Original Article

# Pharmacoeconomics of parenteral nutrition in surgical and critically ill patients receiving structured triglycerides in China

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**Background and Objectives:** A prior meta-analysis showed favorable metabolic effects of structured triglyceride (STG) lipid emulsions in surgical and critically ill patients compared with mixed medium-chain/long-chain triglycerides (MCT/LCT) emulsions. Limited data on clinical outcomes precluded pharmacoeconomic analysis. We performed an updated meta-analysis and developed a cost model to compare overall costs for STGs vs MCT/LCTs in Chinese hospitals. **Methods and Study Design:** We searched Medline, Embase, Wanfang Data, the China Hospital Knowledge Database, and Google Scholar for clinical trials comparing STGs to mixed MCT/LCTs in surgical or critically ill adults published between October 10, 2013 and September 19, 2015. Newly identified studies were pooled with the prior studies and an updated meta-analysis was performed. A deterministic simulation model was used to compare the effects of STGs and mixed MCT/LCT's on Chinese hospital costs. **Results:** The literature search identified six new trials, resulting in a total of 27 studies in the updated meta-analysis. Statistically significant differences favoring STGs were observed for cumulative nitrogen balance, prealbumin and albumin concentrations, plasma triglycerides, and liver enzymes. STGs were also associated with a significant reduction in the length of hospital stay (mean difference, −1.45 days; 95% confidence interval, −2.48 to −0.43; $p$=0.005) versus mixed MCT/LCTs. Cost analysis demonstrated a net cost benefit of ¥675 compared with mixed MCT/LCTs. **Conclusions:** STGs are associated with improvements in metabolic function and reduced length of hospitalization in surgical and critically ill patients compared with mixed MCT/LCT emulsions. Cost analysis using data from Chinese hospitals showed a corresponding cost benefit.

**Key Words: lipid emulsion, parenteral nutrition, intensive care unit, cost-effectiveness**

## INTRODUCTION

The nutritional management of critically ill patients in the intensive care unit (ICU) in Chinese hospitals is a complex challenge involving both clinical and economic considerations. Due to the increased metabolic demands associated with critical illness, many patients admitted to the ICU enter a state of negative energy balance that rapidly progresses during the course of the ICU stay.[1] The resulting energy deficits are associated with an increased risk of complications, prolonged duration of mechanical ventilation, and increased length of stay in the hospital and the ICU.[1-4] In China, patients are required to pay out of pocket for hospital expenditures; therefore, considerations related to acquisition costs for nutrition therapy might significantly influence therapeutic decisions.[5]

Parenteral nutrition (PN) is indicated in critically ill patients who are malnourished or at risk of malnutrition and have a dysfunctional gastrointestinal tract that is not suitable for enteral feeding.[6] Lipids are an integral component of PN, serving as an energy-dense source of calories and essential fatty acids. Additionally, lipids are key structural components of cell membranes and precursors of important bioactive mediators such as leukotrienes and prostaglandins.[1,6-8] Finally, lipids regulate the expression of a variety of genes and modulate cell signalling pathways involved in apoptosis, inflammation, and cell-mediated immune response.[8]

The primary components of parenteral lipid emulsions are medium- and long-chain triglycerides (MCT and LCT, respectively), which are comprised of three fatty acids attached to a glycerol backbone. First generation lipid emulsions were based on LCTs derived primarily from soybean oil; however, evidence of an association between soybean oil-based lipid emulsions and adverse immunological effects led to the development of lipid emulsions in which LCTs were partially replaced with MCTs derived from coconut or palm oil.[9] Parenteral lipid

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emulsions containing both LCTs and MCTs are available as either a mixture of LCTs and MCTs or as synthetically structured triglycerides (STGs) containing randomly mixed triglyceride molecules with both medium-chain and long-chain fatty acids bound to the same glycerol backbone.[10]

Studies evaluating STG-based lipid emulsions in surgical and critically ill patients have consistently demonstrated favorable effects on measures of nutritional status and metabolic function compared with pure LCT or mixed MCT/LCT emulsions.[11,12] In a recent meta-analysis of 21 clinical trials comparing STG-based lipid emulsions with mixed MCT/LCT emulsions, Wu et al reported that STG-based emulsions were associated with significant improvements in cumulative nitrogen balance, decreased plasma triglyceride concentration, and improved liver tolerability.[11] However, few studies have evaluated the effects on clinical outcomes such as infectious complications and length of stay in the hospital or ICU. Of the 21 studies included in the meta-analysis by Wu et al, only four reported data on length of stay in the hospital or ICU, and there was insufficient data on other clinical outcomes to perform a quantitative meta-analysis of the results. As a consequence of the limited availability of data on clinically relevant outcomes, the effects of STGs and mixed MCT/LCT emulsions on total hospitalization costs are unknown. In the present study, we performed a systematic review of the literature to identify studies published since the prior meta-analysis evaluating STGs and mixed MCT/LCT emulsions in surgical and critically ill patients. Newly identified studies were pooled with those in the previous meta-analysis to derive more precise estimates of the magnitude of effect on clinical and metabolic outcomes. The results were then used as inputs for model parameters in a cost minimization model comparing STG-based lipid emulsions with mixed MCT/LCT emulsions in post-surgical and critically ill patients in the ICU setting in Chinese hospitals.

## METHODS

### *Systematic literature search and meta-analysis*

#### Search strategy and selection criteria

The search strategy for the original systematic literature review has been previously described.[11] Briefly, we searched Medline, Embase, Wanfang Data, China Hospital Knowledge Database, and Google Scholar for articles published in English, German, French, Spanish, Italian, or Chinese between October 10, 2013 and September 19, 2015 (the original search included articles published prior to October 10, 2013). The search terms were "structured triglyceride OR structural lipid OR structured lipid AND parenteral" with limits established for selected search parameters according to the specific database (the full search protocol is available in the data supplement). Eligible studies were comparative clinical trials in surgical or critically ill adult patients receiving PN for ≥5 days with at least one arm assigned to receive STGs (Structolipid®, Fresenius Kabi GmbH, Bad Homburg, Germany) and one arm assigned to receive a mixed MCT/LCT emulsion (Lipofundin®, B. Braun, Melsungen, Germany; Lipovenoes MCT®, Fresenius Kabi). Additionally, eligible studies were required to evaluate at least one of the prespecified laboratory and clinical outcomes (see data supplement). We excluded editorials, narrative reviews, abstracts without full text articles, and studies that lacked sufficient information regarding the study population or analytic methods. Titles retrieved by the search were screened by two independent reviewers to identify potentially relevant articles; selected articles were then independently reviewed and assessed for eligibility. Disagreement between reviewers was resolved by consensus through interactive discussion.

#### Data extraction

Information on study design, patient population, and prespecified laboratory and clinical outcomes was extracted and recorded on data extraction forms by two independent reviewers. In cases where the result of a prespecified outcome was only reported graphically, the curves were digitized and numerical values were extrapolated using Engauge Digitizer® software (version 6.0).

#### Data synthesis

Extracted data from the included studies were pooled with data from studies in the original meta-analysis by Wu et al.[11] For continuous outcome variables, the mean difference between treatment groups was used as the measure of effect size; in cases in which a continuous outcome variable was measured inconsistently across studies, standardized mean difference was used. Relative risk was used as the measure of effect size for dichotomous outcome variables.

Meta-analysis of results was performed using RevMan® version 5.3 (The Cochrane Collaboration, London, UK). A fixed-effect model was used to perform the meta-analysis; when substantial heterogeneity ($i^2$ >50%) was detected, a random effect model was adopted. Studies were weighted according to the inverse variance method for continuous variables and the Mantel-Haenszel method for dichotomous variables. Weights were adjusted in the random effect model according to the extent of heterogeneity among the varying intervention effects using the DerSimonian and Laird method. Inter-study variation was estimated by comparing the result of each study with either the Mantel-Haenszel (dichotomous variables) or inverse variance (continuous variables) fixed-effect meta-analysis result.

### *Pharmacoeconomic analysis*

A cost-minimization model was developed to compare resource utilization and overall hospitalization costs in surgical or critically ill ICU patients receiving PN with STG-based emulsions versus mixed MCT/LCT emulsions in Chinese hospitals. Cost items included daily medication costs and the daily cost of stay in the general ward and in the ICU. The model simulates the clinical pathway of a patient from admission to the ICU until hospital discharge. Model parameters included body weight, duration of PN therapy, and length of stay in the ICU and hospital ward. The mean (±SD) body weight of patients from the studies included in the meta-analysis (61.02 [±10.98] kg) was used as a proxy body weight for Chinese patients. Values for duration of PN were obtained from a recent study in Chinese ICU patients receiving PN therapy.[5]

Values for length of stay in the ICU and hospital ward for patients receiving a mixed MCT/LCT emulsion (standard PN) were derived from the same study; for the STG arm, the duration of hospitalization (ICU + ward) was derived by subtracting the mean difference in the length of hospital stay observed in the meta-analysis from the mean total duration of hospitalization (ICU + ward) for patients receiving standard PN. The total number of lipid bags was determined assuming a fat supply of 1 g/kg body weight (BW)/day.[13] The total number of consumed units was calculated by multiplying the daily fat supply by the mean duration of PN therapy and rounding up to the nearest integer; therefore, only the unused portion of the last bag was considered wasted.

The primary cost analysis was based on a deterministic simulation model using mean values for model parameters. All costs are reported in renminbi (¥). Unit cost inputs for one day in the ICU (¥2261) and the hospital ward (¥1550) were obtained from the aforementioned study by Wu et al.[5] Acquisition costs for STG and mixed MCT/LCT emulsions were based on the mean acquisition costs reported by select hospital centers in China (Table 1).

A probabilistic sensitivity analysis was performed to assess the effect of uncertainty surrounding parameter values by repeating the main analysis 1000 times, with each iteration using a new set of values sampled from the probability distribution (expressed as the standard error of the mean) for each model parameter. A one-way deterministic sensitivity analysis was also performed to assess the sensitivity of the estimated cost difference to variations in base case estimates. Finally, a two-way threshold scenario analysis was used to evaluate the relationship between the maximum duration of PN therapy and the reduction in overall costs as a function of the reduction in the length of stay in the hospital.

**Table 1.** Daily unit costs for STG-based and mixed MCT/LCT emulsions at selected hospitals in China†

| Location/source | MCT/LCT (¥) | STG (¥) |
|---|---|---|
| Shang Hai | 98.36 | 278.00 |
| Bei Jin | 88.16 | 266.58 |
| Tian Jin | 94.76 | 280.12 |
| Jiang Su | 89.41 | 270.25 |
| Zhe Jiang | 82.65 | 254.28 |
| Guang Dong | 90.30 | 275.88 |
| NDRC | 98.70 | 291.00 |
| Mean (SEM) | 91.76 (5.84) | 273.73 (11.57) |

LCT: long-chain triglycerides; MCT: medium-chain triglycerides; NDRC: National Development and Reform Commission; SEM: standard error of measurement; STG: structured triglycerides.
†Based on a 250 mL bag containing either 20% Structolipid® or 20% MCT/LCT emulsion.

## RESULTS

The systematic literature search retrieved a total of 13 citations (Figure 1). A review of the titles identified one study that did not meet eligibility criteria due to the study population. Of the 12 full articles that were assessed for eligibility, six met the criteria for inclusion.[13-18]

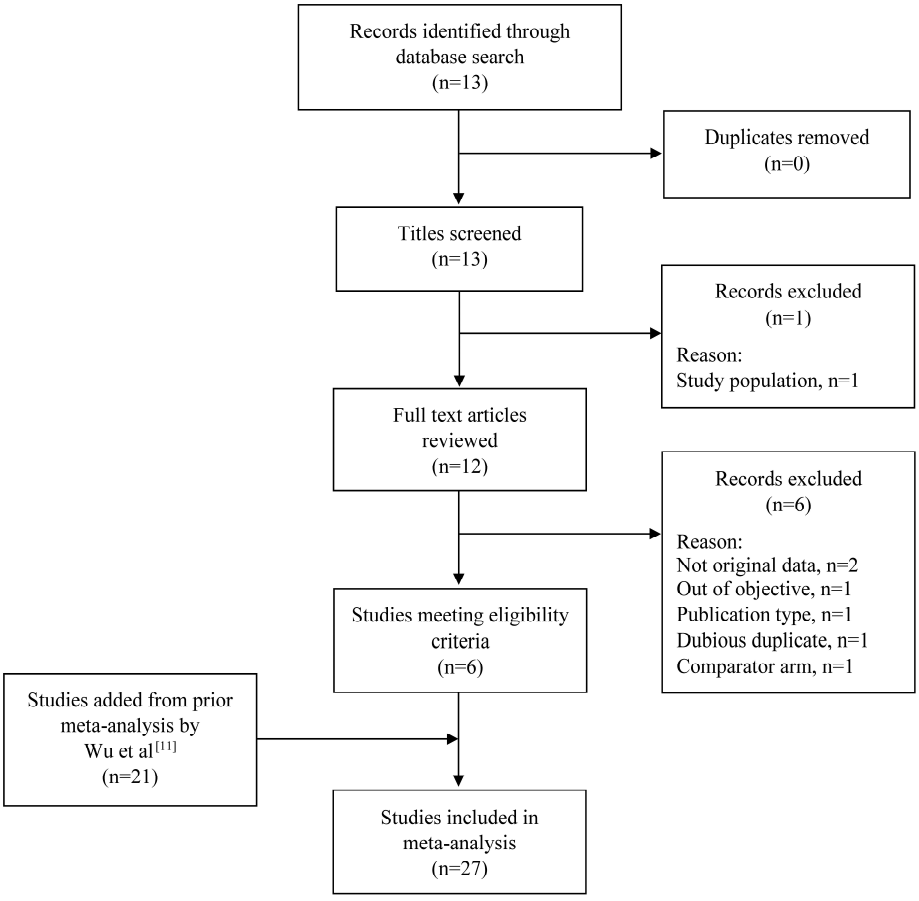



**Figure 1.** Study flow diagram.

***Meta-analysis***

The six studies identified in the updated systematic literature search were pooled with the 21 studies from the prior meta-analysis by Wu et al.[11,19-39] Study characteristics for the 27 studies included in the updated analysis are summarized in Table 2.

Meta-analysis of metabolic outcomes showed statistically significant differences favoring the STG emulsion compared with mixed MCT/LCT emulsions for cumulative nitrogen balance (Figure 2A), pre-albumin (Figures 2B and 2C), plasma triglyceride concentration (Figure 2D), and several parameters of liver function, including alanine transaminase, aspartate aminotransferase, and gamma-glutamyl transferase (Figures 2E). Meta-analysis showed a trend to increased serum albumin concentration in patients receiving STG compared with mixed MCT/LCT emulsions. There was no metabolic parameter for which the outcome favored mixed MCT/LCT emulsions compared with the STG emulsion.

A minority of studies included in the analysis reported clinical outcomes; however, five studies including a total of 118 patients reported data on the length of stay in the hospital or ICU.[18,22,23,27,34] Meta-analysis of data from these five studies showed a statistically significant reduction in the mean length of stay in patients receiving STGs compared with mixed MCT/LCT emulsions (mean difference, −1.45 days; 95% confidence interval [CI], −2.48 to −0.43; $p$=0.005; Figure 3).

***Cost analysis***

Resource consumption parameters for the deterministic simulation model are shown in Table 3 and Figure 4. Patients in both arms enter the model upon admission to the ICU and receive PN therapy for a mean (±SD) duration of 8.3 (±10.0) days. Patients are discharged to the ward after a mean (±SD) duration of 10.4 (±10.1) days. The length of stay on the ward is then determined based on the nutritional therapy. Patients receiving standard PN are discharged from the ward after 14.6 (±14.2) days. Based on the observed mean difference in the length of hospital stay in the meta-analysis, the length of stay is reduced by 1.45 (±0.52) days for patients receiving an STG emulsion, resulting in a total length of hospitalization of 23.55 and 25.00 days in the STG and standard PN groups, respectively.

Model results showed that PN with STGs was associated with a net cost benefit of ¥675 per patient compared with mixed MCT/LCT emulsions (Table 4). Although the acquisition cost was higher for the STG emulsion than the mixed MCT/LCT emulsion (¥3011 versus ¥1009), the shorter duration of hospitalization in patients receiving an STG emulsion resulted in a lower cost of stay (¥43,468 versus ¥46,144), thereby offsetting the difference in acquisition costs.

Probabilistic sensitivity analysis based on 1000 repetitions of the main analysis using randomly sampled values from the probability distribution for each model parameter confirmed the robustness of the result from the deterministic simulation model. The mean estimated reduction in hospital costs associated with STGs was ¥769 (95% CI, ¥709–¥829; Table 5). The estimated reduction in hospital costs in the original model (¥675) was below the 95% CI

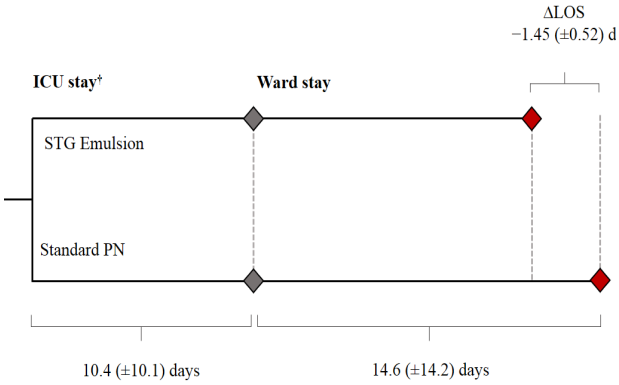



**Figure 4.** Schematic of the model for ICU patients receiving PN therapy †Parenteral nutrition administered for 8.3 (±10.0) days in both arms.

for the estimate in the sensitivity analysis, suggesting that the cost reduction observed in the original simulation model represents a conservative estimate.

Results from the deterministic sensitivity analysis are depicted in Figure 5 in the form of a tornado diagram. In this graph, the effect of uncertainty surrounding variable values on the final outcome is presented in the order of decreasing influence: the most influential parameters result in the widest interval between low and high estimates and appear at the top of the figure. Consistent with the finding of the simulation model, only variation in the length of stay parameter to its minimum value resulted in a change in the result from the primary analysis. The two-way threshold analysis depicted in Figure 6 shows the relationship between the duration of PN administration and the reduction in the length of hospital stay as it relates to overall cost savings; specifically, the longer the maximum duration of PN administration, the larger the necessary reduction in the length of hospital stay to realize a cost benefit with STGs. Based on the estimated mean acquisition costs in China, the use of STGs can be expected to result in an overall cost savings as long as it results in one less day of hospitalization for each week of PN administration.

## DISCUSSION

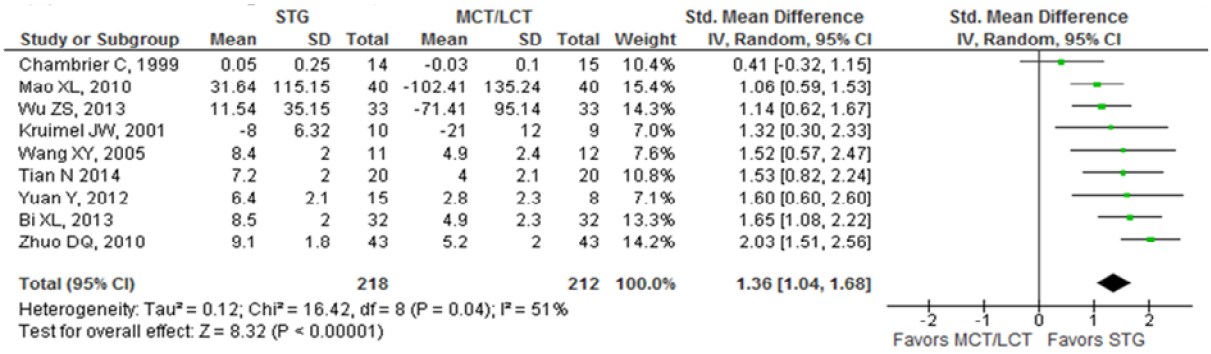
The management of surgical and critically ill patients in the ICU setting represents a substantial source of hospital resource consumption. Due to the increased metabolic demands associated with trauma and critical illness, energy deficits can accumulate rapidly in patients admitted to the ICU, leading to malnutrition and subsequent adverse clinical consequences. Parenteral lipid emulsions containing either a physical mixture of LCTs and MCTs or synthetic STGs provide an efficient source of energy and essential fatty acids. STG-based lipid emulsions have been shown to improve biochemical measures of metabolic function compared with mixed MCT/LCT emulsions; however, few studies have investigated whether such improvements in laboratory parameters translate into clinical or cost benefits. As a consequence, the higher acquisition cost of STGs might limit usage in countries such as China where patients bear full responsibility for the costs of hospitalization. In the present analysis, we performed a meta-analysis of 27 studies evaluating STGs

**Table 2.** Characteristics of included studies

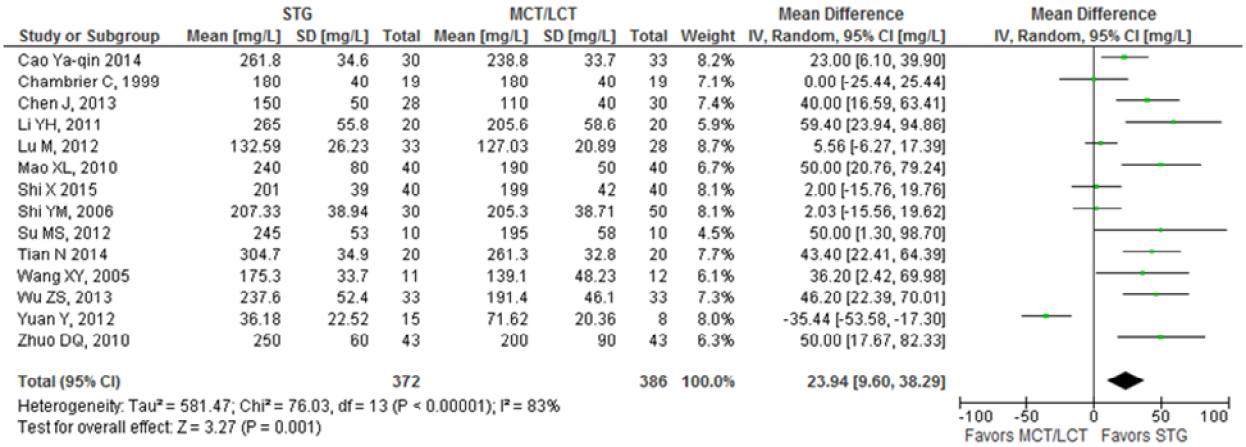
| Studies included in the prior review by Wu et al[11] | | | | | |
|---|---|---|---|---|---|
| Study | Population | Design | N | Observation index | Reported outcomes |
| Bi, 2013[19] | Surgical (GI cancer) | Randomized, controlled | 64 | POD 1–6 | NB, REE, CRP, GSH-px, MDA |
| Chambrier, 1999[20] | Surgical (elective GI) | Randomized, double-blind, controlled | 40 | POD 1–6 | NB, PA, Alb, AST, ALT, ALP, T Bil |
| Chen, 2013[21] | ICU | Randomized, controlled | 80 | Day 0–5 | AST, ALT, ALP, T Bil, TG, C, HDL, LDL |
| Chen, 2013[22] | ICU (severe sepsis) | Randomized, controlled | 64 | Day 1–7 | AST, ALT, TG, PA, Alb, C, G, CRP, LOS ICU, Apache II, Mortality |
| Jing, 2010[23] | Surgical (hepatectomy) | Randomized, double-blind, controlled | 125 | POD 1–3/5 | AST, ALT, T Bil, Alb, C, Serum Cre, LOS H |
| Kang, 2011[24] | Surgical with hyperbilirubinemia | Retrospective, controlled, matched | 50 | POD 1–5 | AST, ALT, ALP, GGT, T Bil, TG |
| Kruimel, 2001[25] | Surgical (aortic prosthesis) | Randomized, double-blind, controlled | 25 | POD 1–5 | NB, TG, FFA |
| Li, 2011[26] | ICU | Randomized, controlled | 40 | Day 0–6 | AST, ALT, GGT, TG, PA, C, Serum Cre |
| Lu, 2012[27] | ICU | Randomized, controlled | 61 | Day 0–5 | TG, PA, Alb, C, G |
| Lu, 2012[28] | Surgical (GI cancer) | Randomized, double-blind, controlled | 80 | POD 1–7 | LOS H, Inf |
| Luo, 2011[29] | Surgical (major abdominal) | Randomized, controlled | 40 | Day 0–4 | TG, Inf |
| Mao, 2010[30] | Surgical (GI cancer) | Randomized, double-blind, controlled | 80 | POD 1–7 | NB, PA, Alb, Inf |
| Puiggros, 2009[31] | Surgical (major GI) | Randomized, double-blind, controlled | 14 | POD 1/2–5 | AST, ALT, ALP, GGT, T Bil, TG, C, HDL, LDL |
| Shi, 2006[32] | Surgical (GI) | Randomized, blind, controlled | 60 | POD 1–6 | TG, PA, C |
| Su, 2012[33] | Surgical with blood loss >3000 mL | Randomized, controlled | 20 | POD 2(T0)–7 | ALT, T Bil, TG, PA |
| Wang, 2005[34] | Surgical (abdominal) | Randomized, double-blind, controlled | 24 | POD 1–6 | NB, PA, LOS H |
| Wang, 2006[35] | Surgical (abdominal) | Randomized, blinded, controlled | 40 | Pre-/post-injection, day 2 | TG, C |
| Wu, 2013[36] | Surgical (liver cancer) | Randomized, controlled | 66 | POD 0–7 | NB, AST, ALT, T Bil, PA, Alb |
| Yu, 2008[37] | Surgical (abdominal) | Randomized, controlled | 50 | POD 5 | AST, ALT |
| Yuan, 2012[38] | Cirrhosis | Controlled | 26 | Day 1–6 | NB, AST, ALT, T Bil, PA, Alb |
| Zhuo, 2010[39] | Surgical (hepatic) | Randomized, double-blind, controlled | 86 | POD 1–7 | NB, T Bil, PA, Alb |
| Fan, 2013[14] | Hepatitis | Randomized, controlled | 75 | Day 1–11 | AST, ALT, TG, C |
| Cao, 2014[15] | MOJ | Randomized, controlled | 63 | Day 0–6 | ALT, T Bill, TG, PA, Alb, C |
| Tang, 2014[16] | ICU | Randomized, controlled | 98 | day 0–15 | AST, ALT, ALP, T Bil, TG, C, HDL, LDL |
| Tian, 2014[17] | ICU | Randomized, double-blind, controlled | 40 | Day 0–7 | NB, PA |
| Chen, 2015[18] | ICU (ANP) | Randomized, double-blind, controlled | 30 | Day 0–5 | AST, ALT, ALP, GGT, TG, C, Serum Cre |
| Shi, 2015[13] | Surgical | Randomized, prospective, double-blind, controlled | 80 | POD 1–7 | AST, ALT, GGT, TG, PA, C, LOS H |

Alb: albumin; ALT: alanine transaminase; ALP: alkaline phosphatase; ANP: acute necrotizing pancreatitis; AST: aspartate aminotransferase; C: cholesterol; CRE: creatinine; CRP: C-reactive protein; FFA: free fatty acids; G: glucose; GGT: gamma-glutamyl transferase; GI: gastrointestinal; GSH-px: glutathione peroxidase; H: hospital; HDL: high density lipoprotein; ICU: intensive care unit; Inf: infection; LDL: low density lipoprotein; LOS: length of stay; MDA: malondialdehyde; MOJ: malignant obstructive jaundice; NB: nitrogen balance; PA: pre-albumin; POD: postoperative day; REE: resting energy expenditure; TG: triglycerides; T Bil: total bilirubin.

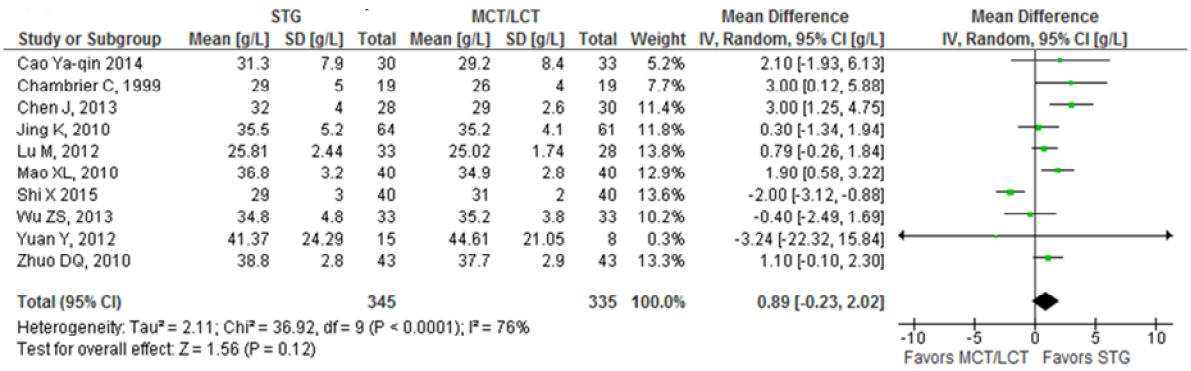
(A) Cumulative nitrogen balance[†]




(B) Pre-albumin concentration[‡]




(C) Serum albumin concentration[‡]




(D) Plasma triglyceride concentration[§]

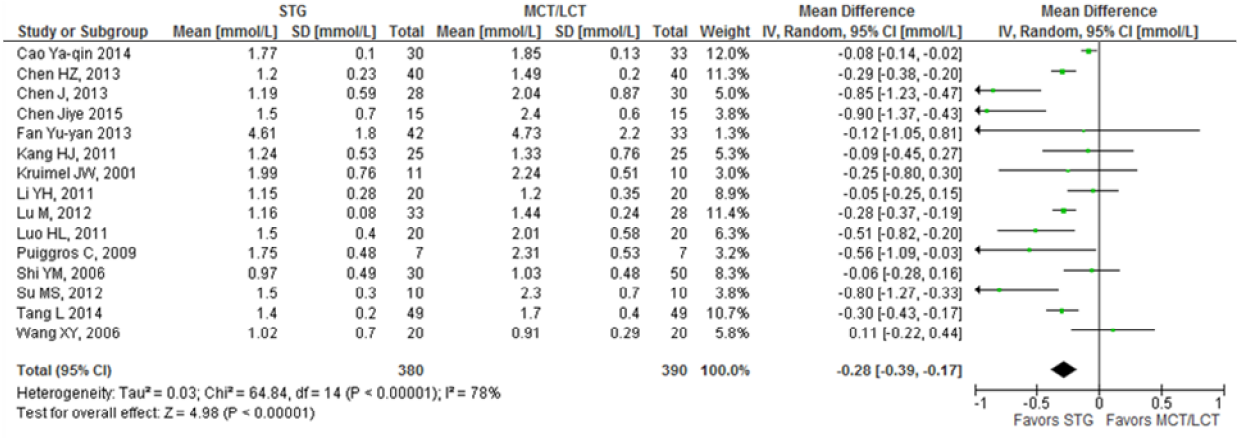
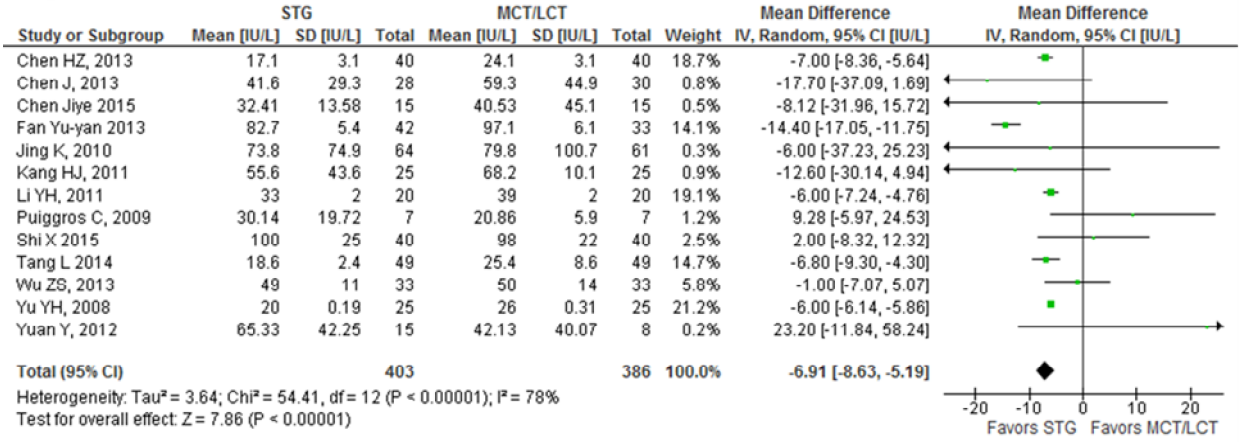



**Figure 2.** Forest plots of the meta-analysis of the effect of STG versus mixed MCT/LCT on laboratory parameters. [†]Assessed over 5–7 days; [‡]Measured after a PN period ranging from 5 to 7 days; [§]Assessed after a PN period ranging from 5 to 7 days, except for Wang et al (assessed after infusion on day 2) and Tang et al (assessed on day 15 of PN administration). CI: confidence interval; LCT: long-chain triglycerides; MCT: medium-chain triglycerides; PN: parenteral nutrition; SD: standard deviation; SE: standard error; Std.: standardized; STG: structured triglycerides.

(E) Liver enzymes[§]

- Aspartate aminotransferase




-Alanine transaminase

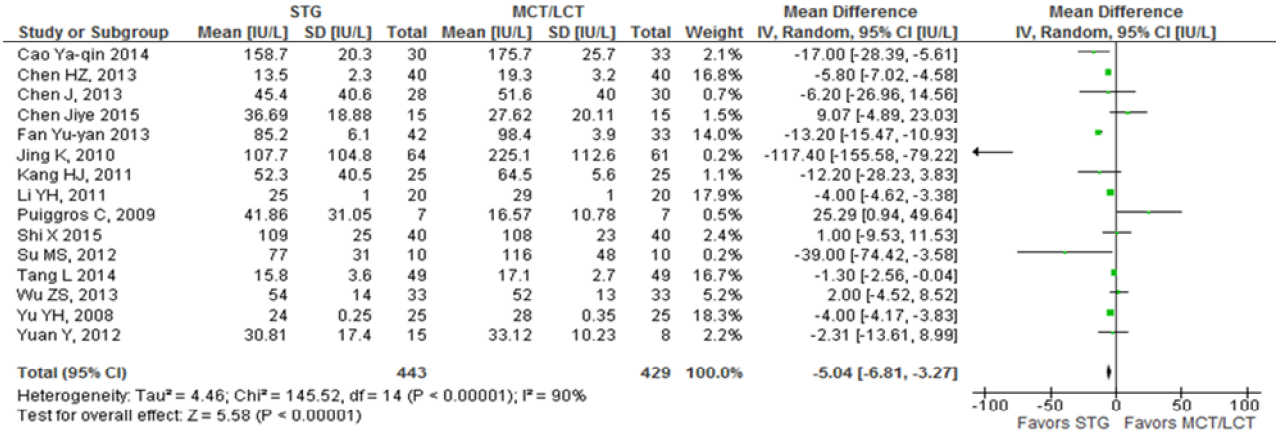



**Figure 2.** Forest plots of the meta-analysis of the effect of STG versus mixed MCT/LCT on laboratory parameters (cont.). [†]Assessed over 5–7 days; [‡]Measured after a PN period ranging from 5 to 7 days; [§]Assessed after a PN period ranging from 5 to 7 days, except for Wang et al (assessed after infusion on day 2) and Tang et al (assessed on day 15 of PN administration). CI: confidence interval; LCT: long-chain triglycerides; MCT: medium-chain triglycerides; PN: parenteral nutrition; SD: standard deviation; SE: standard error; Std.: standardized; STG: structured triglycerides.

**Length of stay in hospital**[†]

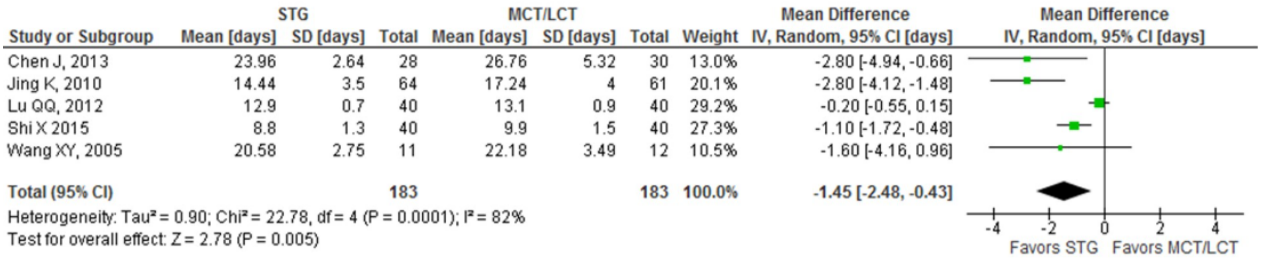



**Figure 3.** Forest plots depicting the results of the meta-analysis of the effect of STG vs mixed MCT/LCT on clinical outcomes. [†]Includes studies evaluating length of stay in the ICU (Chen J, 2013) and length of stay in the hospital (Jing K, 2010; Lu QQ, 2012; Shi X, 2015; and Wang XY, 2005). CI: confidence interval; LCT: long-chain triglycerides; MCT: medium-chain triglycerides; PN: parenteral nutrition; SD: standard deviation; SE: standard error; STG: structured triglycerides.

and mixed MCT/ LCT emulsions in post-surgical or critically ill adult patients and developed a cost minimization model to evaluate the cost benefit of STGs in the ICU setting in Chinese hospitals.

Consistent with prior research,[11,12] meta-analysis of data from studies comparing STGs with mixed MCT/LCT emulsions in surgical and critically ill patients showed statistically significant differences favoring STGs for several measures of metabolic function, including cumulative nitrogen balance, plasma triglyceride concentration, and liver tolerability. The improvements in metabolic outcomes were accompanied by a corresponding reduction in the length of stay in the hospital.

The effect size estimate for the length of stay in the hospital provided a quantitative measure of the effect of STGs on a highly clinically relevant outcome to which an economic value could be assigned. Length of hospital stay was then used as a model parameter for a determin-

**Table 3.** Resource consumption parameters

| Model Parameter | Value | Source |
|---|---|---|
| Mean body weight, kg (±SD) | 61.02 (±10.98) | Meta-analysis |
| Mean duration of PN therapy, d (±SD) | 8.3 (±10.0) | Wu et al, 2016[5] |
| Mean ICU LOS, d (±SD) | 10.4 (±10.1) | Wu et al, 2016[5] |
| Mean Ward LOS, d (±SD) | 14.6 (±14.2) | Wu et al, 2016[5] |
| Mean difference in total LOS, d (95% CI) STG versus standard PN | −1.45 (−2.48 to −0.43) | Meta-analysis |

CI: confidence interval; d: days; ICU: intensive care unit; LOS: length of stay; PN: parenteral nutrition; SD: standard deviation; STG: structured triglyceride.

**Table 4.** Cost outcomes based on the deterministic simulation model

| Parameter | Standard PN | STG | Difference† |
|---|---|---|---|
| PN duration, days | 8.30 | 8.30 | 0 |
| Hospital LOS, days | 25.0 | 23.6 | −1.45 |
| PN acquisition cost, ¥‡ | 1009 | 3011 | 2002 |
| Cost of hospital stay, ¥§ | 46144 | 43468 | −2676 |
| Total cost, ¥ | 47154 | 46479 | −675 |

LOS: length of stay; PN: parenteral nutrition; STG: structured triglycerides.
†Expressed as STG value minus standard PN value.
‡Calculated as the daily acquisition cost multiplied by the duration of PN.
§Calculated as (mean daily cost of ICU stay x mean ICU LOS) + (mean daily cost of ward stay x mean ward LOS).

**Table 5.** Probabilistic sensitivity analysis results

| Parameter | Standard PN | STG | Difference |
|---|---|---|---|
| PN duration, d | | | |
| Mean (SE) | 8.29 (0.56) | 8.29 (0.56) | – |
| 95% CI | 7.20–9.38 | 7.20–9.38 | – |
| Hospital LOS, d | | | |
| Mean (SE) | 25.0 (0.03) | 23.5 (0.05) | −1.46 (0.02) |
| 95% CI | 24.9–25.1 | 23.5–23.6 | −1.49 −1.43 |
| PN acquisition cost, ¥ | | | |
| Mean (SE) | 975 (2.88) | 2908 (7.41) | 1933 (4.62) |
| 95% CI | 969–981 | 2893–2922 | 1924–1942 |
| Cost of hospital stay, ¥ | | | |
| Mean (SE) | 46194 (76.41) | 43492 (96.65) | −2702 (30.17) |
| 95% CI | 46044–46344 | 43309–43676 | −2761 to −2643 |
| Total cost, ¥ | | | |
| Mean (SE) | 47169 (76.56) | 46400 (94.17) | −769 (30.5) |
| 95% CI | 47109–47319 | 46216–46585 | −829 to −709 |

CI: confidence interval; LOS: length of stay; PN: parenteral nutrition; SE: standard error; STG: structured triglycerides.

istic simulation model evaluating the effect of STGs on resource consumption in the ICU setting of Chinese hospitals. The cost analysis showed that the use of STGs in post-surgical and critically ill ICU patients results in a reduction of nearly ¥700 compared with mixed MCT/LCT emulsions. While the acquisition cost is higher for STGs, the difference is offset by a reduction in cost due to the shorter length of hospital stay associated with STGs. Sensitivity analyses confirmed the robustness of the finding and suggested that the estimated cost reduction from the simulation model represents a conservative estimate based on the 95% confidence interval for the estimated cost reduction in the probabilistic model (¥709−¥829). Further cost analysis using a two-way threshold model based on average costs in Chinese hospitals showed that STGs could be expected to result in lower overall hospital costs as long as the length of stay was reduced by one day compared with mixed MCT/LCT emulsions for every seven days of PN administration.

To our knowledge, these findings represent the first available evidence demonstrating that the improvements in biochemical measures of metabolic function observed in ICU patients receiving PN with STG-based lipid emulsions confer clinical benefits that result in reduced resource consumption and lower hospital costs. In light of the substantial clinical and economic consequences associated with suboptimal management of energy deficits in post-surgical and critically ill patients, this finding has important implications for the use of parenteral nutrition in the ICU setting in Chinese hospitals.

The findings of the present study should be interpreted with due consideration of certain limitations. The limited number of studies evaluating length of stay necessitated pooling of the single study evaluating length of stay in the ICU with those that evaluated length of stay in the hospital. The specific reductions in the length of stay in the

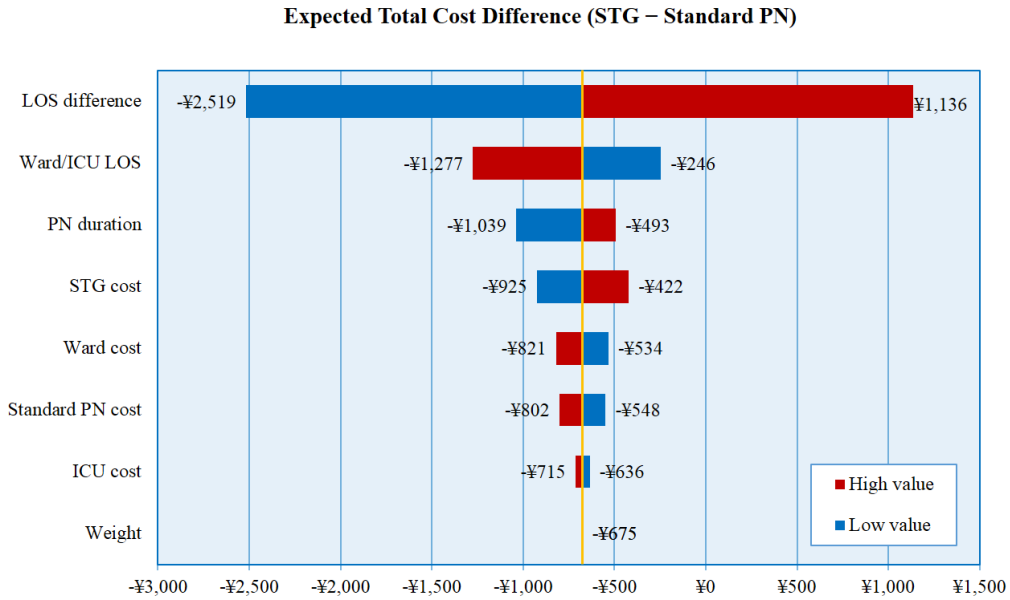



**Figure 5.** Tornado diagram depicting the results of the deterministic sensitivity analysis. ICU: intensive care unit; LOS: length of stay; PN: parenteral nutrition; STG: structured triglycerides.

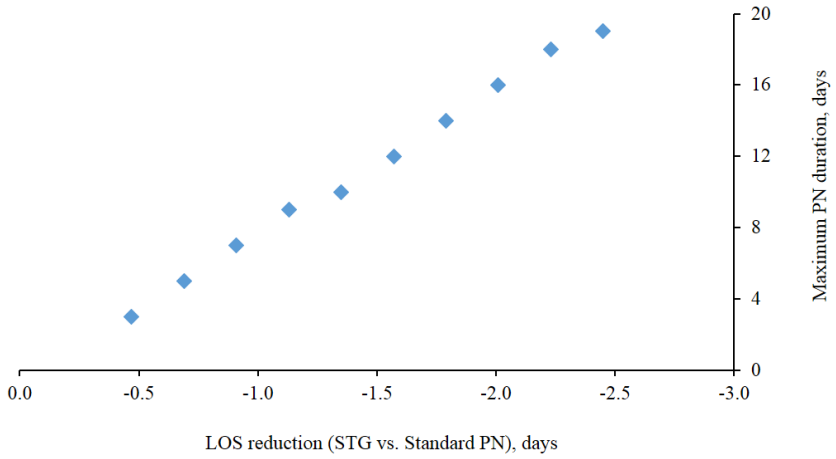



**Figure 6.** Two-way threshold analysis depicting the maximum PN duration associated with a cost savings as a function of the reduction in the length of stay. LOS: length of stay; PN: parenteral nutrition; STG: structured triglycerides.

ICU and on the ward associated with STGs is therefore uncertain. In light of differences in costs between the ICU and the ward, further study is necessary to derive more precise estimates of the magnitude of effect of STGs on the lengths of stay in the ICU and ward, respectively. Additionally, while point estimates favored STGs in each of the five studies evaluating length of stay in the hospital or ICU, there was considerable heterogeneity across the individual studies. Finally, due to the limited availability of published data regarding the cost of care in the ICU in Chinese hospitals, cost estimates for the ICU and ward in the deterministic simulation model were based on a regression analysis of hospital costs in a single institution in Shanghai.[5] The extent to which these estimates are representative of the actual costs in hospitals throughout China is unknown.

### *Conclusion*

In conclusion, the findings of the present study demonstrate that the improvements in biochemical measures of metabolic function in surgical and critically ill ICU patients receiving STG-based lipid emulsions are associated with a corresponding reduction in the length of stay in the hospital. A cost minimization analysis based on cost data from Chinese hospitals shows that the improvement in clinical outcomes results in decreased resource utilization and a net cost savings compared with mixed MCT/LCT emulsions.

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### AUTHOR DISCLOSURES

GW declares no conflict of interest; AE is an employee of Fresenius Kabi, the manufacturer of Structolipid®, MB and LP are employees of AdRes, which has received project funding from Fresenius Kabi.

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