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