

# SURGICAL NUTRITION INTERVENTION: STANDARD OF CARE

Mary Miranowski RDN CNSC Medical Affairs Manager Nestlé Health Science <u>Disclosure</u>: This presentation has been prepared by and is being presented by an employee of Nestlé Health Science. The material herein is accurate as of the date it was presented, and is for educational purposes only and not intended as a substitute for medical advice.

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#### **Surgical Complications**

#### The Facts

- In the US, 48% of hospital costs are related to surgery.
- 1 in 4 colon resections is readmitted in 90 days.
- Risk of 30 day readmission after general surgery increases
   4-fold if there is a complication; Surgical site infection is among those most commonly sited.
- Soft tissue surgical site infections attribute to \$1.6 billion in direct costs annually.
  - A surgical site infection on average increases the cost of hospital stay by \$20,842.



#### **CMS** Initiatives

#### ■ Triple Aim

- Better Care, Better Health, and Lower Costs Through Improvement
- 5 components:
  - partnership with individuals and families, redesign of primary care, population health management, financial management, and macro system integration
- HAC Present on Admission Indicator
  - Hospitals will not receive additional payment for cases in which one of the listed conditions was not present on admission
- Hospital Readmissions Reduction Program (HRRP)
  - Hospitals will receive reduced payments from Medicare if they have excess readmissions within 30 days of discharge for certain diagnoses including coronary artery bypass graft (CABG) and hip replacement.

Berwick D et al. 2008. The Triple Aim: Care, Health, And Cost. Health Affairs, 759-69.

https://www.cms.gov/Medicare/Medicare-Fee-for-ServicePayment/HospitalAcqCond/Downloads/FY 2013 Final HACsCodeList.pdf
https://www.federalregister.gov/articles/2015/11/24/2015-29438

### **HAC Reduction Program**

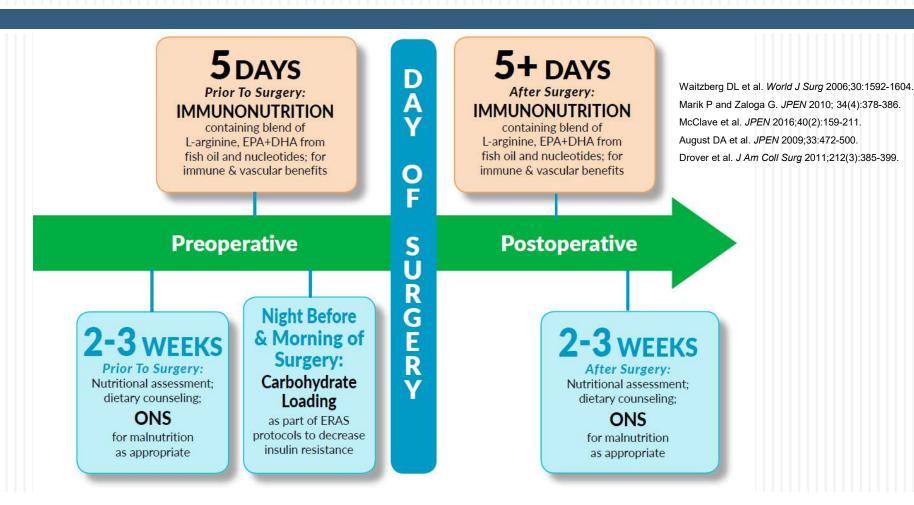
Hospitals performing in the bottom 25% have a 1% reduction in payment from CMS

#### **Measures:**

- PSI 90 Composite Measure (15 HACs)
  - Includes wound dehiscence rate
- CDC NHSN Measures
  - Central Line Associated Bloodstream Infections (CLABSI)
  - Catheter Associated UTIs (CAUTI)
  - SSIs colonic surgeries and abdominal hysterectomies (added in 2016)
  - Methicillin-resistant Staphlococcus aureus (MRSA)
  - Clostridium difficile infection (CDI)



6



# Today's Focus: Major Elective Surgery Consensus of Benefit for 15+ years

- Meta-analyses; Arginine-supplemented Immunonutrition
  - □ Heyland, JAMA 2001
  - Waitzberg, World J Surg 2006
  - □ Cerantola, Brit J Surg 2010
  - Marik and Zaloga, JPEN 2010
  - Drover, J Am Coll Surgeons JACS 2011
  - Marimuthu, Ann Surg 2012
  - □ Zhang, Surg Onc 2012
  - Osland, JPEN 2014
  - Mazaki, Ann Surg 2015
  - Wong and Aly, Int J Surg 2016

# Arginine-supplemented Immunonutrition: Major Elective Surgeries Studied

- ☐ GI Cancer: Upper and Lower
- Cardiac- CABG and Valves
- □ Head/Neck Cancer
- Bladder Cancer
- □ Gyn-Onc Cancer
- □ Orthopedic- Hip, Knee, Shoulder
- □ Non-small cell Lung Cancer
- □ Ventral Hernia Repair

### **Objectives**

- □ Explain the basic science for use of supplemental immunonutrients in helping to reduce the risk of post-operative infectious complications
- Describe the clinical outcomes demonstrated in the literature when perioperative use of arginine supplemented immunonutrition is applied in major elective surgery

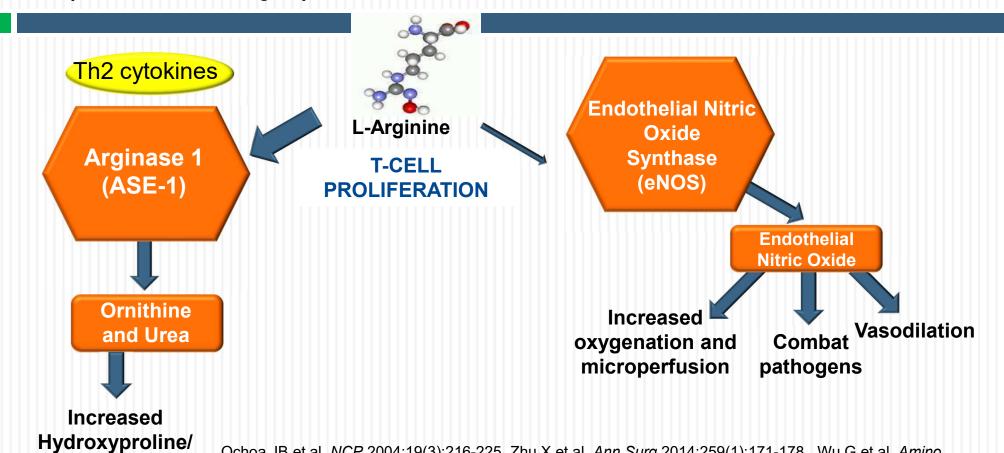
 Discuss how the health economics associated with this nutrition intervention support the implementation of quality initiatives in major elective surgery

### The Science behind the Standard

- □ Surgical trauma induces a state of Arginine Depletion
- Arginine depletion causes T lymphocyte dysfunction and effects microperfusion
- Immunonutrition intervention that includes supplemental arginine helps to restore immune function and optimize oxygen supply to the surgical wound

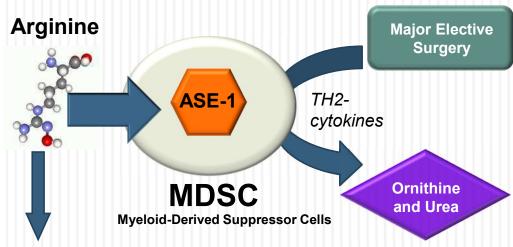
collagen

# Arginine Metabolism after Immune Activation from Major Elective Surgery



Ochoa JB et al. *NCP* 2004;19(3):216-225. Zhu X et al. *Ann Surg* 2014;259(1):171-178. Wu G et al. *Amino Acids* 2009;37:153-168. Forstermann and Sessa. Eur Heart J 2012;33:829-837.

# Arginase-1 in MDSCs Depletes Arginine after Major Surgery



#### **Arginine depletion =**

- Increased risk of infection
- Increased risk of inadequate microperfusion

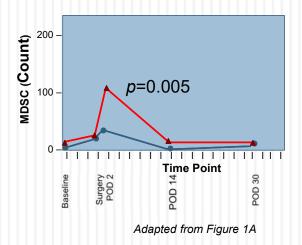
Hamilton-Reeves JM et al. Euro Urol 2016 69(3):389-392. Gentile LF et al. J Trauma Acute Care Surg 2012;72(6):1491-1501. Zhu X et al. Ann Surg 2014;259(1):171-178.. Makarenkova VP et al. J Immun 2006;176:2085-2094.

# Effects of Peri-op Immunonutrition for Cystectomy on Immune Response and Infection Rates: A Pilot RCT



Specialized Immunonutrition\*

Oral Nutrition Supplement Control



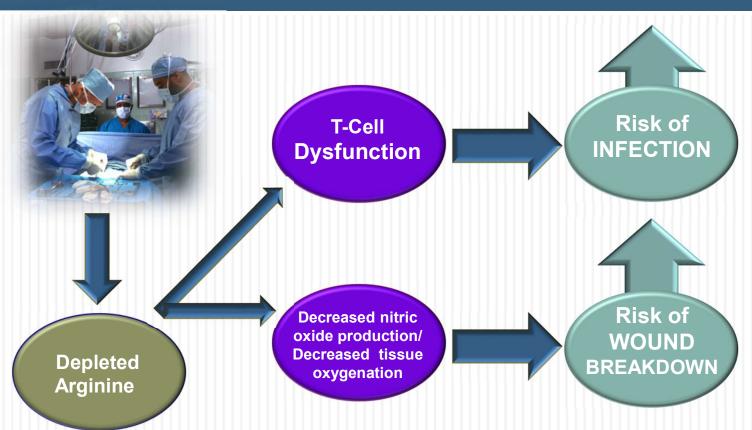
Antibiotic Use	IM	ONS
90 days	14%	53%

p=0.027 Adapted from Table 1

\*The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

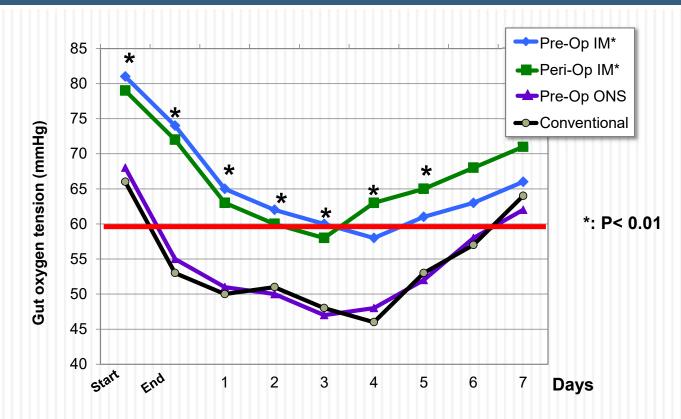
Hamilton-Reeves JM et al. Euro Urol 2016;69(3):389-392.

### Arginine Depletion in Surgery Patients Increases Risks of Infection and Wound Breakdown



Popovich PJ et al. J of Nutr 2006;137:1681S-1686S. Taylor BE et al. CCM 2016; 44(2):390-438. Zhu X et al. Ann Surg 2014;259(1):171-178. Braga M et. al. Surgery 2002;132:805-14.

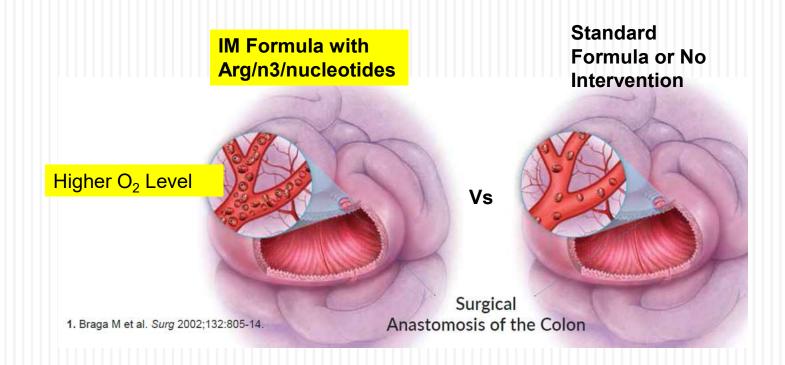
# Arginine-supplemented Immunonutrition increases Tissue Oxygenation



\*The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

Braga et al. Surgery 2002;132:805-14.

# IM Formula Shown to Increase Oxygenation to the Surgical Wound



## Arginine Is Not the Whole Story

- n-3 fatty acids
  - EPA and DHA from Fish Oil
    - Minimize inflammatory response by decreasing production of inflammatory mediators, and increasing production of resolvins, protectins and maresins
    - Increase immune response by enhancing lymphocyte function
    - Interaction with Arginine

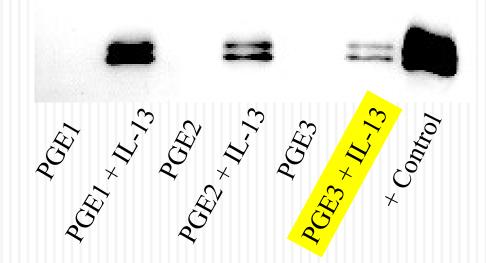


# Proof of Concept – Fish Oil may Blunt Arginase-1 Expression

PGE1 – Borage Oil

PGE2 – Corn Oil

PGE3 – Fish Oil

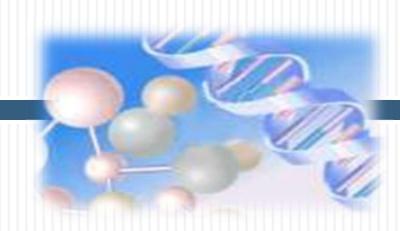


Arginase expression may be modified by the type of Fatty Acid

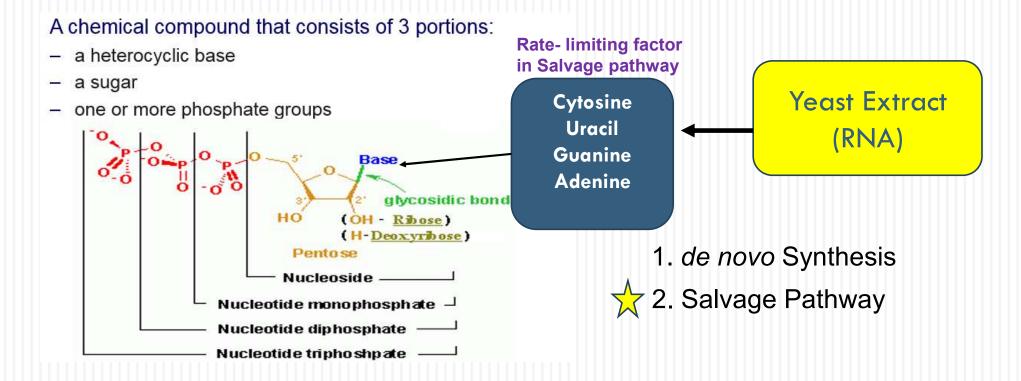
#### The Role of Nucleotides

- Building blocks for DNA and RNA
- Indispensable in stressed states
- □ Essential for rapidly replicating cells to help support immune function
  - Gut Associated Lymphoid Tissue (GALT) and immune cells in the blood are overlapping entities
- Preview: Drover et al found the combination of arginine, fish oil and nucleotides required for statistically significant benefit in major elective surgical patients

Hess JR and Greenberg NA. *NCP* 2012;27(2):281-294. Santora and Kozar et al. J Surg Res 2010;161:288-294. Gil A. Eur J Clin Nutr 2002;56(Suppl 3):S1. Drover et al. *J Am Coll Surgeons* 2011;212(3):385-399.



### Nucleotide Metabolism



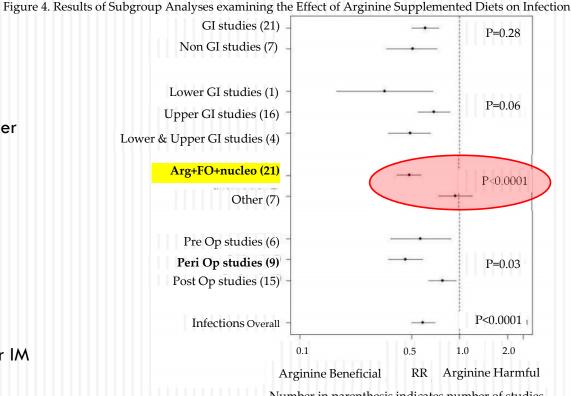
Santora and Kozar et al. J Surg Res 2010;161:288-294. Gil A. Eur J Clin Nutr 2002;56(Suppl 3):S1.

# Perioperative Use of Arginine-supplemented Diets in Major Elective Surgery: A Systematic Review of the Evidence Drover Meta-analysis (n=3438)

- □ Primary outcome: Infectious complications
  - 41% reduction across 28 pre, peri and post-op studies (p<0.0001)
- Secondary outcomes:
  - Hospital LOS
    - Reduced 2.38 days across 29 pre, peri and post-op studies (p<0.00001)
  - Mortality
    - No change

## Sub-analyses of Arginine supplemented diets on Infection

- Same benefit shown for GI surgery vs non GI surgery
- Same benefit shown for Lower and Upper GI surgeries
- Peri-operative use showed greatest benefit (1 54%)
  - •Preop- ↓43% •Postop- ↓22%
- •Arg-n3-nucleotide formula showed significant benefit vs. standards (p<0.0001). Other IM formulas did not (NS)



Number in parenthesis indicates number of studies

Adapted from Drover et al. J Am Coll Surgeons Mar 2011

### Arginine-Supplemented Formulas Studied by Drover

Supplemented Immunonutrients per 1000 kcal except as indicated	Arginine (g)	Glutamine (g)	EPA + DHA (g)	Nucleotides (g)	
Impact <sup>®</sup>	12		1.7	1.2	Containing added
Impact Advanced Recovery® Drink (3 cartons; 600 kcal; 534 mL)	12.6		3.3	1.3	arginine, n-3 fatty acid from fish oil and nucleotides
Stresson <sup>®</sup>	7.1		3.0		
Reconvan®	6.7	10	2.5		
Nutrison <sup>®</sup> Intensive	5				
Standard formula plus free Arg	3.9,5,7.8,8.1, 8.5,9.9,18.2				

Van Bokhorst- De van der Schueren MA et al. AJCN 2001;73:323-332. Daly JM et al. CCM 1990;18(Suppl):S86-S93. Casas-Rodera P et al. Nutr Hosp 2008;23:105-110. de Luis DA et al. Eur J Clin Nutr 2002;56:1126-1129. de Luis DA et al. Eur J Clin Nutr 2004;58:1505-1508. de Luis DA et al. Eur J Clin Nutr 2007;61:200-204. de Luis DA et al. Eur Rev Med Pharmacol Sci 2009;13:279-283. Lobo DN et al. Clin Nutr 2006;25:716-726. Klek S et al. Clin Nutr 2008;27:504-512.; Riso S et al. Clin Nutr 2000;19:407-412.

## Lower vs. Higher Carbohydrate IM Formula Shows Decreased Plasma Glucose and Insulin Response

n= 12 nl volunteers	Lower	Higher
	ONS-r	ONS
Serving size	6 oz	8 oz
Calories	200	340
Protein (intact & L-arginine) (g)	18.1	18.1
L-arginine (g)	4.2	4.2
Nucleotides (mg)	430	430
Total fat (g)	7.9	9.2
MCT (g)	1.3	2.6
Total carbohydrate (g)	15	45
Sugar (g)	13	29.2
Fiber (g)	0	3.3

Schwartz S et al. CNW 2017 abstract

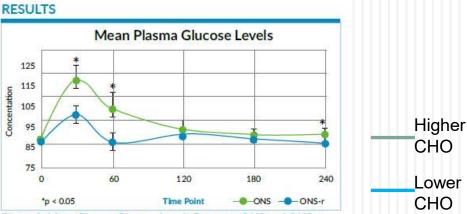


Figure 2. Mean Plasma Glucose Levels Between ONS and ONS-r

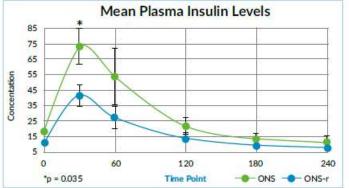
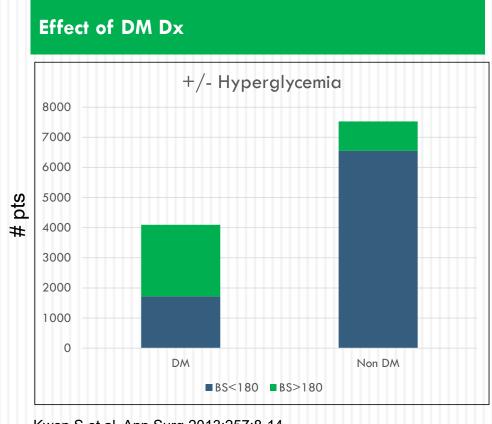
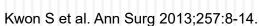
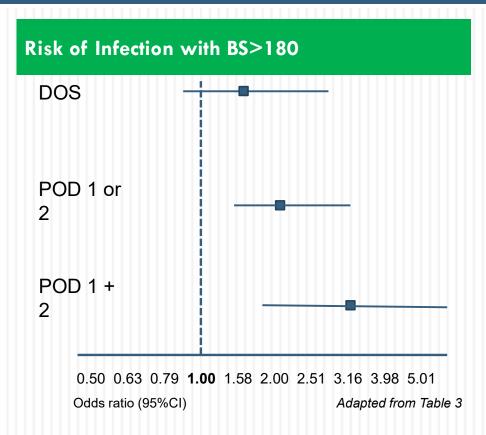


Figure 3 Mean Plasma Insulin Levels Retween ONS and ONS-r

### Hyperglycemia Increases Risk Postop







### Preop Arg-supp IM and Bladder Cancer Surgery

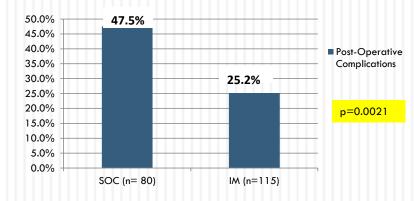
- □ Case-control pilot study (n=60) in bladder cancer patients
- Compared to retrospective control, the group consuming preop argsupp IM\* showed:
  - Lower 30 day post-operative complication rate (40% vs. 76.7%; p = 0.008)
  - Lower infection rate (23.3% vs. 60%; p = 0.008)
  - Lower rate of paralytic ileus at day 7 (6.6% vs. 33.3%; p = 0.02)

\*The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

Bertrand J et al. World J Urol 2014;32:233-237. Engel DR et al. Nature Med 2010;16:1407-1413.

# Utility and Feasibility of a Perioperative Nutritional Intervention High-Risk Head and Neck Cancer Patients- UPMC QI

- Prospective, non-randomized interventional cohort study (n= 195)
  - Study group was ordered an IM\* drink preoperatively for 5 days and IM tube feeding postoperatively, whereas the comparative cohort (SOC) received standard tube feeds post-op
- Post operative complication rates:
  - 25.2% in those receiving IM
  - 47.5% in those not receiving IM
- Pharyngeal leaks/fistulas
  - most common cx
  - more frequent in the SOC group
- Length of Stay:
  - Reduced by 2.8 days on average in immunonutrition group

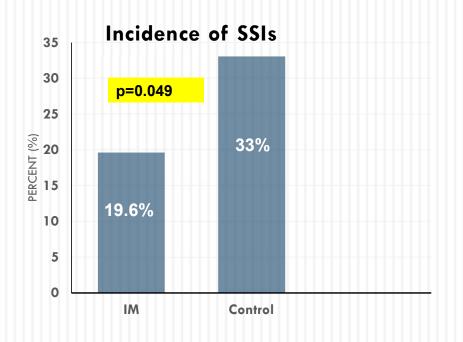


p=0.02

\*The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

Rowan NR et al. Oral Onc 2016;54:42-46.

# Post-operative Enteral Immunonutrition for Gynecologic Oncology Patients Undergoing Laparotomy Decreases Wound Complications (SSI) n=338



- 41% Reduction in SSIs with IM\* compared to control
- 78% less likely to develop CDC SSI class 2&3 infections (p=0.044)
- Patients on IM had fewer morbid
   SSIs (11.6% vs. 21.2%;p=0.03) and
   required fewer interventions such as:
  - IV antibiotics, readmissions, operative procedures, interventional radiology, wound packing, neg pressure wound tx

<sup>\*</sup>The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

## Surgical Immunonutrition Protocol



**5 Days Preoperatively** 

At least 5 Days Postoperatively if feasible

3 servings IM oral formula or at least 1000 kcal IM enteral formula/day

Waitzberg DL et al. *World J Surg* 2006;30:1592-1604. Marik P and Zaloga G. *JPEN* 2010; 34(4):378-386. McClave et al. *JPEN* 2016;40(2):159-211. August DA et al. *JPEN* 2009;33:472-500. Drover et al. *J Am Coll Surg* 2011;212(3):385-399. Wischmeyer PE et al. *Anesth Analg* 2018;126(6): 1883-1895.

3 servings IM oral formula or at least 1000 kcal IM enteral formula/day

IM= Immunonutrition Formula containing arginine-n3 fatty acid-nucleotides

# Critical Care Nutrition Guidelines — Immunonutrition and Surgery

- Immune-modulating enteral formulations (arginine with other agents including EPA, DHA, glutamine, nucleic acids) should be considered for perioperative use in the surgical ICU (E2, O3)
  - EN to be provided within 24 hours of surgery as appropriate (O2)
- Immune-modulating formulas containing arginine and fish oils are suggested for routine use in the post-operative patient in the surgical ICU and suggested for the severe trauma patient (O3)
- When advancing the diet postoperatively, it is suggested that patients be allowed solids as tolerated and that clear liquids are NOT required as the first meal (O6)

# A Standard to Optimize Care

- □ Immunonutrients appear to synergize in alleviating arginine depletion
- Complication rates, LOS and readmission have all shown improvement with the use of a proven surgical immunonutrition intervention
- A potential financial upside can be illustrated for the use of perioperative immunonutrition in major elective surgery

## Surgical Immunonutrition: What's it Worth?

- Reductions in infectious complications and LOS and readmission provide:
  - Better outcomes for patients, clinicians, institutions and the Healthcare system
  - Health economic savings potential
    - Opportunity to demonstrate this to:
      - Surgeons, Surgical Clinic nurses
      - Administrators
      - Payers
        - FYI- Peri-operative immunonutrition is fully reimbursed by the government for GI Cancer Surgery patients in France

# The Challenge: Integrate Immunonutrition with Surgical Protocols

- The evidence-base is strong but awareness and implementation lags behind
- Seize this opportunity to improve care and get some well deserved recognition for the value of surgical immunonutrition
- How? Quality Improvement (QI) is the best way to demonstrate feasibility and value to decision-makers

# Strong for Surgery

- Started as a public health campaign in Washington State, with an initial focus on colo-rectal surgeons, patients and other important stakeholders.
- Now an initiative of the American College of Surgeons

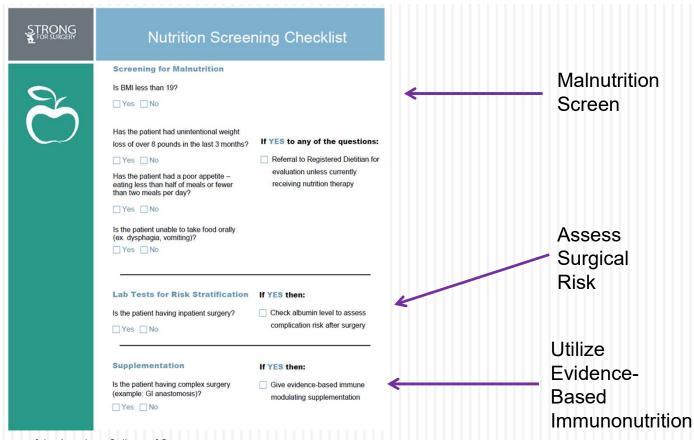


- Interactive tools to help optimize patients prior to surgery
  - Pre-Surgical Checklists
    - Optimizing Nutrition- Utilizes Preoperative Arginine-supp IM, evidence based
    - Smoking Cessation
    - Medications
    - Blood sugar control
- A 23% lower risk of prolonged LOS was shown in the nutrition check listed group receiving IM. (RR 0.77;95%CI,0.58-1.01 p=0.05)

Thornblade LW et al. Dis Colon Rect 2017;60:1.

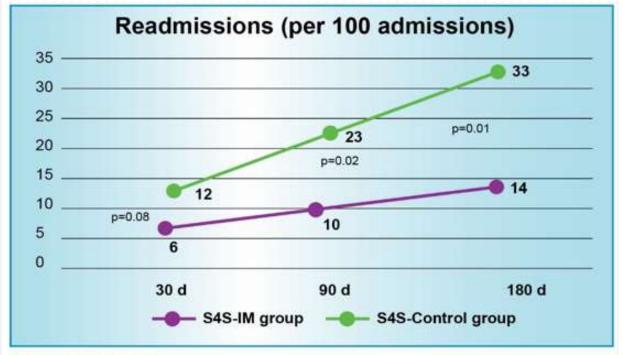
www.facs.org/quality-programs/strong-for-surgery

### Strong for Surgery Nutrition Checklist



Strong for Surgery® is a Quality Program of the American College of Surgeons

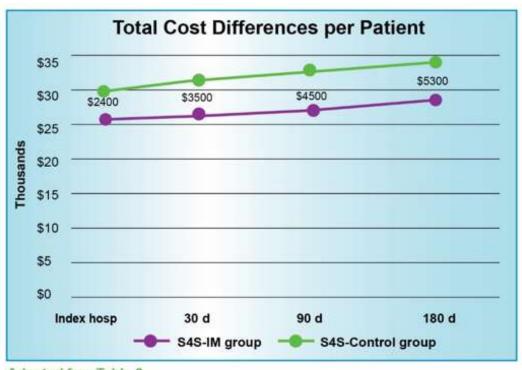
Effects of arginine-based immunonutrition on inpatient total costs and hospitalization outcomes for patients undergoing colorectal surgery



Adapted fom Table 4

- n= 716 colorectal surgery patients
- Strong for Surgery (S4S) study group- Provided with preop IM containing supplemental arginine, n-3 fatty acids and nucleotides
- Clinical Outcomes
  - Readmission decreased 50-58%
  - Decreased risk of SSI (0% vs 2.65%; p=0.04)
  - Decreased risk of thromboembolism (1.3% vs. 5%; p=0.05)

Effects of arginine-based immunonutrition on inpatient total costs and hospitalization outcomes for patients undergoing colorectal surgery



From Index
 Hospitalization to 180
 days post-discharge,
 mean cost of care was
 \$5300 less for the
 Strong for Surgery
 (S4S)-IM group vs.
 (S4S)-control group.

Adapted fom Table 2

37 Banerjee et al. Nutr 2017; 42: 106-13. Strong for Surgery is a Quality Program of the American College of Surgeons

#### Health Economics – Perioperative

#### Estimated Potential Cost Savings/GI Cancer Surgery Patient\*\* 4500 \$3811 4000 Potential Savings (\$) per patient stay \$3240 3500 \$2671 3000 \$2192 \$2101 2500 2000 \$1530 1500 \$961 1000 \$391 \$163 500 5 10 15 20 20.8 3 25 30 35 Base Complication Rate (%)

Waitzberg DL et al. *WJS* 2006;30:1592-1604. Drover JW et al. *JACS* 2011;212(3):385-399. Mauskopf J et al. *WJSO* 2012;10(136) e-pub 7/6/2012. HCUP Nationwide Inpatient Sample 2008.

\*Containing arginine, n-3 fatty acids and nucleotides; Cost of perioperative immunonutrition not included.

<sup>\*\*</sup>Estimated potential cost savings included in this health economics model are for illustrative purposes only and are not intended to guarantee any specific reductions in cost at a particular facility.

# Impact of a Novel Preoperative Patient-Centered Surgical Wellness Program

Kristen E. Kelley, MPH, RN, CIC,\* Alyssa D. Fajardo, MD, FACS, FASCRS,†
Nancy M. Strange, RDN, CNSC, CD,‡ Carol A. Harmon, MSN, RN,§ Kim Pawlecki, MSN, RN,§
Marnie Sieber, MSN, RN,\* Nikki Walke, MBA, RN,§ William F. Fadel, PhD,¶ William A. Wooden, MD, FACS,||
Josh Sadowski, BS,\* Thomas J. Birdas, MD, FACS,|| Larry H. Stevens, MD, FACS,||
Grace S. Rozycki, MD, FACS,|| and C. Max Schmidt, MD, PhD, MBA, FACS\*\*††

Outcome Measure	Pre-intervention (n= 9202)	Intervention (n=6538)	P value
Surgical site infection (SSI)	52	22	0.044
Catheter associated urinary			
tract infection (CAUTI)	27	6	0.007
Clostridium difficile infection			
(CDI)	78	34	0.016
Patient safety indicators (PSI)	55	0	< 0.001
Ventilator associated event	14	6	0.367
(VAE)			
Central line associated			
bloodstream infection (CLABSI)	7	3	0.538
Methicillin resistant staph			
aureaus (MRSA)	3	2	1.000

#### **Preop Wellness Bundle Contents:**

- Chlorhexidine
- Mupirocin
- Incentive spirometer
- Smoking cessation information
- Immunonutrition drink containing arginine, n-3 fatty acids and nucleotides

#### **Types of Surgery:**

- General
- Neuro
- ENT
- Urology
- Plastics
- Ortho
- Gyn
- Thoracic
- Oral Maxillofacial
- Cardiovascular

#### **Outcomes:**

- SSI, CAUTI, CDI and PSI were significantly reduced
- Total compliance to bundle elements lowered risk of HAI by 50% (p=0.003)
- Cost of Wellness Bundle kits was recovered in addition to 1 Mill. in cost savings

## What is an Enhanced Recovery Protocols (ERP) Bundle?

#### Protocol components implemented Pre-, Intra- and Postoperatively



Lassen K et al. Clin Nutr 2012;31:817-830. Zhuang CL et al. Dis Colon Rectum 2013;56(5):667-678.

#### Clinical Outcomes with an ERP Bundle

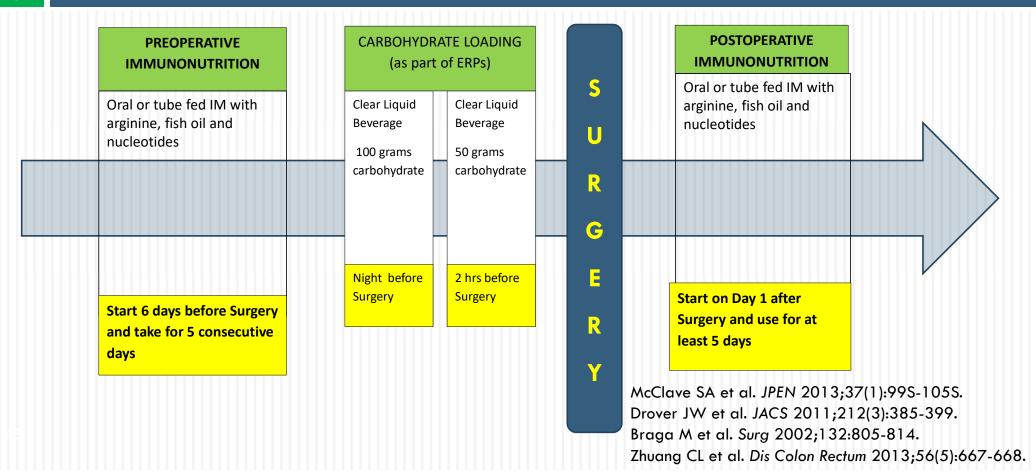
- Implementation of the ERP bundle of protocols in colorectal surgery have demonstrated a reduction in complications by 30%-50% and a 2-3 day reduction in LOS.
  - QI studies from Duke and UVA support these findings.
- □ The bundle of protocols has been required to achieve significant improvements in clinical outcomes.
- Use of carbohydrate loading shows limited evidence of clinical benefit when used as a separate intervention in elective surgery.
  - No difference in LOS when compared with water or placebo.

# **ASER Implementation Guide**

http://aserhq.org/

- □ American Society of Enhanced Recovery (ASER)
  - 1. Reduce the preoperative starvation period
  - Carbohydrate loading may be given 12 hrs prior to surgery and up to two hours before anesthesia\*
  - 3. Immunonutrition containing supplemental arginine, n-3 fatty acids (EPA & DHA) and nucleotides found beneficial when given 5-7 days preoperatively and 5-10 days postoperatively

#### Immunonutrition (IM) & Carbohydrate Loading in ERPs: Complementary Protocols for Major Elective Surgery



#### Multi-modal Perioperative Care Plus Immunonutrition versus Traditional Care in Total Hip Arthroplasty: A Randomized Pilot Study

- Methods (n=32)
  - □ n=15 in ACERTO Group
    - Pre-op IM\* for 5 days leading up to surgery
    - 2 hours before surgery 200mL-12.5% maltodextrin beverage
    - Restricted IV fluids-only 1000mL fluids post-op
  - n=17 in Control Group
    - Standard diet-NO IM
    - Fasting until surgery
    - IV hydration until Post-op Day 1

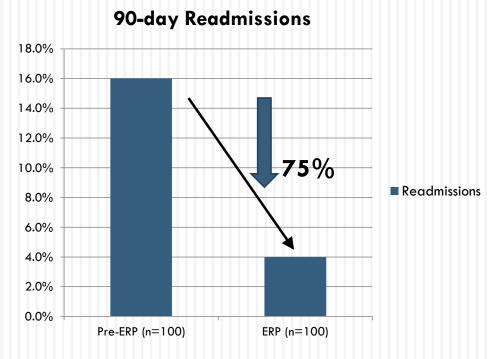
#### Results

Shows ERP Bundle (including preoperative IM and carb loading) enhanced recovery by decreasing LOS and lowering inflammation. adapted from Table 3

Variable	Control Group		ACERTO Group		
	Mean	Median	Mean	Median	
LOS		6 days		3 days	p<0.01
CRP (mg/L)					
Preop	10.2	8	10.1	8	p=0.96
Postop Day 2	80.6	79	66.5	66	p<0.01

\*The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

# ERP Bundle Plus Immunonutrition- Ventral Hernia Repair (n=200)



\*The IM intervention contained supplemental L-arginine, fish oil, and nucleotides

- A 75% reduction in 90day readmission was associated with the ERP bundle, including evidence-based IM.
- Other associated outcomes were:
  - Reduced LOS
  - More rapid diet advancement and time to flatus and bowel movement
  - Shorter time to oral narcotics

Majumder A et al. J Am Coll Surg 2016;222:1106-1115.

## ERP Bundle with Immunonutrition (IM) in GI Surgery -Grant funded vs. Self-Pay IAR

Cross Sectional- Retrospective Study of Real World Evidence

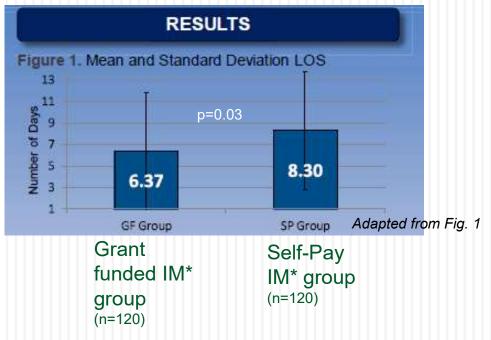
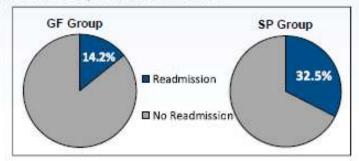


Figure 3. Incidence of SSI **GF Group** SP Group 15.1% SSI 29.2% ■ No SSI

Adapted from Fig. 3

Figure 4. 30-day readmission rates



Kavanaugh E et al abstract at ERAS USA 2018

## It's All About Outcomes

□ Clinical

□ Health Economic



# Summary

- Pre-, Peri- and Post-operative use of supplemental arginine, n3 fatty acids and nucleotides are proven effective vs. other combinations studied to improve outcomes following major elective surgery.
- All three immunonutrients discussed have a mechanistic role in the support of immune function.
- The health economics associated with this studied blend of immunonutrients support the implementation of quality initiatives in major elective surgery

## Thank You

#### Questions

Nutrition-related resources and tools are available from Nestlé Nutrition Institute: www.nestlenutrition-institute.org

Visit the New and improved MyCE site at MyCEeducation.com
Offering CE to dietitians and nurses

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