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# Impact of nutrition support on clinical outcome and cost-effectiveness analysis in patients at nutritional risk: A prospective cohort study with propensity score matching

Hui Zhang M.S., R.N. [a,b,c], Yang Wang M.S. [d,**], Zhu-Ming Jiang M.D., F.A.C.S. [a,*], Jens Kondrup M.D. [e], Hai Fang Ph.D. [f], Martha Andrews Ph.D. [g], Marie T. Nolan Ph.D., R.N. [g], Shao-Yu Mu R.N. [b], Jun Zhang M.D. [h], Kang Yu M.S. [i], Qian Lu Ph.D. [j], Wei-Ming Kang M.D. [a]

[a] *Department of General Surgery, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China*
[b] *Department of Nursing School, Chongqing Medical University, Chongqing, China*
[c] *Guizhou Provincial People's Hospital, Guizhou, China*
[d] *Medical Research & Biometrics Center, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*
[e] *Nutrition Unit, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark*
[f] *China Center for Health Development Studies, Peking University, Beijing, China*
[g] *School of Nursing, Johns Hopkins University, Baltimore, Maryland*
[h] *Department of General Surgery, the First Affiliated Hospital of Chongqing Medical University, Chongqing, China*
[i] *Department of Nutrition, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China*
[j] *Department of Medical & Surgical Nursing, School of Nursing, Peking University, Beijing, China*

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ABSTRACT

*Objectives:* There is a lack of evidence regarding the economic effects of nutrition support in patients at nutritional risk. The aim of this study was to perform a cost-effectiveness analysis by comparing an adequate nutrition support cohort with a no-support cohort.
*Method:* A prospective observational study was performed in the surgical and medical gastroenterology wards. We identified patients at nutritional risk and the provision of nutrition support by the staff, unaware of the risk status, was recorded. Cost data were obtained from each patient's statement of accounts, and effectiveness was measured by the rate of infectious complication. To control for potential confounding variables, the propensity score method with matching was carried out. The incremental cost-effectiveness ratio was calculated based on the matched population.
*Results:* We screened 3791 patients, and 440 were recruited for the analysis. Patients in the nutrition support cohort had a lower incidence of infectious complications than those in the no-support cohort (9.1 versus 18.1%; $P = 0.007$). This result was similar in the 149 propensity matched pairs (9.4 versus 24.2%; $P < 0.001$). The median hospital length of stay was significantly reduced among the matched nutrition support patients (13 versus 15 d; $P < 0.001$). The total costs were similar among the matched pairs (US $6219 versus $6161). The incremental cost-effectiveness analysis suggested that nutrition support cost US $392 per patient prevented from having infectious complications.

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ZMJ, MTN, and JK designed this protocol in 2006; monitored the study, collaborated with data statistical analysis, and descriptions. They also approved manuscript drafts and the final manuscript. MA worked as nutritionist for MTN and focused on clinical nutrition. HF designed the health economic-related data analysis, reviewed the data calculations and prepared the health-economic related sections of the manuscript. JZ, SYM, KY, QL, and WMK assisted HZ and YW in carrying out the study, reviewing, and advising on the manuscript. All authors read and approved the final manuscript. The authors have no conflicts of interest to declare.

* Corresponding author. Tel.: +86 186 0114 8800; fax:+86 106 5253 037.
*E-mail address:* jiangzm@imicams.ac.cn (Z.-M. Jiang).
** Co-first author.

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*Conclusion:* Nutrition support was associated with fewer infectious complications and shorter length of stay in patients at nutritional risk. The incremental cost-effectiveness ratio indicated that nutrition support had not increased costs significantly.



## Introduction

Nutrition screening, assessment, and intervention are major components of hospital nutritional care. This concept is recommended by several professional guidelines [1–3]. Nutritional Risk Screening 2002 (NRS 2002) was developed and used to identify patients at nutritional risk who would likely benefit from nutrition support [4]. This tool had been confirmed and validated by several studies [5,6]. Our group's previous work [7,8] also suggested that nutrition improves clinical outcome among patients at nutritional risk.

Medical care is a resource in high demand and decision makers seek to reduce medical care that is not documented to justify its cost. The outcome of a health intervention must be compared with the resources needed for the intervention [9,10], and this also applies to nutrition support [11,12].

The knowledge of whether nutrition support is cost-effective is limited. In this study, we added an analysis of cost-effectiveness in a protocol otherwise similar to our previous cohort studies of patients at nutritional risk [7,8].

### Participants and methods

#### *Participants*

This was a prospective observational study conducted in the surgical and medical gastroenterology wards of the First Affiliated Hospital of Chongqing Medical University. Recruitment was carried out among patients admitted consecutively to the wards from July 2011 to the end of June 2012.

The patients were considered eligible if they were admitted with one of the following diagnoses:

- Gastric cancer (with surgery),
- Colorectal cancer (with surgery),
- Intestinal obstruction (with surgery),
- Crohn's disease or ulcerative colitis (without surgery),
- Gastric cancer or colorectal cancer (without surgery),
- Mild intestinal obstruction (without surgery),
- Moderate pancreatitis, or
- Alcoholic cirrhosis.

All diagnoses were made according to the guidelines of the Chinese Society of Gastroenterology (similar to the guidelines of American Gastroenterological Association). Participants also were included if they were at nutritional risk (with a NRS-2002 score $\geq$3), age $\geq$18 y, scheduled to stay in the hospital for at least 5 d, willing to participate in the study, and able to communicate with the researchers.

Patients, who were pregnant, admitted emergently, experiencing impaired cognitive functions, and transferred from other hospitals or wards were excluded. Patients who had not been interviewed within 48 h after admission, or had infectious complications when admitted to the hospital also were excluded from the analysis.

The study protocol was approved by the ethics committee of Peking Union Medical College Hospital (No. S-054), IRB of Johns Hopkins University Hospital (2005-2008) and also the ethics committee of the first Affiliated Hospital of Chongqing Medical University (No. 2011-14). The protocol was registered on Clinicaltrials.gov as NCT00289380. Moreover, the study was conducted according to the STROBE Statement and the Declaration of Helsinki [13] and informed consent was obtained from all patients participating in the study.

#### *Procedures*

The first interviews with and examinations of patients were performed by the research group within 24 h after admission. Nutritional risk was determined by using NRS 2002, which was recommended for hospital patients by the European Society for Clinical Nutrition and Metabolism (ESPEN) and Chinese Society of Parenteral and Enteral Nutrition (CSPEN).

NRS 2002 consists of scores for impaired nutritional status and severity of disease, and an additional score if age $\geq$70 years [4]. Impaired nutritional status was scored from 0 to 3 according to changes in body mass index (BMI) and weight and food intake. Severity of disease was scored 0 to 3 according to different kinds of disease. If age was $\geq$70 y, 1 was added to the total score. NRS 2002 has been validated in the Chinese population [7,8].

All patients who met the inclusion criteria and completed the first evaluation were seen at least four times per week before discharge. Data concerning complications and nutrition support were collected from medical records, nursing records, and interviews with the patients. Finally, the date of discharge and the discharge destination were recorded.

The computerized statement of the fiscal account of each patient was obtained from the Discharge Office within 3 d postdischarge, and cost calculation was performed. Two individuals independently evaluated the data before entering the information into the electronic database.

#### *Initiation and adequacy of nutrition support*

Physicians and nurses caring for the patients were blinded to the result of the nutrition screening. The decision made by the physicians to initiate nutrition support was seemingly based on patients' or family's attitude toward nutrition support, health insurance coverage, and the clinical judgment of the physicians according to their attitude toward nutrition support. After the physicians decided to initiate the nutrition support, nurses with expertise in this area carried out the procedures. The decision to provide nutrition support obviously did not follow the guidelines recommended by the CSPEN, probably because of lack of awareness of the guideline. This produced the "natural experiment" that enabled us to carry out the cohort study.

The nutrition support cohort included those patients who had received adequate support. According to CSPEN [3], adequacy of nutrition support was defined as 25 to ~30 kcal/kg daily of nonprotein calories (carbohydrate, fat, or a combination of the two) and 0.15 to ~0.20 g/kg daily of nitrogen. Patients received nutrition support for $\geq$5 consecutive days. Because spontaneous food intake was not monitored systematically, the energy supplied via parenteral nutrition (PN) or enteral nutrition (EN) had to be judged to exceed 90% of the total energy provision.

PN solutions were given in either multichamber bags (Kabiven, Fresenius Kabi, Bad Homburg, Germany and SSPC Wuxi, China) or all-in-one bags prepared by the pharmacy under standard laminar airflow conditions (Class 100). The vascular access for PN was either a peripheral venous catheter (BD Pegasus, Franklin Lakes, NJ, USA), or a peripherally inserted central catheter (PICC; Bard, 605 North 5600 west, Salt Lake City, UT, USA). The PN regimen was continuously infused for 16 to 24 h by adjusting the flow-rate. Tolerance to PN support was monitored by blood tests for liver and kidney function, electrolytes, and blood glucose.

EN was administered by commercial tube feeding (Fresubin, SSPC, and Wuxi, China). Tube feeding was continuously infused for no less than 18 h/d by adjusting the flow rate.

#### *Definition of nutrition support and no-support cohort*

The two cohorts of patients were divided according to the nutrition support therapy they actually received. The nutrition support cohort consisted of patients who received adequate nutrition support, as defined above. The no-support cohort consisted of patients who received only intravenous 5 to 10% glucose and electrolyte infusions. According to the exclusion criteria of the protocol for analysis, patients who received inadequate PN, inadequate EN, $<$5 d nutrition support, and patients who had an oral intake $>$10% of total intake were excluded from the analysis. If a patient was given adequate nutrition support only after the occurrence of a complication, the patient was included in the no-support cohort.

#### *Clinical outcomes*

The primary outcome of this study was defined as the occurrence of infectious complications, according to clinical, radiologic, and hematologic evidence

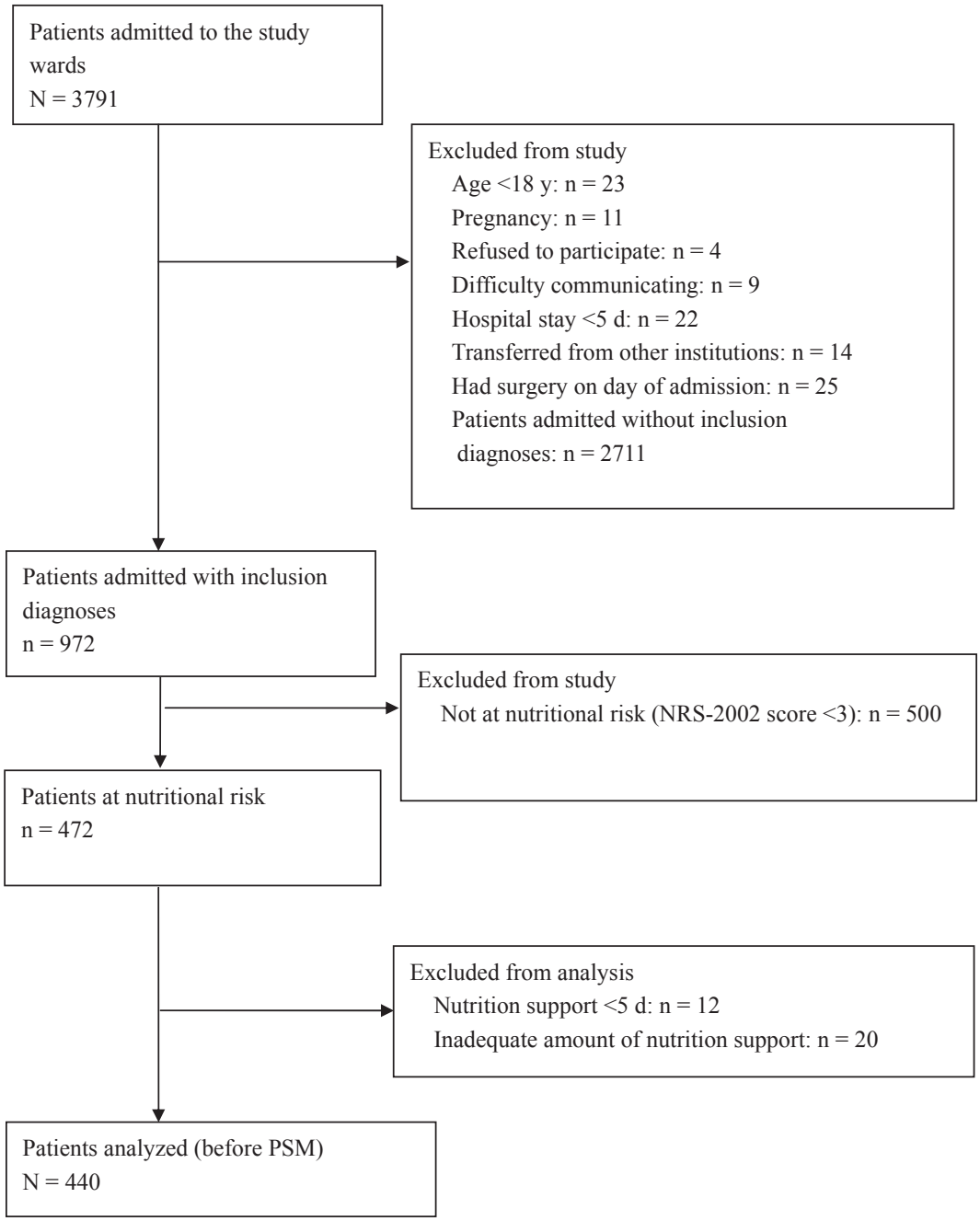


**Fig. 1.** Patient flowchart. PSM, propensity score matching.

of infection [14]. If the patient had more than one infectious complication, he or she was regarded as only one case with infectious complications. Noninfectious and overall complication rates also were collected and treated as secondary outcomes. The hospital length of stay (LOS) also was recorded.

*Costs and cost-effectiveness*

In this study, all actual costs during the in-hospital period were obtained from the statement of accounts no matter what kind of payment was used (insurance or no insurance). Thus, the cost-effectiveness analysis was performed from the payer's perspective (focus on direct medical costs) [15,16].

Total costs were divided into three areas:

1. Nutrition support, including nutrition solutions, nursing, physician, and other staff supervision of preparation, administration, and catheter placement and maintenance.
2. Infectious complication(s), including diagnostic procedures and treatment, nursing care, and physician treatment related to infectious complications.
3. "Other," including costs associated with the hospital admission, calculated from the total costs from which the cost of nutrition support and infectious complications were subtracted.

The total costs were used for the cost-effectiveness analysis. Cost data were collected from each patient within 3 d after discharge. Cost is expressed in US dollars, and the exchange rate used was US $1 equals 6.37 China Yuan (CNY) in July 2012.

The percentage of patients without infectious complication(s) (free of infectious complication rate) was used as a measure of effectiveness [17]. The incremental cost-effectiveness ratio (ICER) was calculated by dividing the total cost difference between the two cohorts by the difference in effectiveness [18]. In our study, the difference in effectiveness is equal to the effectiveness measure (such as infection rate) for the group with nutrition support minus the effectiveness measure for the group without nutrition support, the difference in cost

**Table 1**
Baseline characteristics of the patients at nutritional risk (N = 440)

| Item | Nutrition support, n = 186 n (%) | No support, n = 254 n (%) | *P* value |
|---|---|---|---|
| Men | 110 (59.1) | 146 (57.5) | 0.727 |
| Age (y) | 62.2 ± 11.7 | 60.4 ± 14.7 | 0.156 |
| BMI (kg/m$^2$) | 20.9 ± 3.3 | 20.9 ± 3.2 | 0.821 |
| Admissions in Medical Department | 38 (20.4) | 102 (40.2) | <0.001 |
| Insurance | 168 (90.3) | 218 (85.8) | 0.151 |
| Nutritional risk score | | | 0.026 |
| 3 | 74 (39.8) | 125 (49.2) | |
| 4 | 61 (32.8) | 85 (33.5) | |
| 5 | 41 (22) | 40 (15.7) | |
| 6 | 10 (5.4) | 4 (1.6) | |
| Severity of disease score | | | <0.001 |
| 1 | 37 (19.9) | 100 (39.4) | |
| 2 | 149 (80.1) | 154 (60.6) | |
| Nutritional status score | | | 0.189 |
| 0 | 14 (7.5) | 21 (8.3) | |
| 1 | 74 (39.8) | 88 (34.6) | |
| 2 | 38 (20.4) | 74 (29.1) | |
| 3 | 60 (32.3) | 71 (28) | |
| Age score | | | 0.640 |
| 0 | 122 (65.6) | 172 (67.7) | |
| 1 | 64 (34.4) | 82 (32.3) | |
| Diagnosis group* | | | <0.001 |
| A | 35 (18.8) | 46 (18.1) | |
| B | 113 (60.8) | 106 (41.7) | |
| C | 1 (0.5) | 9 (3.5) | |
| D | 34 (18.3) | 71 (28) | |
| E | 3 (1.6) | 22 (8.7) | |

BMI, body mass index
* A, gastric cancer (with surgery); B, colorectal cancer and intestinal obstruction (with surgery); C, Crohn's disease, ulcerative colitis (without surgery); D, gastric cancer, colorectal cancer (without surgery), mild intestinal obstruction (without surgery); E, moderate pancreatitis, alcoholic cirrhosis.

**Table 2**
Baseline characteristics of the patients at nutritional risk after propensity score matching (N = 298)

| Item | Nutrition support, n = 149 n (%) | No support, n = 149 n (%) | *P* value |
|---|---|---|---|
| Men | 82 (55) | 86 (57.7) | 0.640 |
| Age | 61.4 ± 11.9 | 62 ± 13.1 | 0.698 |
| BMI (kg/m$^2$) | 21 ± 3.4 | 21.4 ± 3.1 | 0.210 |
| Admissions in Medical Department | 35 (23.5) | 33 (22.1) | 0.783 |
| Insurance | 134 (89.9) | 136 (91.3) | 0.691 |
| Nutritional risk score | | | 0.519 |
| 3 | 64 (43) | 69 (46.3) | |
| 4 | 51 (34.2) | 55 (36.9) | |
| 5 | 29 (19.5) | 23 (15.4) | |
| 6 | 5 (3.4) | 2 (1.3) | |
| Severity of disease score | | | 0.783 |
| 1 | 35 (23.5%) | 33 (22.1%) | |
| 2 | 114 (76.5%) | 116 (77.9%) | |
| Nutritional status score | | | 0.623 |
| 0 | 13 (8.7) | 17 (11.4) | |
| 1 | 57 (38.3) | 64 (43) | |
| 2 | 35 (23.5) | 30 (20.1) | |
| 3 | 44 (29.5) | 38 (25.5) | |
| Age score | | | 0.806 |
| 0 | 100 (67.1) | 98 (65.8) | |
| 1 | 49 (32.9) | 51 (34.2) | |
| Diagnosis group* | | | 0.946 |
| A | 31 (20.8) | 29 (19.5) | |
| B | 83 (55.7) | 87 (58.4) | |
| C | 1 (0.7) | 0 (0) | |
| D | 31 (20.8) | 29 (19.5) | |
| E | 3 (2) | 4 (2.7) | |

BMI, body mass index
* A, gastric cancer (with surgery); B, colorectal cancer and intestinal obstruction (with surgery); C, Crohn's disease, ulcerative colitis (without surgery); D, gastric cancer, colorectal cancer (without surgery), mild intestinal obstruction (without surgery); E, moderate pancreatitis, alcoholic cirrhosis.

equals cost for the group with nutrition support minus cost for the group with no nutrition support. ICER defines the cost of avoiding one patient having infectious complication(s). The formula of the ICER is as follows [19]:

$$\frac{Cost\ (nutrition\ support) - Cost\ (no\ nutrition\ support)}{Effectiveness\ (nutrition\ support) - Effectiveness\ (no\ nutrition\ support)}$$

*Sample size determination (power analysis)*

We planned to include ≥400 eligible patients in the final analysis. Based on our previous study [7], we assumed there would be 20% infectious complication rate among patients without nutrition support. The proportion of participants exposed to nutrition support was estimated as 50% in the cohort. With a two-sided 0.05 $\alpha$ level, a sample of ≥400 would offer >80% power to detect a minimum 50% relative reduction (RR) on the occurrence of infectious complications attributed to the nutrition support.

*Statistical analysis*

Data were expressed by frequencies and percentages for categorical variables and means ± SD for continuous variables. Categorical variables were compared using $\chi^2$ or Fisher's exact tests. Normally distributed continuous variables were compared using Student's *t* test, and non-normally distributed data were compared using the Wilcoxon rank-sum test. A specific test was used to validate whether the distribution was normality.

As is demonstrated in the results section, the two groups differed substantially with respect to baseline characteristics. These differences may, by themselves, have contributed to the observed difference in outcome (infectious complications), independently of adequate nutrition support. To minimize the confounding effect of these differences, the method of propensity score with matching was applied. The propensity score [20] for an individual is defined as the conditional probability of being treated given his or her covariates. In the present study, the propensity score is the probability of a patient being assigned to the nutrition support cohort given a set of observed covariates (age, sex, BMI, department of admission, nutritional status score, disease severity score, and health insurance coverage). The propensity score was calculated by logistic regression analysis with nutrition support or no support as dependent variable and baseline age, sex, BMI, department of admission (medical or surgical), nutritional status score, disease severity score, and health insurance coverage as independent baseline variables. The Hosmer–Lemeshow test showed a $P = 0.459$, which suggests an acceptable discrimination effect of the model. A matched sample within the two cohorts was obtained from the propensity score with the use of the caliper matching procedure with a precision of 0.01. The balance of baseline characteristics between the two cohorts was finally assessed using the statistical tests mentioned above.

The ICER was calculated on the matched population (from the differences in cost and complication rate respectively). Monte Carlo simulation [21] was carried out to demonstrate the validity of those observed economic results. This generated 10 000 bootstrapping samples and the 95% confidence intervals (CIs) of those resamplings were established. $P < 0.05$ was considered statistically significant. Statistical analysis was performed by SAS 9.3 software (SAS, Institute Inc, Cary, NC, USA).

## Results

### *Patient characteristics*

In all, 3791 patients were registered during the data collection period and 440 fulfilled the inclusions criteria (Fig. 1). Adequate nutrition support was given to 186 patients, whereas 254 patients were given no support. There was no significant difference among the follow-up time between two cohorts.

Compared with no-support patients, those in the nutrition support group were less frequently admitted to the medical wards (20.4 versus 40.2%) and had a higher nutritional risk and severity of disease score (Table 1). Moreover, the baseline diagnosis groups were significantly different between the groups. After application of propensity score matching (149 pairs

**Table 3**
Clinical outcome before and after propensity matching

| Item | Before matching | | | After matching | | |
|---|---|---|---|---|---|---|
| | Nutrition support, n = 186 % | No support, n = 254 % | *P* value | Nutrition support, n = 149 % | No support, n = 149 % | *P* value |
| Infectious | 9.1 | 18.1 | 0.007 | 9.4 | 24.2 | <0.001 |
| Pulmonary infection | 3.2 | 8.3 | | 4 | 11.4 | |
| Wound infection | 3.2 | 3.9 | | 3.4 | 4.7 | |
| Urinary tract infection | 2.7 | 4.3 | | 2 | 6.7 | |
| Gastrointestinal infection | 0 | 1.6 | | 0 | 1.3 | |
| Noninfectious | 1.1 | 2 | 0.704 | 1.3 | 2.7 | 0.684 |
| Anastomosis minor bleeding | 0.5 | 0.4 | | 0.7 | 0.7 | |
| Gastrointestinal part obstruction | 0.5 | 0 | | 0.7 | 0 | |
| Wound effusion | 0 | 0.4 | | 0 | 0.7 | |
| Urine retention | 0 | 1.2 | | 0 | 1.3 | |
| Overall complications | 10.2 | 20.1 | 0.004 | 10.7 | 26.8 | <0.001 |
| Hospital length of stay (d)* | 15 (12–18) | 15 (12–19) | 0.598 | 13 (11–18) | 15 (13–20) | <0.001 |

* Length of stay is presented as median and interquartile ratio (Q1, Q3).

of patients remained), there were no significant differences of baseline characteristics between groups among the matched population (Table 2).

*Complications and hospital LOS*

Before matching, the nutrition support cohort had a significantly lower rate of infectious (9.1 versus 18.1%; $P = 0.007$) and overall complications (10.2 versus 20.1%; $P = 0.004$) compared with the no support group. LOS was similar between the two groups (Table 3).

After matching, the support cohort showed a larger decrease in infections and overall complications and a shorter LOS (Table 3).

Both matched and unmatched data showed no difference in the rate of noninfections complication.

*Cost, cost-effectiveness (ICER)*

The total costs were higher in the support cohort in the unmatched population (US $6642 versus $5843, data not shown). After matching, the difference of total costs was US $58 (Table 4). The increased cost of nutrition support did not result in a total increase of cost because the support group had lower overall complications costs and reduced costs of infectious complications.

Cost-effectiveness results based on the matched population are shown in Table 4.

The bootstrap 95% CI demonstrated that the overall costs were not significantly different between the cohorts (Fig. 2). The difference of effectiveness (free of infectious complication rate) was 14.8% (bootstrap 95% CI, 4–23.6%). The ICER was calculated as US $392.

## Discussion

The results from the present study suggested that nutrition support reduces the number of patients with one or more infectious complication(s), in agreement with our earlier studies [7,8] and that the cost is $392 for each case prevented.

Moreover, the nutrition support cohort had a shorter LOS compared with the no-support cohort. These findings agree with those of Khan et al. [22], whose study suggested that each of the postoperative complications studied were associated with substantial increases in total hospital cost and LOS, even after adjusting for type of surgery, urgency of surgery, and preoperative patient comorbid conditions.

The World Health Organization (WHO) has proposed that if the ICER is less than three times the gross domestic product (GDP) per capita, the medical intervention should be considered cost-effective [23]. When using the 2011 Chinese GDP level [24], this threshold would be 105 000 CNY, equal to about US $16,484. Our data showed an ICER of US $392 and even the upper limit of the bootstrapping interval was US $9598. This amount is considerably less than the WHO recommended threshold.

The effect of nutrition support on the rate of infections seemed to be larger in the matched sample than in the unmatched sample (Table 3). It may be that nutrition support is particularly effective in preventing infections in the cohort selected by the propensity score method, i.e. more patients undergoing surgery and therefore a higher score for Severity of disease and total NRS 2002 score, cf. Table 2 versus Table 1.

The present study included only three patients using PN combined with EN. None of the cases was using adequate EN support alone. This result was similar to those from a previous

**Table 4**
Cost-effectiveness analysis of nutrition support versus no support for patients at nutritional risk*

| Item | Nutrition support, n = 149 | No support, n = 149 | Difference (support–no support) | Difference bootstrap 95% CI† |
|---|---|---|---|---|
| Cost (US$) | 6219 | 6161 | 58 | (−559 to 736) |
| Effectiveness (1-infectious complication rate) | 90.6% | 75.8% | 14.8% | (4 to 23.6) |
| ICER = (58/0.148) = $392 | | | | |
| Bootstrap 95% confidence interval of ICER (−4344 to 9598) | | | | |

ICER, incremental cost-effectiveness ratio
* The propensity matched population, see text.
† The 95% CI was calculated by the bootstrap simulation; 10 000 bootstrapping samples were generated.

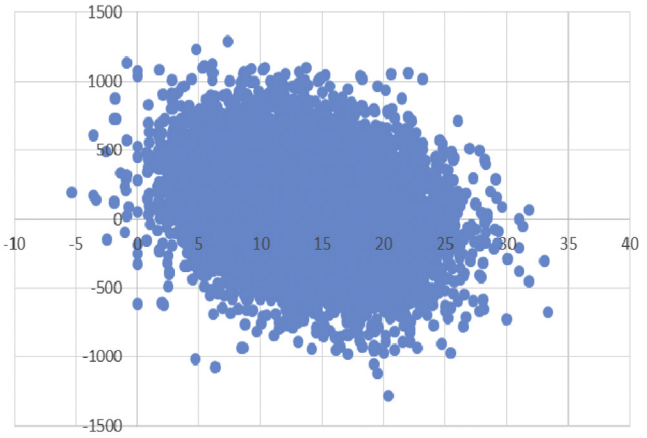


**Fig. 2.** Scatter plot of the simulation results from 10 000 bootstrapping samples. The x axis represents the difference on infectious complication rate between the nutrition support and no-support cohorts. The y axis represents the difference on average total cost between the two cohorts.

study [25]. Due to the higher cost of PN, our results would probably have been more favorable for nutrition support if EN had been used to a greater extent.

The rate of catheter sepsis was 0%, which was probably related to the fact that all patients received PICC or a fine-needle peripheral vein infusion at a slow rate. In our hospital's surgical and medical wards, line infections from PICC and peripheral vein infusions are very low for all hospitalized patients.

*Limitations and strengths of the study*

There are some limitations to be considered in the present study. First, it was a single-center study. Conditions vary among hospitals and regions and the observed results should be interpreted and extrapolated cautiously for other populations.

Second, this was not a randomized controlled trial (RCT). An RCT is considered unethical in China among patients who are at nutritional risk. Physicians should not randomize at-risk patients to an inadequate nutrition support group.

By the nature of an observational study, it suffers from the influence of unknown confounders. However, a consecutively recruited observational study has the advantage of avoiding the bias of highly selected participants, which is commonly seen in RCTs. Additionally, the propensity score matching method was employed to minimize the effect of all known confounders. We also found that although patients were treated by a limited number of physicians, each having their individual practice of prescribing nutrition support, this did not affect the results (by means of a generalized linear analysis, data not shown).

The present cost analysis was performed from the payer's perspective and only the direct costs during the in-hospital period were collected. If the costs of primary care, loss of work ability, and postdischarge costs had been included (societal perspective), the results would be different.

## Conclusion

This study suggested that nutrition support decreases the rate of infectious complications as well as the hospital LOS among patients at nutritional risk according to NRS 2002. Nutrition support also appears to be cost-effective in current clinical practice in China.

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## References

[1] Mueller C, Compher C, Ellen DM, American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. A.S.P.E.N. clinical guidelines: nutrition screening, assessment, and intervention in adults. JPEN J Parenter Enteral Nutr 2011;35:16–24.
[2] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22:415–21.
[3] Chinese Medical Association. Clinical Practice guidelines parenteral enteral nutrition section. Beijing: People's Medical Publishing House; 2008:16–8. 47.
[4] Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22:321–36.
[5] Johansen N, Kondrup J, Plum LM, Bak L, Nørregaard P, Bunch E, et al. Effect of nutritional support on clinical outcome in patients at nutritional risk. Clin Nutr 2004;23:539–50.
[6] Starke J, Schneider H, Alteheld B, Stehle P, Meier R. Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients. Clin Nutr 2011;30:194–201.
[7] Jie B, Jiang ZM, Nolan MT, Efron DT, Zhu SN, Yu K, et al. Impact of nutritional support on clinical outcomes in patients at nutritional risk: a multicenter, prospective cohort study in Baltimore and Beijing teaching hospitals. Nutrition 2010;26:1088–93.
[8] Jie B, Jiang ZM, Nolan MT, Kondrup J. Impact of preoperative nutritional support on clinical outcome in abdominal surgical patients at nutritional risk. Nutrition 2012;28:1022–7.
[9] Jiang ZM, Zhong ZH. Nutritional risk, undernutrition (malnutrition) and nutritional support. Chin J Clin Nutr 2008;16:331–2.
[10] Dougherty D, Conway H. The "3 T's" road map to transform US health care: the "how" of high quality care [J]. JAMA 2008;299:2319–21.
[11] Kernick DP. Has health economics lost its way? BMJ 1998;317:197–9.
[12] Waitzberg DL. Efficacy of nutritional support: Evidence-based nutrition and cost-effectiveness. Nestle Nutr Workshop Ser Clin Perform Programme 2002;7:257–71. discussion 271–6.
[13] World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Seoul: 59th WMA General Assembly; 2008. version 2013. Available at: http://jamanetwork.com/journals/jama/fullarticle/1760318.
[14] American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992;20:864–74.
[15] Eisenberg JM, Glick H, Hillman AL, Baron J, Finkler SA, Hershey JC, et al. Measuring the economic impact of perioperative total parenteral nutrition: principles and design. Am J Clin Nutr 1988;47:382–91.
[16] McGhan WF, Boatman JL. Pharmacoeconomics, health policy, and limited resources. In: Boatman JL, Townsend RJ, McGhan WF, editors. Principles of Pharmacoeconomics. 3rd Edition. Cincinnati, OH: Harvey Whitney Books Co; 2005. p. 401–8.
[17] Braga M, Gianotti L. Preoperative immunonutrition: cost-benefit analysis. JPEN J Parenter Enteral Nutr 2005;29:S57–61.
[18] Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. 3rd Edition. New York, the USA: Oxford University Press; 2005:40.
[19] Preedy VR, Watson RR. Incremental cost-effectiveness ratio. Handbook of Disease Burdens and Quality of Life Measures. New York, USA: Springer; 2010:4235.

[20] Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res 2011;46:399–424.
[21] Kroese DP, Taimre T, Botev ZI. Handbook of Monte Carlo Methods. Hoboken, New Jersey, USA: John Wiley & Sons, Inc.; 2011.
[22] Khan NA, Quan H, Bugar JM, Lemaire JB, Brant R, Ghali WA. Association of postoperative complications with hospital costs and length of stay in a tertiary care center. J Gen Intern Med 2006;21:177–80.
[23] WHO-CHOICE. Choosing interventions that are cost-effective. Geneva: WHO; 2014. Available at: http://www.who.int/choice/en/. Accessed December 31, 2016.
[24] National Bureau of Statistics of China. Bulletin on the final verification data of GDP in 2011. Available at: http://www.stats.gov.cn/english/PressRelease/201301/t20130111_72246.html. Accessed December 31, 2016.
[25] Zhang H, Wang Y, Mu SY, Jiang ZM, Shi D, Yu K. Prevalence of nutritional risks, undernutrition and application of nutritional support at a Chongqing teaching hospital. Natl Med J China 2012;48:3417–9.