

# Use of a Lipid Screening Tool to Identify Patients at Greater Risk of Infusion Reactions to Lipids in the Home Setting

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## ABSTRACT

### Background

Parenteral nutrition (PN) containing lipid has potential for causing hypersensitivity-related reactions due to the components that make up the intravenous lipid emulsions (ILE). There are 5 different brands of lipids approved in the U.S. for use in PN: Intralipid® (Fresenius Kabi) and Nutrilipid® (B. Braun), SMOF® (Fresenius Kabi), Clinolipid® (Baxter), and Omegaven® (Fresenius Kabi). As reported in the literature, rates of infusion reactions increase in patients with higher risk of hypersensitivity to fish, egg, soybean, or peanut protein. At present, there is limited clinical guidance specific to the home setting for monitoring and administration of the first dose of lipid. Due to this, home infusion organizations have traditionally imposed strict protocols, including required nursing observation time, when administering new ILE formulations. A lipid risk screening tool was previously implemented by this organization to ascertain patients at minimal risk for reaction and allow greater flexibility in patient care surrounding first doses of lipids. Secondary benefits of the lipid risk screening tool included the optimization of limited nursing time available and decreased costs and waste associated with unused anaphylaxis kits. The lipid risk screening tool assesses the potential level of risk the patient may experience based on previous use of ILE products; history of reaction to components such as eggs, soybean products, peanuts, and fish; history of anaphylaxis reactions to ILE or components; history of mild to moderate reactions or no history of reactions to ingredients or potential ingredients. Although there is high potential for hypersensitivity, the reporting shows low incidence of hypersensitivity reactions from previous published literature.

### Purpose

The primary objective of this study was to compare the resources utilized when using a lipid risk screening tool versus the resources utilized previously without the use of a lipid risk screening tool. Specifically, this study assessed nursing time and drug costs related to the dispensing of anaphylaxis kits. The secondary objective was to assess the tolerability of ILE first doses in the home. It was hypothesized that ILE first doses in the home would be well tolerated after clinical review of patients using the lipid risk screening tool.

### Methods

This was a multi-center, retrospective chart review and analysis. Data was collected from electronic medical records and internal surveillance software. Inclusion criteria were patients with whom the lipid risk screening tool was utilized over a period of 12 months. Exclusion criteria included patients less than 18 years of age, and ILE conversion that did not meet risk stratification (i.e., soy-based product conversion to soy-based product). A cost analysis was completed to assess nursing time reduced, and medication dispenses avoided as a result of utilizing the lipid risk screening tool, as compared to the previous process. The patient charts were reviewed for infusion reactions of ILE first dose administration.

*Abstract continues on next page*

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## Results

During the 12-month period reviewed, there was a reduction in resources utilized as a result of the lipid risk assessment tool. Drug utilization related to anaphylaxis kit usage decreased, which resulted in a 99.3% drug cost reduction. There was also a 98.2% reduction in nursing time with the use of the lipid risk screening tool versus the previous method. For the secondary objective of ILE first dose tolerability, the percentage of patients determined to be at any level of risk for ILE infusion reactions was 1.2%. The at-risk population for infusion reactions was determined to have 66.7% of patients at low risk, 11.1% at mild-moderate risk and 22.2% at high risk (see Figure 2). There were no hypersensitivity reactions reported with the at-risk population. The types of allergies for the at-risk population are shown in Figure 3.

## Discussion

Hypersensitivity to the components of parenteral nutrition (PN) is a rare but important complication of PN. Resources used in connection with hypersensitivity reaction were expected to be lower when utilizing the lipid assessment tool prior to first doses of ILEs in the home. As hypothesized the results showed lower cost utilization and nursing time with the lipid assessment tool. A limitation of the study was voluntary reporting and manual documentation of adverse events.

## Conclusions

This study demonstrated the utility of the lipid risk screening tool in appropriately assessing level of risk and potential need for additional resources. The lipid risk screening tool significantly reduced cost as well as time required by nurses to monitor patients for potential reactions. This study shows there is an opportunity to develop further training, education, and insight for optimal usage of the lipid risk screening tool.

## Background

Parenteral nutrition (PN) containing lipid has potential for causing hypersensitivity related reactions due to the components that make up the intravenous lipid emulsion (ILE).<sup>1</sup> ILE is provided to patients as a source of calories and fat, and although hypersensitivity reactions are rare occurrences, this is an important complication to consider when administering lipid containing PN. There are 5 different brands of lipids approved in the US for use in PN: Intralipid® (Fresenius Kabi), Nutrilipid® (B. Braun), SMOF® (Fresenius Kabi), Clinolipid® (Baxter), and Omegaven® (Fresenius Kabi).<sup>2-6</sup> Intralipid® and Nutrilipid® are composed of 100% soybean oil. SMOF® is an ILE formulated with 4 different oils in different concentrations: soybean oil (30%), medium chain triglycerides (30%), olive oil (25%), and fish oil (25%). Clinolipid® is an olive oil (80%) based ILE formulated with soybean oil (20%). Omegaven® is composed of 100% fish oil.<sup>4</sup> Previous literature has reported an increase of infusion-related reactions in patients with a history of hypersensitivity to fish, egg, soybean, or peanut protein.<sup>1</sup> Allergic reactions to PN are uncommon with <1% occurrence, and 60% of symptoms occur within day 1-21.<sup>7</sup> Symptoms may include rash, anaphylaxis, respiratory symptoms, and hemodynamic instability.<sup>7</sup> General principles when considering lipids include avoiding soy ILE in patients with soy and egg allergy, and in patients with peanut allergy as it may cause cross-reactivity.<sup>1,5,6</sup> An additional consideration of note is that olive oil and fish oil ILE formulations are contraindicated in patients with fish and olive allergy.<sup>4,6</sup>

At present, there is limited clinical guidance specific to the home setting for the monitoring and administration of lipids with first dose. Due to this, home infusion organizations have traditionally imposed strict protocols, including required nursing observation time, when administering new ILE formulations. A lipid risk screening tool was previously implemented by this organization to ascertain patients at minimal risk for reaction and allow greater flexibility in patient care surrounding first doses of lipids.

The lipid risk screening tool had secondary benefits, including the optimization of available nursing time, and decreased costs and waste associated with unused anaphylaxis kits. The lipid risk screening tool assesses the potential level of risk the patient may experience based on previous use of ILE products; history of reaction to components such as eggs, soybean products, peanuts, and fish; history of anaphylaxis reactions to ILE or components; and history of mild to moderate reactions or no history

of reactions to ingredients or potential ingredients. Although there is high potential for hypersensitivity based on the ingredients of ILE, the reporting shows low incidence of hypersensitivity reactions.

## Purpose

The primary objective of this study was to compare the resources utilized in this organization with previous stricter protocols of nurse monitoring and anaphylaxis kit availability for all patients, to the utilization after implementation of the lipid risk screening tool. The study assessed nursing time utilized and drug costs related to the dispensing of anaphylaxis kits. The secondary objective was to assess the tolerability of ILE first dose in the home. It was hypothesized that ILE first dose in the home would be well tolerated after clinical review of patients with the risk assessment tool.

## Methods

This study was a multi-center, retrospective, cost-effective analysis of the lipid risk screening tool. Data was collected manually from the electronic medical record and internal surveillance software. The lipid risk screening tool usage over a 1-year period was investigated to determine the utilization of anaphylaxis kits and nursing time for patients receiving first doses of lipids. This study was determined to be IRB exempt.

Data extraction included patient name, medical record number, date of birth, age, location, and lipid risk screening tool information. All data was de-identified prior to analysis, this included patient name, medical record number, date of birth, age, and location. The lipid risk screening tool included current ILE usage, which new product was ordered, if anaphylaxis kits and nursing time were required based on patient level of risk defined in Table 1, and

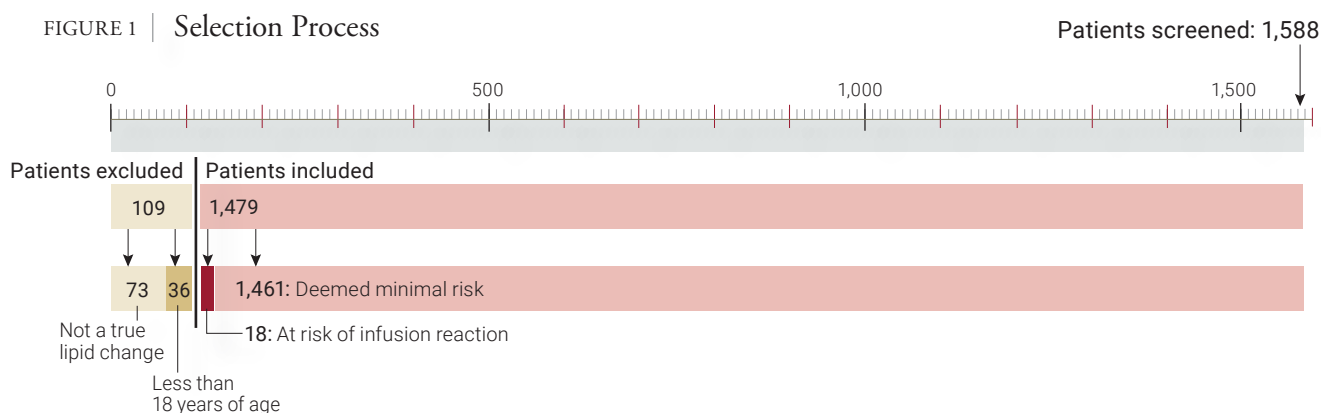
history of reactions to components in ILE products such as eggs, soybean products, peanuts, and fish; history of anaphylaxis reactions to previously used ILE or of their components; history of mild to moderate reactions; or no history of reactions to ingredients or potential ingredients. The tool was developed by the organization as a questionnaire format to be utilized by clinicians, including dietitians and pharmacists, to ascertain patient risk level and allow flexibility around first dose. The previous process involved all patients receiving the stricter protocol of nurse monitoring and anaphylaxis kit availability. The study screened a total of 1,588 records with 1,479 meeting the inclusion criteria. Of the 1,479 records, 1,461 were deemed minimal risk and 18 patients were deemed at-risk for infusion-related reactions (see Figure 1).

A cost analysis was conducted to assess nursing time reduction in minutes, and unnecessary medication dispenses avoided as a result of the lipid risk screening

TABLE 1 | Categories of Patient Level of Risk

Risk Based on Patient History of Hypersensitivity* Reaction			
Minimal Risk	Low Risk	Mild-Moderate Risk	High Risk
No history of allergic reactions.	Known history of mild-moderate reactions to ingredients in ILE.	Known history of mild reactions to ILE product and/or severe reactions to uncooked ingredient.	Known, moderate to severe atopic history and/or anaphylaxis to the ILE product/ingredients.
Appropriate to administer	Appropriate to administer with nursing monitoring, and anaphylaxis kit	Consider Alternative ILE or route of lipids	

\* Hypersensitivity: An immune response that appears as itchy, red and inflamed skin, inflamed airways causing wheezing, shortness of breath, chest tightness, and coughing.



tool, as compared to the previous process (Figure 2). Patient charts were reviewed for infusion reactions of ILE first dose administration. The inclusion and exclusion criteria are described as follows:

**Inclusion criteria:**

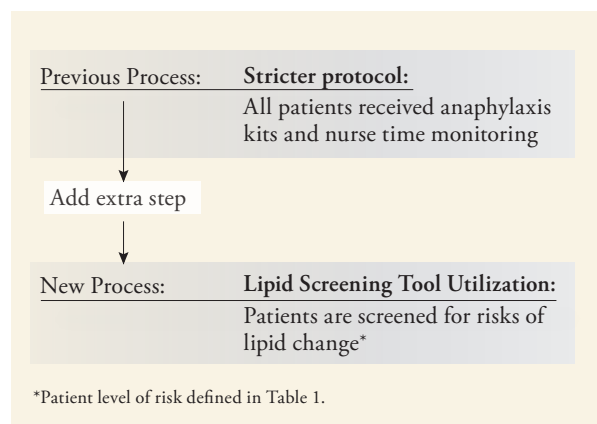
- Patients in whom the screening tool was utilized over a period of 12 months.

**Exclusion criteria:**

- Patients less than 18 years of age at time of screening
- ILE conversion that did not meet risk stratification:
  - Intralipid® to Nutrilipid®
  - Nutrilipid® to Intralipid®
  - SMOF® to Intralipid®, Nutrilipid®, Clinolipid®
  - Clinolipid® to Intralipid®, Nutrilipid®

Of the 1,479 patients included, the initial lipid therapy was 72.7% Intralipid®, 15.3% no initial lipid therapy, 9.9% Clinolipid®, and 2.1% Nutrilipid®. The average ages were 55.9, 55, 55.9, and 54.4 years respectively, and allergies were present in 4.3%, 9.7%, 2.1%, and 19.4% of patients. Of those patients who were initially receiving Intralipid®, 61.1% converted to Clinolipid®, 38.8% converted to SMOF®, and 0.09% converted to Omegaven®. Of those who

FIGURE 2 | Comparison of Previous Process vs. New Process



were initially lipid naive, 41.9% started Clinolipid®, 34.8% started SMOF®, 22.9% Nutrilipid®, and 0.4% Intralipid®. Of those patients who were initially receiving Clinolipid®, 100% converted to SMOF®. Finally, of those patients initially receiving Nutrilipid®, 80.6% converted to Clinolipid® and 19.4% converted to SMOF® (see Table 2 for additional baseline characteristics).

**Results**

Of the 1,479 patients included in the study, 1,461 (98.8%) were determined to be minimal risk and not require nursing observation and anaphylaxis kit availability for the first dose of ILE based on the lipid

TABLE 2 | Baseline Characteristics (n= 1,479)

Baseline Characteristic	No Current Lipid (n=227, 15.3%)	Clinolipid® (n= 146, 9.9%)	Intralipid® (n=1,075, 72.7%)	Nutrilipid® (n= 31, 2.1%)
Age, mean +/- SD	55 +/- 16.1	55.9 +/- 16	55.9 +/-16.3	54.4 +/-16.9
18-49 yrs. (n, %)	88 (38.8)	40 (27.4)	352 (32.7)	11 (35.5)
50-64 yrs. (n, %)	66 (29.1)	60 (41.1)	354 (32.9)	8 (25.8)
65+ yrs. (n, %)	73 (32.1)	46 (31.5)	369 (34.3)	12 (38.7)
Allergies, n (%)	22 (9.7)	3 (2.1)	46 (4.3)	6 (19.4)
Eggs	3 (13.6)	0	3 (6.5)	1 (16.7)
Peanuts	4 (18.2)	1 (33.3)	3 (6.5)	1 (16.7)
Fish	11 (50.1)	2 (66.6)	32 (69.6)	2 (33.3)
Soybean, Soy products	1 (4.5)	0	2 (4.3)	0
Combination of 2 or more	3 (13.6)	0	6 (13)	2 (33.3)
ILE Therapy Change, n (%)				
Clinolipid®	95 (41.9)	0	657 (61.1)	25 (80.6)
Nutrilipid®	52 (22.9)	0	0	0
Intralipid®	1 (0.4)	0	0	0
SMOF®	79 (34.8)	146 (100)	417 (38.8)	6 (19.4)
Omegaven®	0	0	1 (0.09)	0

risk screening tool result, and 18 patients (1.2%) were determined to be at higher risk of hypersensitivity reactions of first dose of the ILE in the home. Of the 18 patients, 12 required both nursing time and an anaphylaxis kit due to lipid risk screening tool determining lipid administration to be appropriate under nurse monitoring and anaphylaxis kit present at the time of infusion. Four patients were determined to be at high risk, and an alternative administration plan was developed rather than providing the first dose in the home. The remaining 2 patients were determined to be at mild to moderate risk, 1 patient had no previous known reactions or allergies and had nurse monitoring without complications. The second patient had a history of allergic reactions to soy and nuts and was administered formulation not containing lipid.

The projected expenditure following the historical process of requiring 30 minutes of nurse monitoring with anaphylaxis kit availability would have resulted in an expenditure of \$212,059 for the 1,479 patients included in the study. With the implementation of the lipid risk screening tool, a 99.3% drug cost reduction was realized, related to avoided anaphylaxis kit dispenses. Nursing time was calculated in minutes, and the projected time spent would have totaled 739.5 hours for the 1,479 patients. As a result of lipid risk screening tool implementation, 726.5 hours of nursing time were saved (98.2%).

For the secondary objective of ILE first dose tolerability, there were no reports of ILE infusion reactions in the internal surveillance software for the studied population during the study period. Of the 18 patients determined to be at-risk by the lipid screening tool, 66.7% were deemed low risk, 11.1% mild-moderate risk, and 22.2% high risk (see Figure 3). The reported allergies of the at-risk population were 27.8% (n=5) had allergies to peanuts, 22.2% (n=4) patients had no known allergies, 22.2% (n=4) had allergies to fish, 16.7% (n=3) had allergies to soybean/soy products, and 11.1% (n=2) had allergies to eggs (see Figure 4).

## Discussion

Cost reduction with implementation of the lipid risk screening tool was expected. The lipid screening tool revealed overall risk was minimal to low within the studied group and provided clear direction on individualized care plans for each patient. Based on

FIGURE 3 | Level of Risk

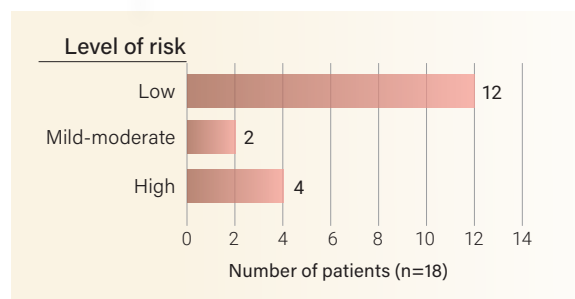
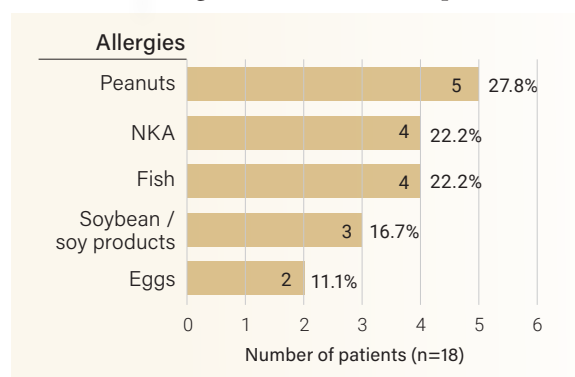


FIGURE 4 | Allergies of the At-Risk Population



these results, the utilization of the lipid risk screening tool allows greater reassurance in the clinical review of risks as an appropriate measure to allow flexibility in care. With limited prior research in this area, new lipid exposure in the home setting previously involved all patients receiving nurse monitoring time and anaphylaxis kit. Implementing a lipid risk screening tool resulted in reduced costs and resources used. This study included patients across an organization over 50 different sites in the U.S. This study provided more information on occurrence on lipid infusion reactions in the home and the implementation of a lipid assessment tool to help guide clinicians with lipids home starts.

A limitation to this study is the voluntary reporting of adverse events from lipid infusion-related reactions which could have resulted in missed events. This study also revealed future usages for how the lipid assessment tool can be implemented. The lipid assessment tool was primarily utilized by pharmacists and dietitians and optimal usage and re-education, and training was revealed as part of the findings. Lipids are an essential component of parenteral nutrition, and this study did not cover further nutrition interventions for patients with history of reactions. Further studies will need to be developed for guidance of higher risk patients.

### Conclusions

This study validated the effectiveness of the lipid risk screening tool in appropriately assessing the level of risk and potential need for additional resources in response to potential hypersensitivity reaction of first dose ILE in the home. Implementation of the lipid risk screening tool significantly reduced cost as well as time required by nurses to monitor patients for potential reactions. Based on the results, the study demonstrated patients tolerate first dose ILE and can be safely stratified based on risks of inducing a reaction with the lipid risk screening tool. Additionally, this study shows there is an opportunity to develop further training, education, and insight for optimal usage of the lipid risk screening tool.

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## Appendix

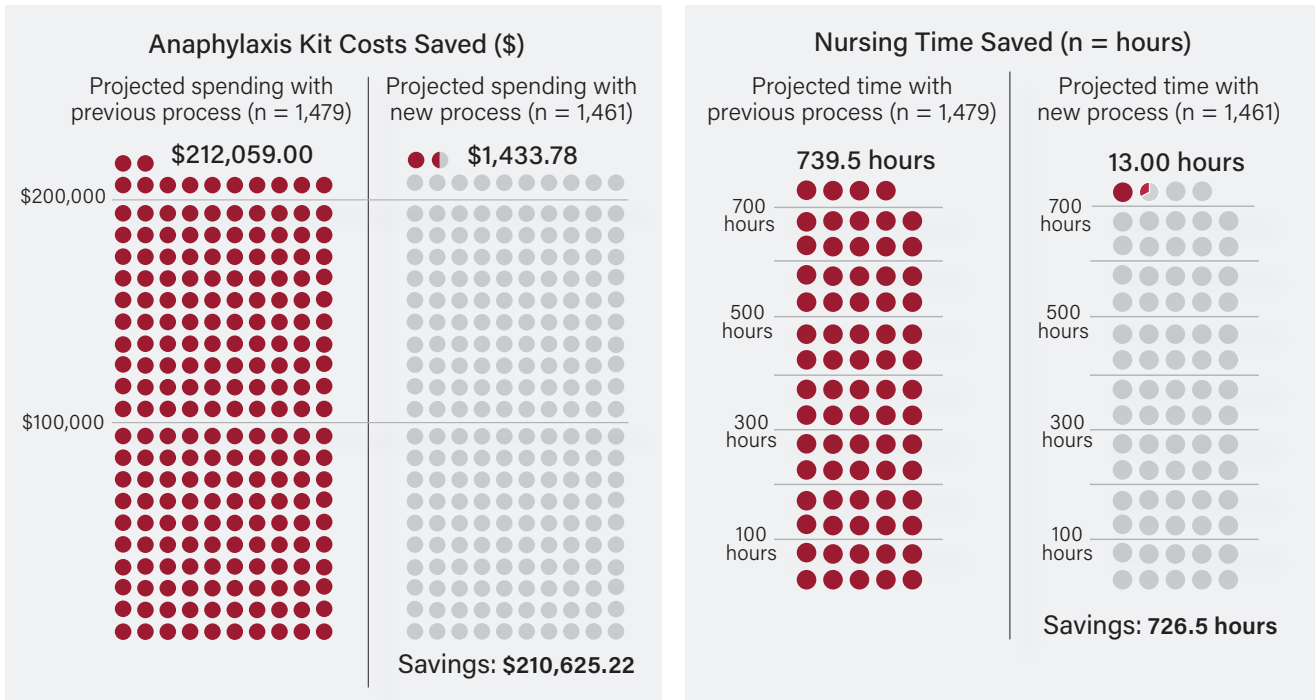
TABLE A1 | Anaphylaxis Contents and Price

Item (total price: \$143.38)
Anaphylaxis Kit Guideline X 1
DiphenhydrAMINE 50 mg/mL 1 mL Vial X 1
EPINEPHrine 1 mg/mL 1 mL SD Amp X 2
Sodium Chloride 0.9% 500 mL X 1
Syringe 1cc LL X 6
Needle 18G 1-1/2in 5Mic X 3
Needle 23G 1in X 4
Needle 25G 5/8in X 3
IV Adm Set 108in 0.2M YSite X 1
Alcohol Prep Pad LG 2-Ply X 4
IV Cath 24Gx.75in Ag X 2
Kit IVStart Frepp/Alc/Teg IV-300LFC X 1

TABLE A2 | Lipid Emulsion Composition

Lipid Product	Intralipid® Nutrilipid®	Smoflipid®	Clinolipid®	Omegaven®
Oil Source	100% soybean oil	30% soybean oil 30% MCT oil 25% olive oil 15% fish oil	80% olive oil 20% soybean oil	100% fish oil

FIGURE A1 | Cost Comparison of Projected Spending and Cost Savings: Drug Cost and Nursing Costs



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