Critical Care Nutrition: Taking Guidelines Directly to the Bedside

Stephen McClave, MD

University of Louisville School of Medicine
Louisville, Kentucky
April 28th, 2016

Critical Care Nutrition

Taking Guidelines Directly to the Bedside

Stephen A. McClave, MD
Louisville, Kentucky

Disclosures

- Nestle
  - Speakers Bureau
  - Educational Grant (Fellowship)
- Abbott
  - Speakers Bureau
- Medtronic
  - Consultant
- Metagenics
  - Speakers Bureau

What We're Hearing: Early EN is Bad!

- No "Forced Mandatory Feeds" first week[1]
- Trophic feeds are better[1]
- Starve to preserve autophagy[2]

Immunonutrition Kills Patients!

- Arginine (Heyland)
- Probiotics (PROPATRIA)[3]
- Fish oil (Omega)[4]
- Glutamine (REDOX)[5]
- "End of Era" (Metaplus)[6]

We Were Wrong About PN!

- PN is back
- Now PN=EN[7]

[1]Dellinger (CCM 2013; 41:580) [2]Schetz (Crit Care 2013; 17:302)
[3]Besselink (Lancet 2008;371:651) [4]Rice (JAMA 2011; 306:1574)
[5]Heyland (NEJM 2013; 368:1489) [6]Van Zanten (*JAMA*. 2014;312:514)
[7]Harvey (NEJM 2014)

Introduction

- Not all patients derive same benefit from nutrition therapy

- Previously well nourished, mild critical illness, short stay ICU
  - Less benefit
- Moderate to severe critical illness, long ICU LOS, malnourished
  - More likely to benefit
  - More likely to be harmed by iatrogenic underfeeding
- Benefit of nutrition Rx depends on:

Route	Timing	Interruptions
Dosing	Content	Mobility

SA McClave, RG Martindale, TW Rice, DK Heyland (CCM 2014:42:2600)

Impact of Clinical Issues

Nutritional Risk
- Disease severity
- Nutritional status

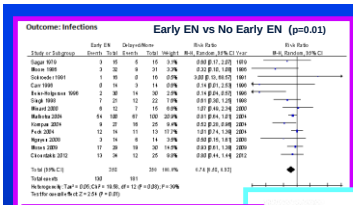
NEW

Timing of nutritional intervention

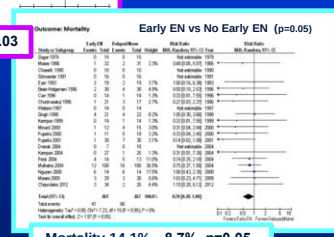
First week
- Argument to AVOID feeding
  - Height of dz process, inflammat, insulin resist, intolerance
  - Evidence that full feeds may be harmful
  - Importance of preserving autophagy
  - Teleologic argument disrupting fight/fright/flight response
- Opposing argument to PROVIDE feeding
  - Window of opportunity to attenuate disease severity, SIRS
  - Provide non-nutritional benefits of nutrition Rx

Second week - Change in priorities, less controversial
- Need for nutritional benefits, impact of increasing caloric deficit
- Iatrogenic underfeeding > 7 days bad, catabolism to anabolism

Value of EN in the Literature: Infection Mortality



Infection 51.7%→36.3%, p=0.03



Mortality 14.1%→8.7%, p=0.05

SA McClave, BE Taylor, RG Martindale ASPEN/SCCM CCN Guidelines

JPEN 2016;40(2):159-211

EN Benefits: Achieved at Different Doses?

- **Non-Nutrition benefits - Lower dose, needed in all patients**

NEW

Gastrointestinal responses
- Trophic on gut integrity
- Gut/lung axis of inflamm
- Motility/contractility
- Commensal bacteria
- Secretory IgA, GALT tissue
- Reduced bact virulence

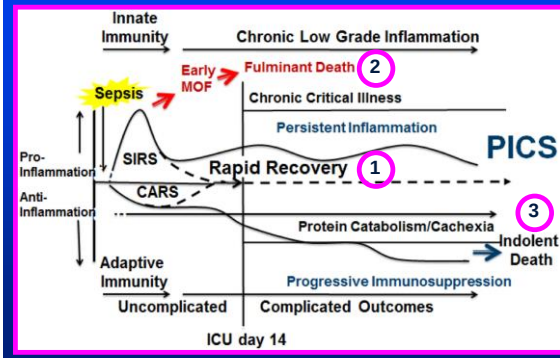
Immune responses
- Modulate regulatory cells
- Stimulate oral tolerance
- Duod colon receptors
- Promote Th-2 >Th-1 lymphocytes
- Maintain MALT tissue
- Modulate adhesion molecules

Metabolic responses
- Incretin to ↑ insulin sens
- Attenuate stress metab
- Reduce hyperglycemia (AGES)
- Enhance fuel utilization

- **Nutrition benefits – Higher dose, needed in high risk patients**
  - Protein, calories
  - Maintain LBM
  - Micronutrients, anti-oxidants
  - Stimulate protein synthesis

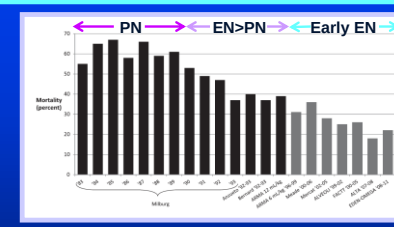
S McClave, R Martindale, T Rice, D Heyland (CCM 2014;42:2600)

Impact of Clinical Issues: Events of First Week May Affect Longterm Outcome



M Rosenthal, F Moore (J Adv Nutr Hum Metab 2015 pii:e784)

ARDSNet Trials: Mortality Rate Over Time



Implications: Medical care in ICU steadily improving with time
- Low TV vent, conserv fluid mgmnt, spont breathing, ↓sedation, NIV
- As mort drops, harder to show Rx effect, much larger RCTs needed
- Aggressive provision of EN presumed part of improved care
- Danger: Large but underpowered negative studies on EN Rx effect

MJ Noto, AP Wheeler (Amer J Respir Crit Care Med 2013;188:128)

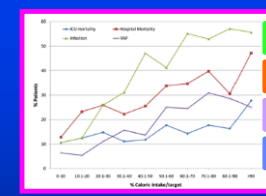
Question #1

Does the literature indicate that underfeeding is BETTER than full feeding in ICU patients?

Answer: No.

Literature that suggests feeding less is BETTER is flawed.

Underfeeding *Better* than Full Feeds: Flawed!



Hosp Mortality (OR)	1st	2nd	3rd	Signif
Arabi [1]				
All patients	1.00	1.23	1.99	p=0.02
Heyland [2]				
All patients	1.00	1.22	1.28	p=0.0005
All pts (no all PO)	1.00	0.77	0.73	p<0.0001

[1] Arabi JPEN 2010;34(3):280 [2] Heyland CCM 2011;39(12):1

Is Underfeeding BETTER than Full Feeding?
Plausibility and Type 1 Error


Braunschweig

- **Braunschweig INTACT Study** [2]

	Intens Rx (n=40)	Stand Rx (n=38)	
%Goal cal	84.7%	55.4%	(p<0.0001)
Mortality	40.0%	16.0%	(p=0.02)

  Hosp LOS, ICU LOS, infections, durat MV no different
  Power analysis indicated (n=200) needed to complete study
  Cause of death no plausible mechanism (% died withdraw of care)
- **Ziegler Example of Type 1 Error:** PN/Glutamine vs PN in post-op pts[3]
  First 50 pts – Less infections with Glutamine
  Next 50 pts (100 total) – More infections with Glutamine
  Last 50 pts (150 total) – No difference between groups
- **Arabi 2011 Single Center Study** [1]

	Under 60-70% (n=120)	Full 90-100% (n=120)
Received	59.0%	71.4%
Hosp Mort	30.0%	42.5% (p<0.05)

[1] Am J Clin Nutr 2011;93:569 [2] JPEN 2014;38:000 [3] NIH Data Safety Monitoring Board

Question #2

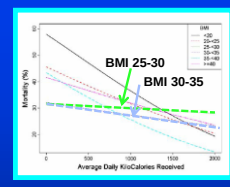
Can underfeeding achieve the SAME OUTCOMES as full feeding in ICU patients?

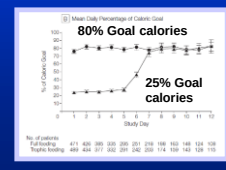
Answer: Yes.

Good quality studies show the same outcomes between underfeeding and full feeding in certain patient populations.

Does Underfeeding *Equal* Full Feeding?

ONLINE FIRST
Initial Trophic vs Full Enteral Feeding in Patients With Acute Lung Injury
The EDEN Randomized Trial





Why would trophic feeds work?
- Age 52 yrs, BMI 30, ICU LOS 5d
- 25% Goals calories is sufficient
- Early initiation more important
- Minimizing interruptions important
- Less fluids in ARDS important [1]
- BMI range less nutrition effect [2]

Significance of Surviving Sepsis Recs
- Extrapolation of ARDS study to all sepsis
- No extemes of age, BMI, disease severity
- Start trophic OK, but not locked in for 7d

[1] T Rice (JAMA 2012) [2] C Alberda (Int Care Med 2009)

Does Underfeeding *Equal* Full Feeding?


YM Arabi

- **Arabi 2015 Multicenter** [1]

Demographics

Mixed ICU		AP II 21.0
Age 50.2-50.9		SOFA 9.9
BMI 29.0		

	Permiss Under (n=894)	Full (n=446)
Intended	40-60%	70-100%
Received	46%	71%
Infection	35.9%	37.9%
ICU LOS	13d	13d
ICU/90d Mort	16.1/27.2%	19.1/28.9%

[1] NEJM 2015;372:2398

NEW Concept of Nutritional Risk


Jens Kondrup

Components: Impaired nutrition status and disease severity

J Kondrup (Curr Opin Clin Nutr Metab Care 2014;17:177)

Nutritional Risk Score 2002
Poor Nutritional Status and Disease Severity

Nutritional Risk Screening 2002 (ESPEN guideline)

Impaired nutritional status		Severity of disease (= requirement/stress-metabolism)	
Mild Score 1	Wt loss >5% in 3 mths Or Food intake <50-75% of normal requirement in preceding week	Mild Score 1	Hip fracture (9). Chronic patients, in particular with acute complications: cirrhosis (11), COPD (12). *Chronic hemodialysis, diabetes, malignant oncology.*
Moderate Score 2	Wt loss >5% in 2 mths Or BMI 18.5 - 20.5 + impaired general condition Or Food intake 25-50% of normal requirement in preceding week	Moderate Score 2	Major abdominal surgery (13-15). Stroke (16). *Severe pneumonia, malignant hematology.*
Severe Score 3	Wt loss >5% in 1 mth (= >15% in 3 mths (17)) Or BMI <18.5 + impaired general condition (17) or Food intake 0-25% of normal requirement in preceding week	Severe Score 3	Head injury (18, 19). Bone marrow transplantation (20). *Intensive care patients (APACHE>10).*
Score:	+	Score:	= TOTAL SCORE:

Age >70 yrs : Add 1 point

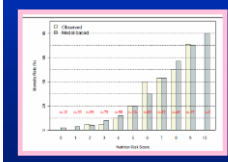
Score ≥3 Consider EN/PN
Score ≥5 High risk

Kondrup J (Clin Nutr 2002)

Concept of Nutritional Risk: Nutric Score

Six factors for Nutric Score:

- **Disease severity:**
  - Age
  - Initial APACHE II score
  - Initial SOFA score
  - Interleukin-6
  - Comorbidities
- **Poor nutritional status:**
  - Hosp LOS prior to ICU



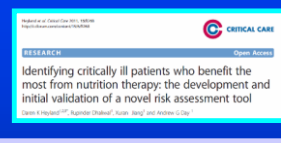


Table 1: NUTRIC Score variables

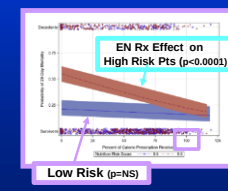
Variable	Range	Points
Age	<50	0
	50 - <75	1
	≥75	2
APACHE II	<15	0
	15 - <20	1
	20-28	2
	≥28	3
SOFA	<6	0
	6 - <10	1
	≥10	2
Number of Co-morbidities	0-1	0
	≥2	1
Days from hospital to ICU admission	0 - <1	0
	≥1	1
IL-6	0 - <400	0
	≥ 400	1

Heyland DK (Crit Care 2011;6:1)

Paradigm Shift: Assess Risk-↑Therapy-↑Response
Observational Studies

- NRS-2002 **Jie Study**[1] - **High Risk** patients (n=120)with NRS Score ≥ 5
  Insufficient (n=77) **Sufficient Nutr Rx**(n=43)
  Overall complications 51% → 26% *
  Nosocomial infection 34% → 16% *
  No benefit (sufficient vs insufficient) **Low Risk** pts (n=965) NRS < 5

- Nutric Score **Heyland Study**[2] (n=1199) (no Interleukin-6 used)



[1] B Jie (Clin Nutr 2012) [2] DK Heyland (Crit Care 2011;15:R268) (Clin Nutr 2015 Jan)

Paradigm Shift: Assess Risk-↑Therapy-↑Response

Randomized
Controlled Trials

- **Starke Study** (NRS Score ≥3) (n=132)

	Energy	Protein	Complic	Re-Hosp
Intervent (n=66)	24 kcal/kg*	1.0 gm/kg*	6.0%*	25.7%*
Controls (n=66)	18 kcal/kg	0.7 gm/kg	19.7%	42.4%

- **Johansen Study** (NRS Score on all pts) (n=212)

	Complic	NRS Score	Hosp LOS
Intervention	(n=18)	3.4	14.07d *
Controls	(n=14)	3.6	19.67d

[1] J Starke (Clin Nutrit 2011;30:194) [2] N Johansen (Clin Nutrit 2004;23:539) *p<0.05

Dosing of EN

NEW

- Low nutritional risk - (NRS 2002 ≤ 3 or Nutric Score ≤5)
  Low dose EN (trophic or none) for first week[1,2]
- Moderate risk - ALI/ARDS, MV ≥ 72 hrs[3]
  Low or high dose EN (Trophic or full feeds)
- High nutritional risk (NRS 2002 ≥5, Nutric ≥6)[1,2]
  High dose EN - Advance to goal as tolerated over 24-48 hrs
  Attempt to provide > 80% goal[4]

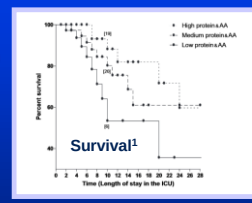
[1]Kondrup J (Clin Nutr 2002) [2]Heyland DK (Clin Nutr 2015)
[3]Rice T (JAMA 2012) [4]Heyland DK (CCM 2011;39:1)

Nutritional Assessment
Set Goals of Therapy

- Caloric requirements
  25-30 Kcal/kg/d
  Published predictive equations no more accurate
  Indirect calorimetry

- Protein requirements
  Greater emphasis
  Higher doses
  1.2–2.0 gm/kg/d
  Fewer restrictions

NEW

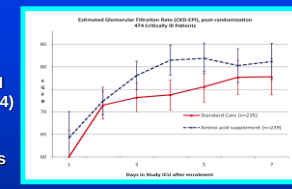


MJ Allingstrup (Clin Nutr 2012;31:462)[1]
P Weijs (JPEN 2012;36:60)[2]

Do Interventional RCTs Support Emphasis on Protein?

- **Doig Nephro-Protect Trial** [1]

  Unblinded multicenter RCT
  Pts expected on MV 48 hrs;
  excluded patients with AKI
  Short-term IV AAs QD (n=474)
  Max protein 2.0 gm/kg/d
  20 endpoints, 4 subsets
  No difference in mort, others



- **Heyland Protein Top-Up Trial** [2]

  Multicenter RCT adding PN vs placebo to enteral tube feeding
  Five centers in Europe, US, Canada (n=167)
  Primary endpoint = 60d mortality; Secondary = LOS, infect, MOF
  Results from pilot trial – No difference in outcomes between groups

[1] Doig (Int Care Med 2015) [2] Heyland (Clinical Trials.gov 2010)

Initiate Enteral Feeding

- EN preferred over PN for nutrition support therapy
- Initiate EN within 24-48 hrs of onset of illness
  - Overt signs of contractility not required to start
  - Absent BS predict intolerance, dz severity, need for vigillence[1]
- Initiate EN in the stomach[2]
  - Divert lower if intolerant, high aspiration risk
- Withhold EN with hemodynamic instability
  - Restart with caution if requiring low dose vasopressor support[3]

[1]Nguyen (J Crit Care 2013;28:537) [2] Deane (Crit Care 2013:17:R125)
[3] Khalid (Amer J Crit Care 2010;19:261)

NEW Monitor Tolerance and Adequacy

- GRVs should not be used as part of routine care[1]

Montejo Multicenter RCT [2]	GI Complications	%Goal Feeds
500cc GRV (n=160)	47.8% *	89% *
200cc GRV (n=169)	63.6%	83%

Reignier Multicenter RCT [3]	VAP	Infect	Mortality	Deficit
No GRV used (n=227) 319 kcal	16.7%	26.4%	27.8%	
Routine GRV (n=222) 509 kcal	15.8%	27.0%	27.5%	

- Focus instead on:
  - Phys exam
  - Passing stool, gas
  - Tracking I&Os
  - Aspirat risk
  - Access site
  - Protein calorie goals

[1]McClave (JPEN 2016;40:159) [2]Montejo (ICM 2010;36:1386) [3]Reignier (JAMA 2013;309:249)

Need for EN in High Risk Patients:
Utilize Strategies to Increase EN Delivery

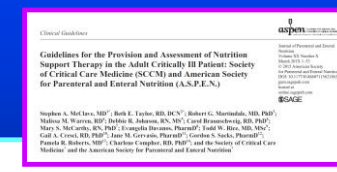
- Compensatory Strategies
  - Over-order calories
  - Timed over 18-20 hrs
  - Volume-based feeding
  - Set catch-up rate

- Multi-Strategy De-escalation (Top-Down or PEP-uP)
  - Start at goal
  - Volume-based feed
  - Caloric balance
  - SB infusion
  - Start with prokinetics
  - Probiotics (oropharynx and tube)
  - Small peptide formula
  - Elevate HOB
- Nurse-driven protocols for EN (Set ramp up, vol, GRV, NPO, etc)
- Alter NPO status for diagnostic tests, procedures, surgery
- Bundle nutrition elements (set of action statements)

SA McClave (JPEN 2015;39:707) DK Heyland (CCM 2013;41:2743)

ASPEN/SCCM CCN Guidelines:
Bundle Statements

NEW



Clinical Guidelines

Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

aspen

SAGE

TABLE 2. Bundle Statements

Assess patients on admission to the ICU for nutrition risk, and calculate both energy and protein requirements to determine goals of nutrition therapy.
Initiate enteral nutrition (EN) within 24–48 hours following the onset of critical illness and admission to the ICU and increase to goals over the first week of ICU stay.
Take steps as needed to reduce risk of aspiration or improve tolerance to gastric feeding (use prokinetic agent, continuous infusion, chlorhexidine mouthwash, elevate the head of bed, and divert level of feeding in the gastrointestinal tract).
Implement enteral feeding protocols with institution-specific strategies to promote delivery of EN.
Do not use gastric residual volumes as part of routine care to monitor ICU patients on EN.
Start parenteral nutrition early when EN is not feasible or sufficient in high-risk or poorly nourished patients.

JPEN 2016;40(2):159-211

NEW Formula Selection in the ICU

- Start with standard polymeric isotonic formula (most ICU pts)
- Consider use of specialty formulas
  - Obesity formulas (Class II and III)
- Cannot recommend certain formulas
  - Organ-failure formulas
    - Rarely use hepatic, renal failure
    - Don't use pulmonary failure
  - Disease-specific (diabetic)

SA McClave, B Taylor SCCM/ASPEN Guidelines (JPEN 2016;40:159-211)

Immunonutrition and Anti-Inflammatory Formulas

- Elective Surgery, SICU – Use arg/fish oil formula [1]
  - Infection ↓ 41% (OR=0.59)
  - Hosp LOS ↓2.38 days

NEW

- Crit Care MICU – Don't recommend arg/FO formula
  - No difference mortality, infection, LOS

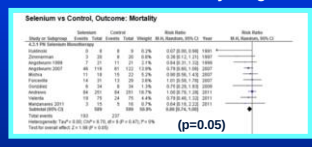
- ALI/ARDS – No recommendation anti-inflammatory lipid profile formula [2-8]
  - Gadek, Singer, Pontes-Arruda, Grau-Carmona
    - Constant infusion – All benefit
  - Rice ARDSNet, Stapleton
    - Bolus infusion – Harm, no benefit
  - Van Zanten Meta-Plus
    - Constant infusion - Harm

[1] JW Drover (JACS 2011;212(3);385) [2] JE Gadek (CCM 1999;27:1409)
[3] P Singer (CCM 2006;34:1033) [4] A Pontes-Arruda (CCM 2006;34:2325)
[5] T Grau-Carmona (Clin Nutr 2011;30:578) [6] T Rice (JAMA 2012;307:795)
[7] R Stapleton (CCM 2011;39:1655) [8] A Van Zanten (JAMA 2014;312:514)

Adjunctive Therapy

- **Soluble prebiotic fiber** – Consider routine use in all pts
- **Probiotics** – Use for select patient populations
  Where RCTs have shown safety and benefit [1]
  Do not use routinely for general ICU pts

NEW



McClave, Taylor, Martindale
(SCCM ASPEN 2016 Guidelines)

- **Antioxidants** – Use for all pts requiring Specialized Nutr Support
  Selenium, zinc, copper, Vit C, Vit E
- **Enteral glutamine** – Do not use

[1] Zhang (World J Gastro 2010;16:3970)

What is the Role of PN in the ICU?

Recent trials have changed our perspective

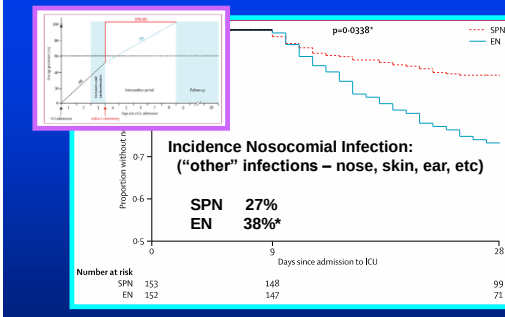
Exclusive PN Can Be Done Safely

Doig Early PN Study ICU Pts with Short Term EN Contraindication

- Early PN in Pts not expected to get EN for 3 days (n=1372)
  Multicenter PRCT PN vs STD
- Results:
  Durat MV shorter in PN by 0.47 d *
  Trend less ICU LOS by 0.8 d
  No different – Mortality, infection, QOL, hosp LOS, function
- Conclusion:
  PN can be given safely early on
  Little benefit realized

Doig GS, Simpson F (JAMA 2013;309:2130)

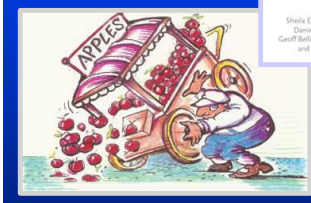
Supplemental PN Can Be Done Safely



Swiss Supp PN Study:Durat MV, Hosp LOS, ICU LOS no different (n=300)
CP Heiddeger, M Berger, C Pichard (Lancet 2012 Dec 3)

Should Exclusive PN Be Used More in the ICU?

The NEW ENGLAND JOURNAL of MEDICINE
ORIGINAL ARTICLE
Trial of the Route of Early Nutritional Support in Critically Ill Adults



Multicenter Trial in England
EN vs PN in 2400 ICU pts
High risk (mortality 34%)
Key protocols in place
Each provided 80% goal feeds
No difference in outcomes

Impact: Under controlled conditions, high risk patients, PN can = EN
EN still preferred over PN, but should lower threshold to use PN

SE Harvey CALORIES Trial Group (NEJM Ahead of Print 10-1-14)

Use of Parenteral Nutrition

NEW

- **Exclusive PN**
  Low Risk - Withhold exclusive PN
  if EN not feasible (NRS 2002 ≤ 3 or Nutric Score ≤5)
  High Risk - Initiate exclusive PN ASAP (esp malnourished)
  if EN not feasible (NRS 2002 ≥5, Nutric Score ≥6)
- **Supplemental PN** - Add after 7-10d if EN < 60% goal high or low risk [1]
- **Maximize efficacy of PN**
  Use Multidisciplinary Nutrition Team, protocols
  Hypocaloric dosing (80%) first week [2]
  Withhold soy-based lipids first week
  Moderate glucose control (140-180 mg/dL)
  Transition off PN when EN provides > 60% goal

[1]Heiddeger (Lancet 2012 Dec 3) [2] Jiang (Clin Nutrit 2011;30:730)

Summary

- Benefit of nutrition Rx derived from provision of early EN
- Standard polymeric formula appropriate for majority
- Use PN earlier in high risk than low risk pts when EN not feasible
- Appropriate monitors to assure safety, tolerance
- Interpret guidelines as they apply to institutional pt populations

Thank You!!

CEU/CPE Instructions

To receive your CEU/CPE Certificate:

1. Go to www.NutriciaLearningCenter.com
2. Click on “CE Credit Request”
3. Enter code: **EWCCN3**
4. Certificate will be visible for download on your NLC personalized dashboard