

# Protein dosing in the ICU: How much, when and why?

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Dr. Gordon S. Doig,  
Associate Professor in Intensive Care  
Northern Clinical School Intensive Care Research Unit,  
University of Sydney, Sydney, Australia  
[gdoig@med.usyd.edu.au](mailto:gdoig@med.usyd.edu.au)  
[www.EvidenceBased.net](http://www.EvidenceBased.net)





# *Overview of Talk*

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- Context
  - Levels of Evidence
  - Types of Outcomes
- Guideline Recommendations
- Current Evidence
- New Evidence
- Summary

Editorials, Expert Opinion



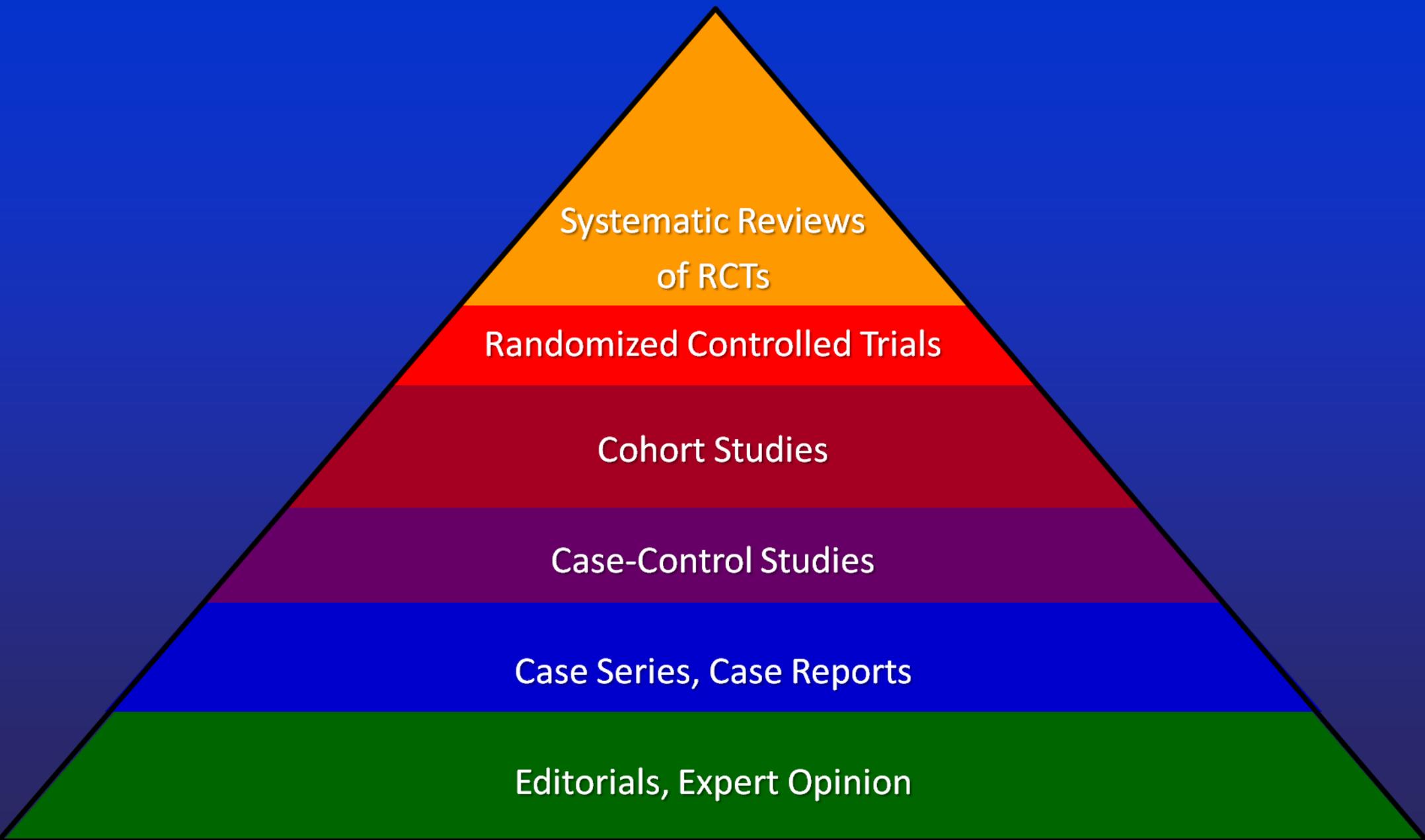
Case Series, Case Reports

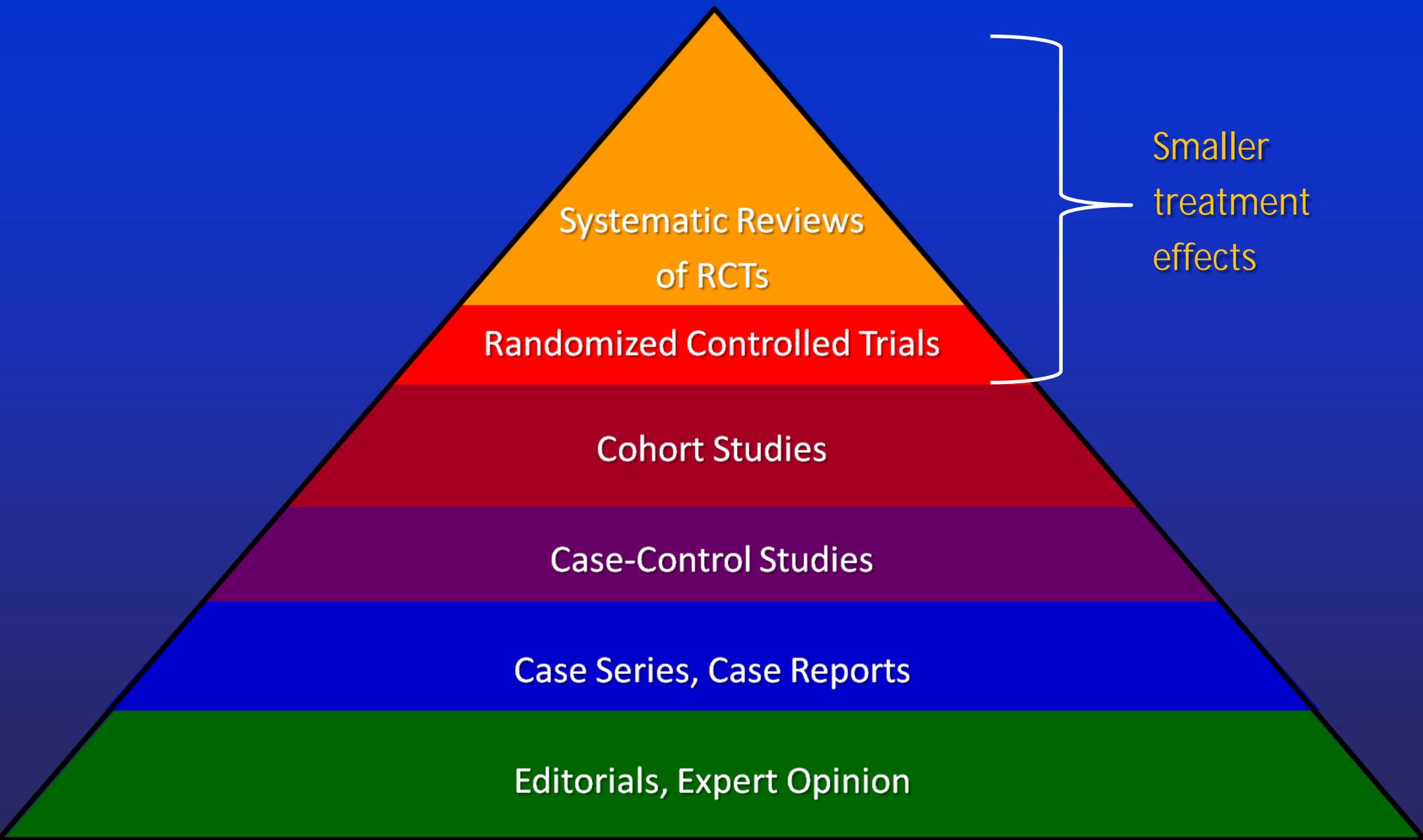
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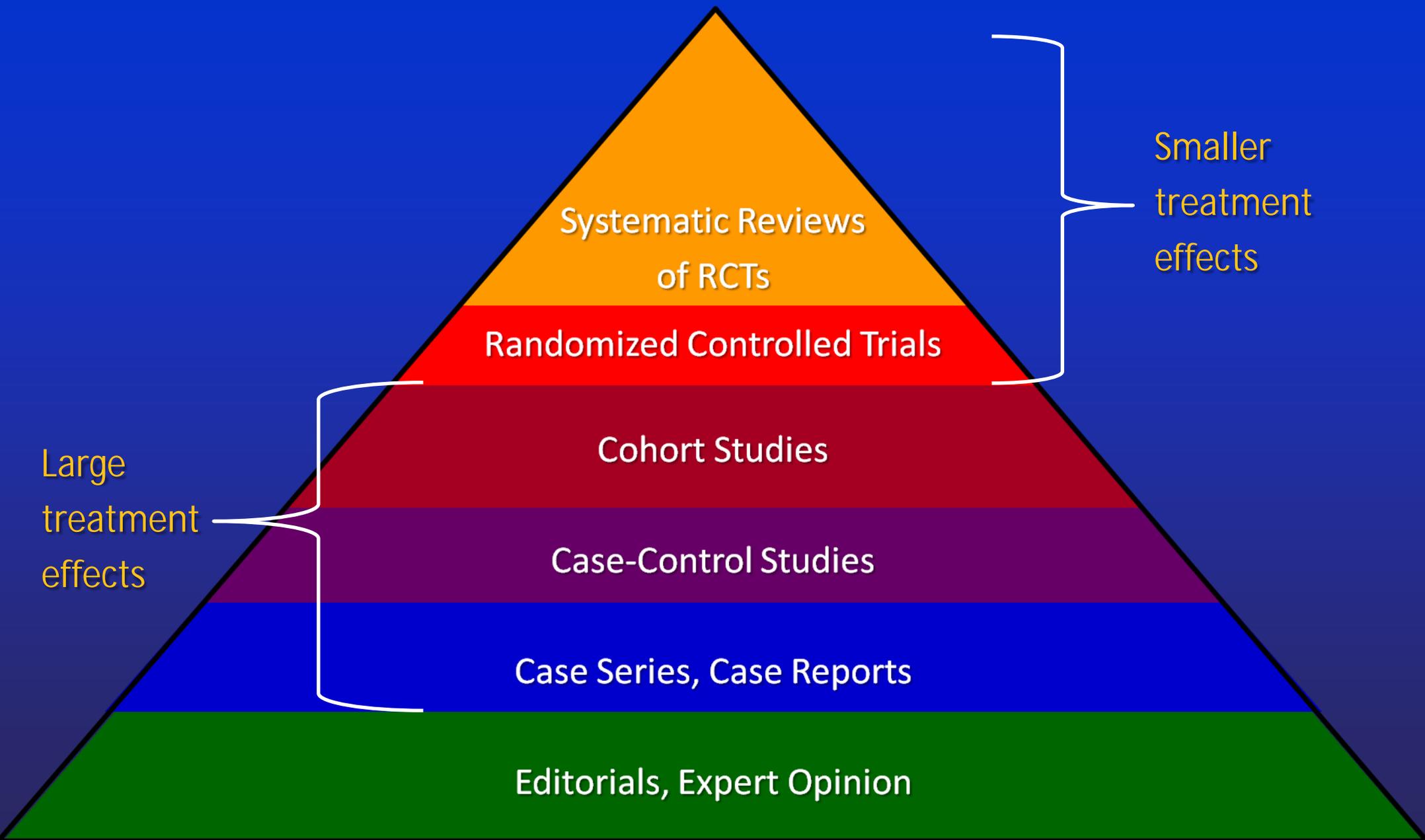


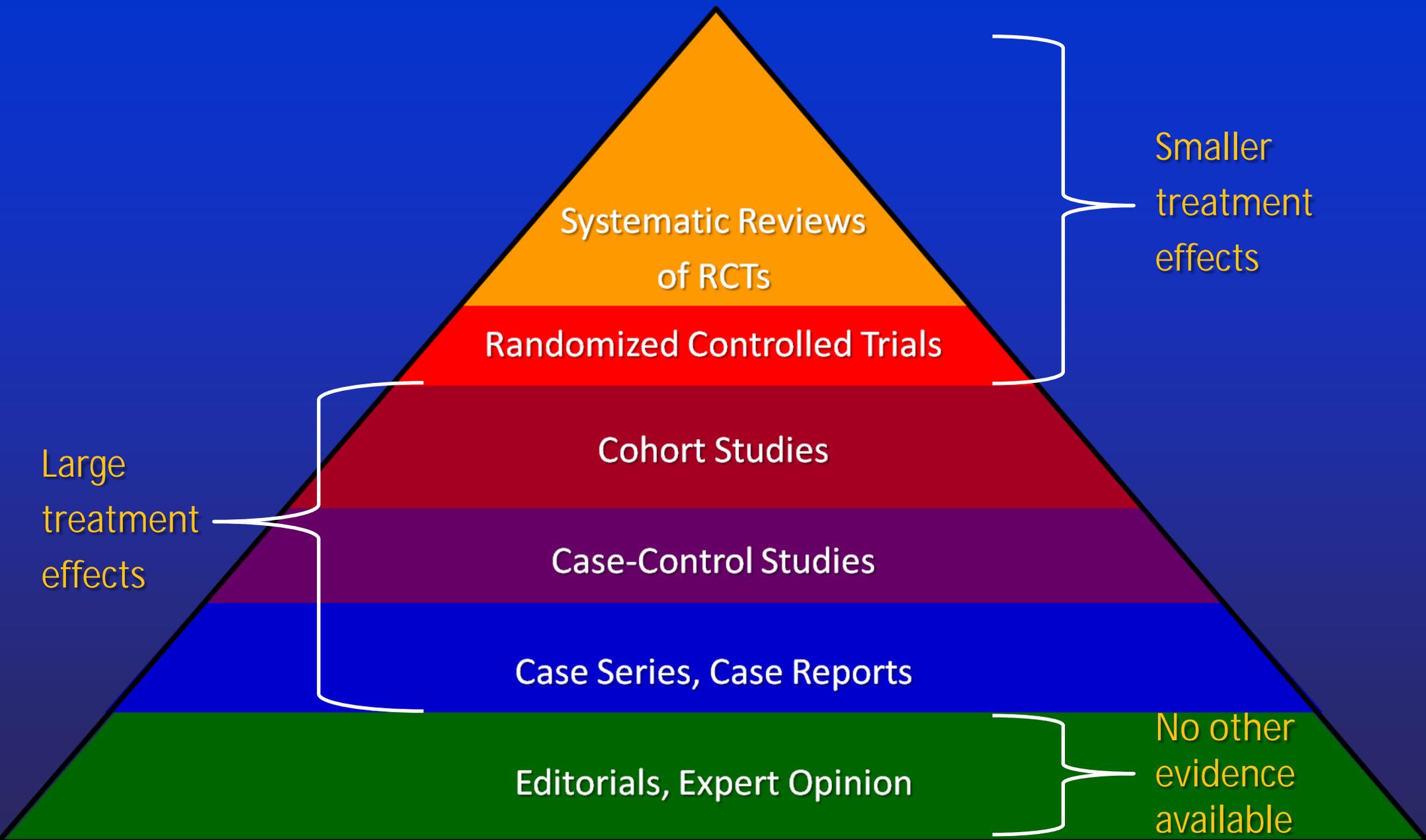














# *Patient vs. Disease oriented outcomes*

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Shaughnessy AF and Slawson DC. What happened to the valid POEMS? A survey of review articles on the treatment of type 2 diabetes. *BMJ* 2003;327:266-271



## *Patient vs. Disease oriented outcomes*

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A *patient oriented outcome* is defined as a direct measure of how a patient feels, functions or survives.



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Before new drugs can be licensed using disease oriented outcomes, **FDA requires** a definitive clinical trial demonstrating an improvement in a disease oriented outcome leads to an improvement in a patient oriented outcome.



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*Improvements in disease oriented outcomes do not always lead to improvements in patient oriented outcomes.*

Before new drugs can be licensed using disease oriented outcomes, **FDA requires** a definitive clinical trial demonstrating an improvement in a disease oriented outcome leads to an improvement in a patient oriented outcome.

- *No measures of 'nutritional efficacy' (Nitrogen balance, caloric intake, percent calories from EN, body composition etc) fulfill this FDA requirement.*



# *Guideline recommendations*

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# Guideline recommendations

Clinical Nutrition 28 (2009) 387–400



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Contents lists available at ScienceDirect

## Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>



## ESPEN Guidelines on Parenteral Nutrition: Intensive care

Pierre Singer<sup>a</sup>, Mette M. Berger<sup>b</sup>, Greet Van den Berghe<sup>c</sup>, Gianni Biolo<sup>d</sup>, Philip Calder<sup>e</sup>, Alastair Forbes<sup>f</sup>, Richard Griffiths<sup>g</sup>, Georg Kreyman<sup>h</sup>, Xavier Leverve<sup>i</sup>, Claude Pichard<sup>j</sup>

ESPEN Guidelines on Parenteral Nutrition: Intensive Care. *Clinical Nutrition* 2009;28(4):359-479.



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1.3–1.5 g/kg ideal body weight per day in conjunction with an adequate energy supply (Grade B)

- **Grade B:** At least one well-designed controlled trial without randomization, a quasi-experimental study or observational study

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# *ASPEN guideline recommendations*

## Special Article

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### Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition: Executive Summary\*

Robert G. Martindale, MD, PhD; Stephen A. McClave, MD; Vincent W. Vanek, MD; Mary McCarthy, RN, PhD; Pamela Roberts, MD; Beth Taylor, RD; Juan B. Ochoa, MD; Lena Napolitano, MD; Gail Cresci, RD; American College of Critical Care Medicine; and the A.S.P.E.N. Board of Directors

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1.2–2.0 g/kg actual body weight per day (Grade E)

- **Grade E:** supported by nonrandomized, historical controls, case series, uncontrolled studies, and expert opinion

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# *RCTs*

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## RCTs

*Food and Nutrition Sciences*, 2013, 4, 201-214

<http://dx.doi.org/10.4236/fns.2013.42028> Published Online February 2013 (<http://www.scirp.org/journal/fns>)



# **Back to Basics: Estimating Protein Requirements for Adult Hospital Patients. A Systematic Review of Randomised Controlled Trials**

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critically ill		1.2 - 1.5	ESPEN [29]
		1.2 - 2.0	ASPEN [31]
		1.1 - 1.3	Mesejo [68]
continuous renal replacement therapy		≥2.0	Scheinkestel [69]
sepsis		1.2 - 2.3	Greig [70], McCowen [71]
obese critically ill (permissive underfeeding: reduced energy intake)	BMI 30 - 40	≥2 g/kgIBW	ASPEN [31]
	BMI > 40	≥2.5 g/kgIBW	

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- Mesejo 2003, critically ill, N=50, 25 patients per group.

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*None reported any positive effects on patient oriented outcomes.*

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## *New data*

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- Observational study conducted in 167 ICUs across 21 countries

Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhaliwal R, Heyland DK. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. *Intensive Care Med.* 2009 Oct;35(10):1728-37.



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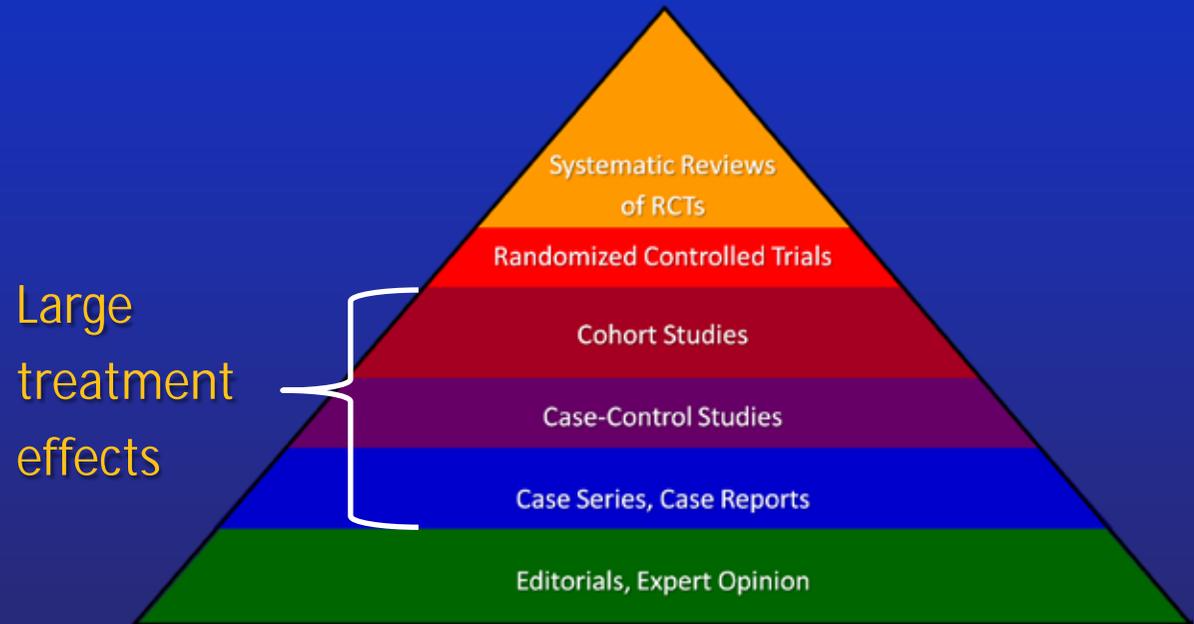


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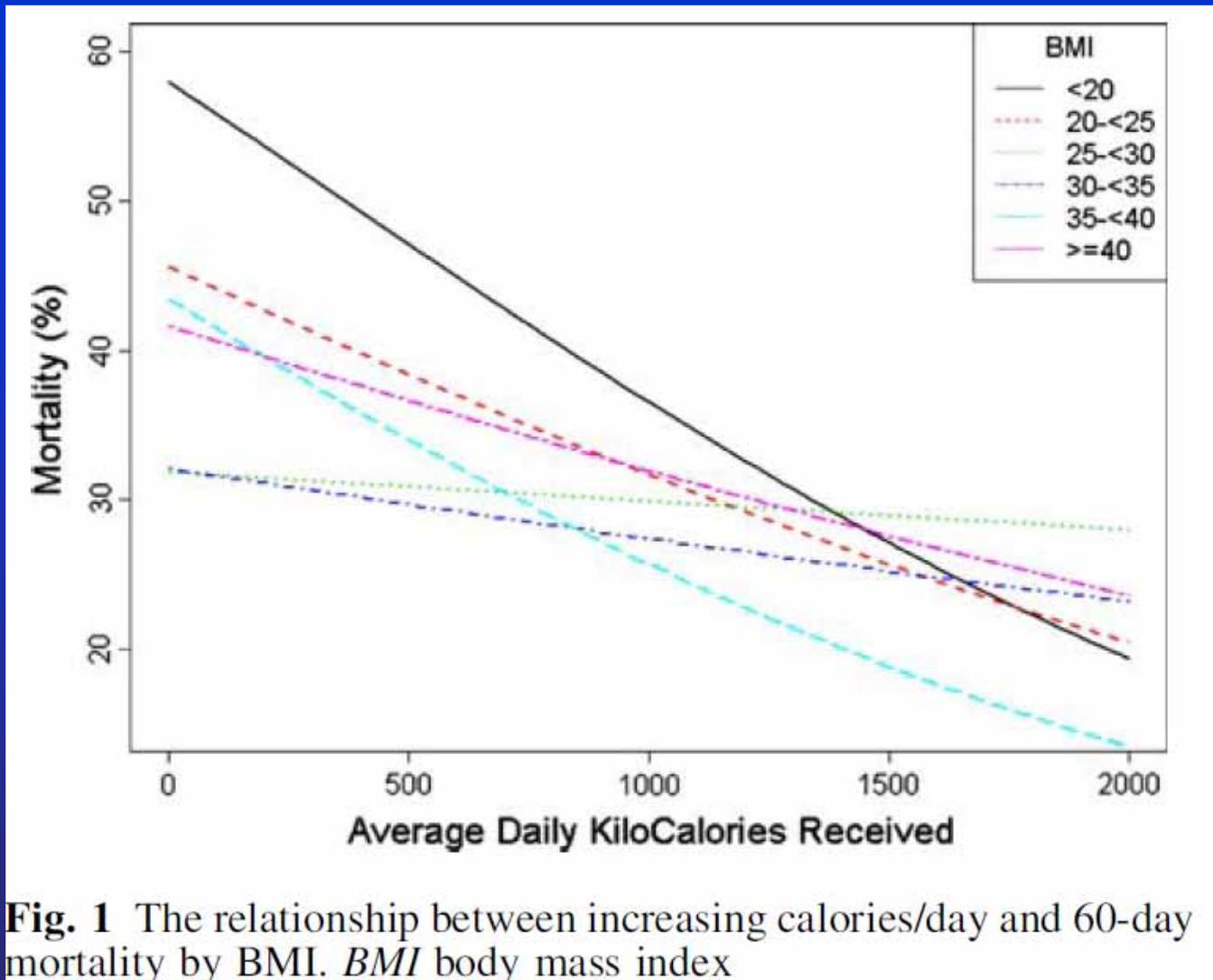


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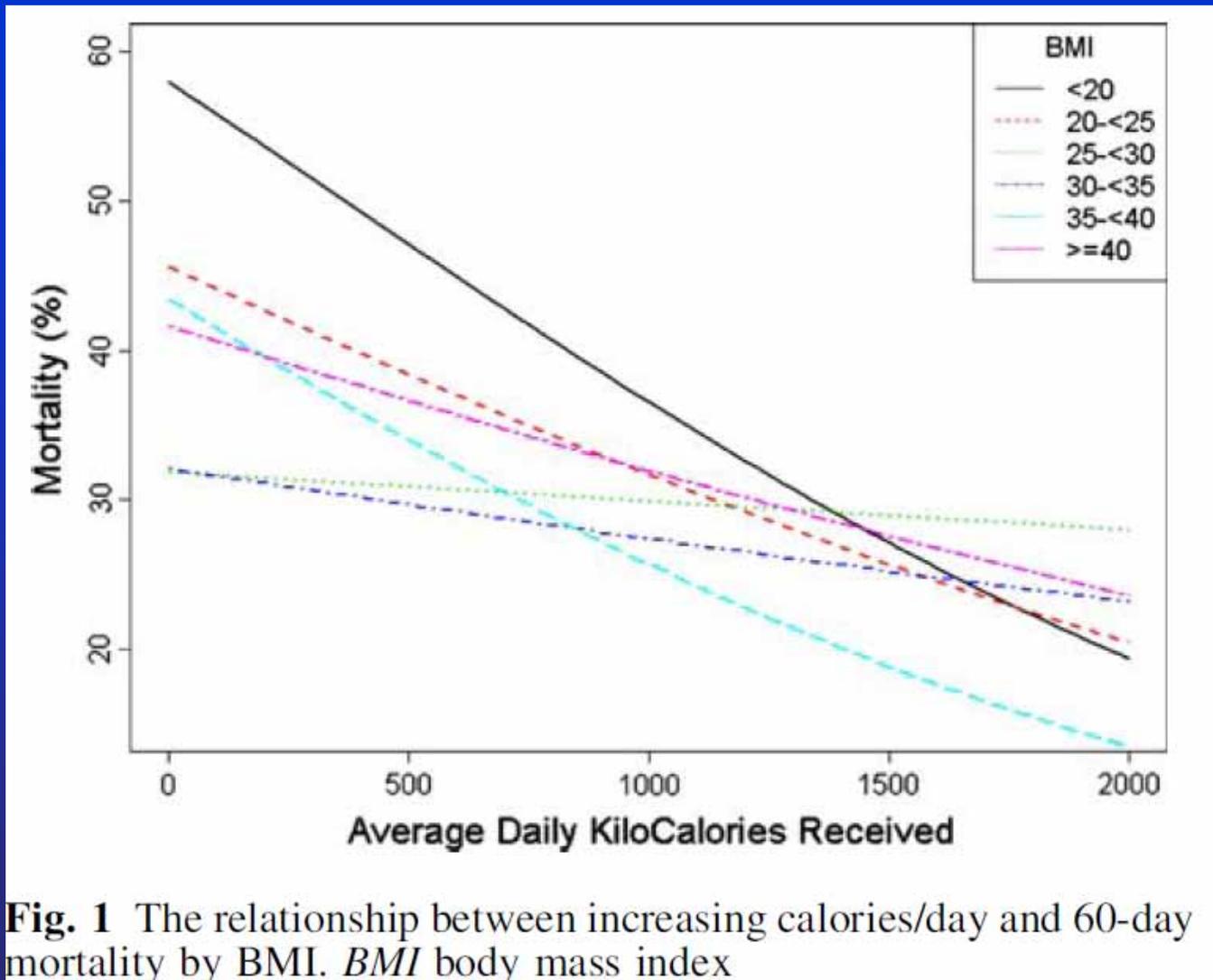
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*Most hospital formulas use a fixed ratio of protein to energy.*



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*All lines slope down and to the right (decreased mortality as energy increases), we should conclude that **ALL classes of BMI benefit**, however some benefit more than others.*

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- A 'Figure 1' for protein was not presented, but throughout the paper the 'protein' effect mirrors the 'energy effect'.



# *Conclusions (Take home message)*

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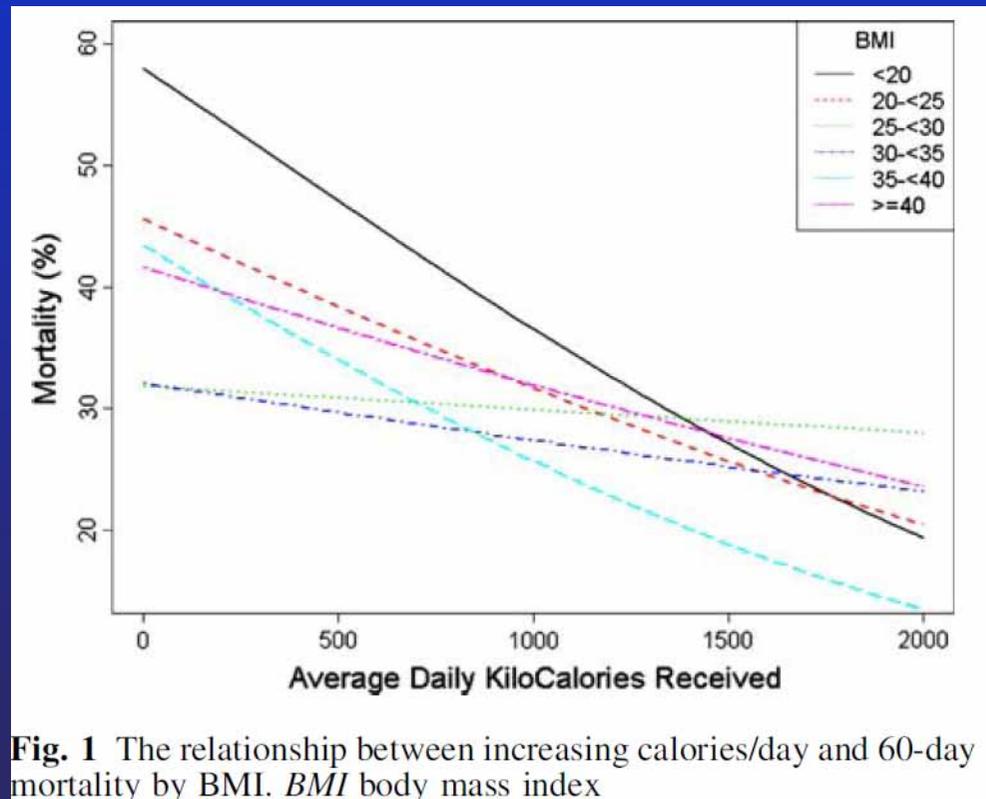
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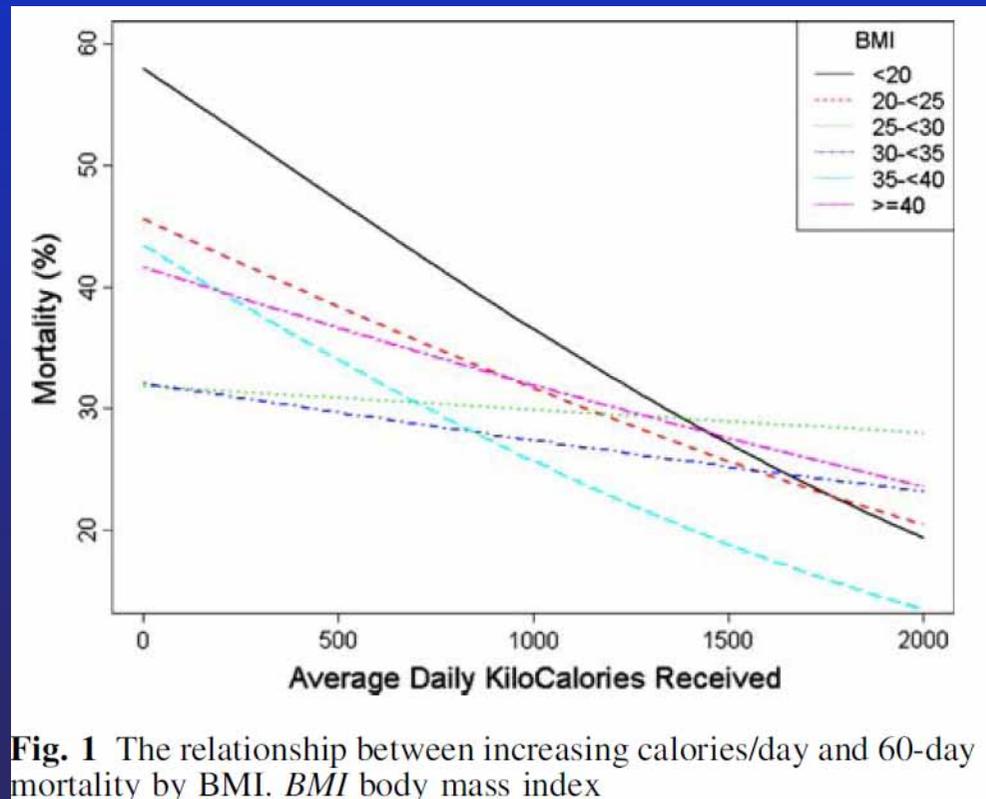


**Fig. 1** The relationship between increasing calories/day and 60-day mortality by BMI. *BMI* body mass index



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**Fig. 1** The relationship between increasing calories/day and 60-day mortality by BMI. *BMI* body mass index



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  - We just completed a 474 patient RCT addressing this question.
  - Patients with unstable renal function at ICU admission *may not* benefit from higher-end protein dosing (2.0 g/kg).
  - But patients without renal dysfunction did show a mortality reduction!!



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*Protein dosing is a **hot topic and may lead to reduced mortality**. We need more well done multi-centre RCTs focussed on patient oriented outcomes to refine our target range.*

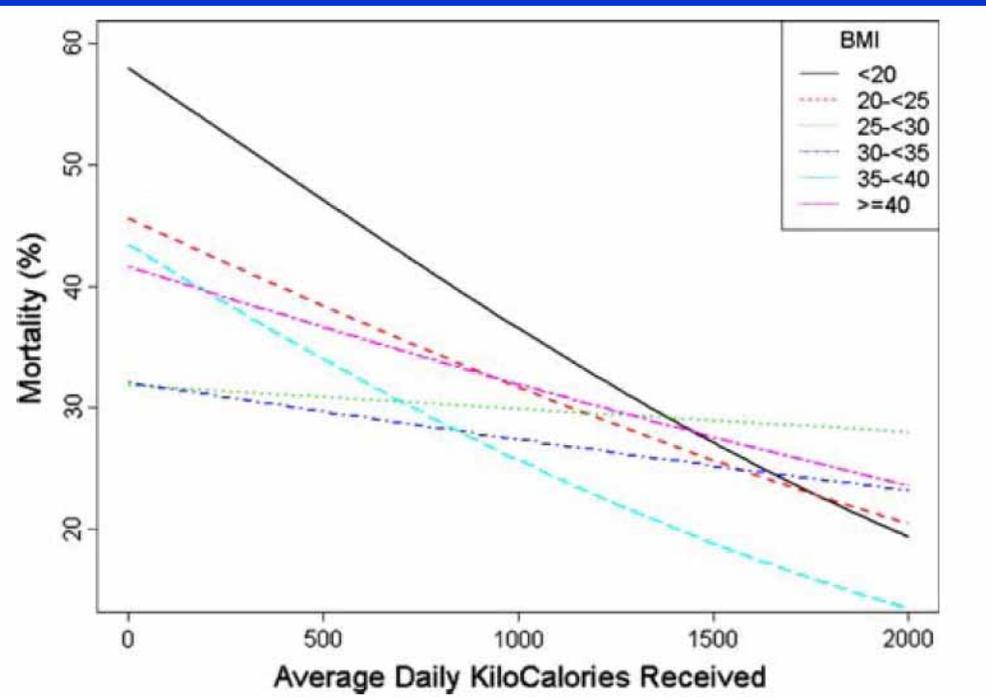


## Questions?

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- Observational studies suggest patients may benefit from 'more' protein.
  - This potential benefit is **NOT** restricted to patients with low BMI.
- Daily protein targets between **1.2–2.0 g/kg**, are reasonable.
  - Some form of adjustment to IBW at a BMI threshold is also reasonable.
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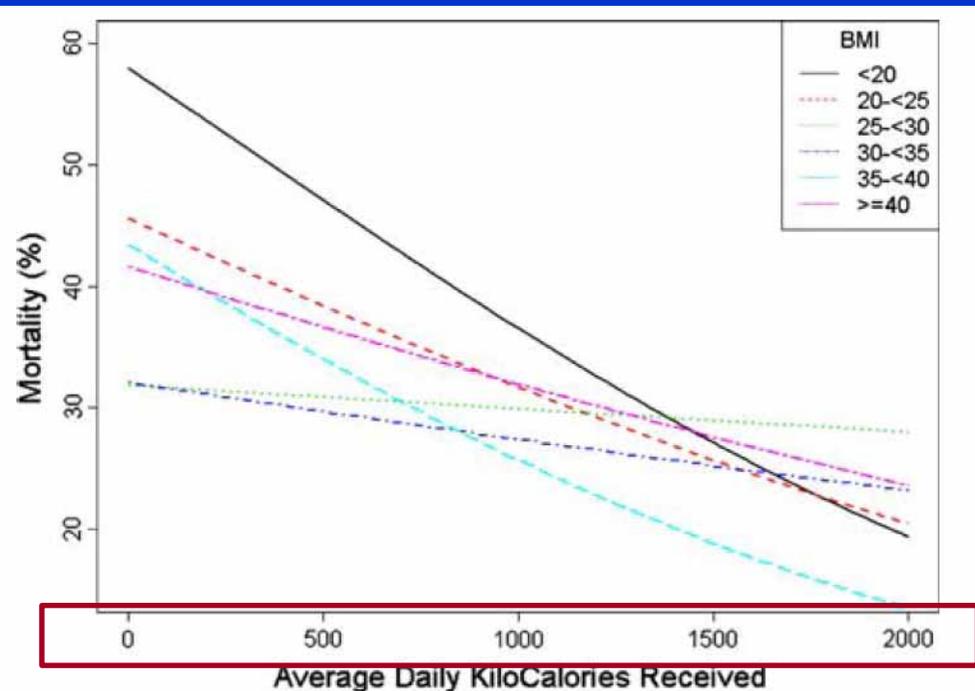


**Fig. 1** The relationship between increasing calories/day and 60-day mortality by BMI. *BMI* body mass index

- The interpretation of interactions in logistic regression models is *complex*.
- Because logistic regression is conducted in the log-odds scale, the magnitude of effect is not *linear* over all values of the interacting variables.
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(a) Increased energy intake

BMI group	Unadjusted ( <i>n</i> = 2,772)			
	Odds ratio	95% CI		<i>p</i> value
		LCL	UCL	
Overall	0.73	0.62	0.87	0.001
<20	0.48	0.28	0.83	0.009
20 to <25	0.61	0.45	0.82	0.001
25 to <30	1.01	0.75	1.36	0.960
30 to <35	0.84	0.54	1.30	0.439
35 to <40	0.47	0.23	0.95	0.036
≥40	0.78	0.41	1.47	0.442



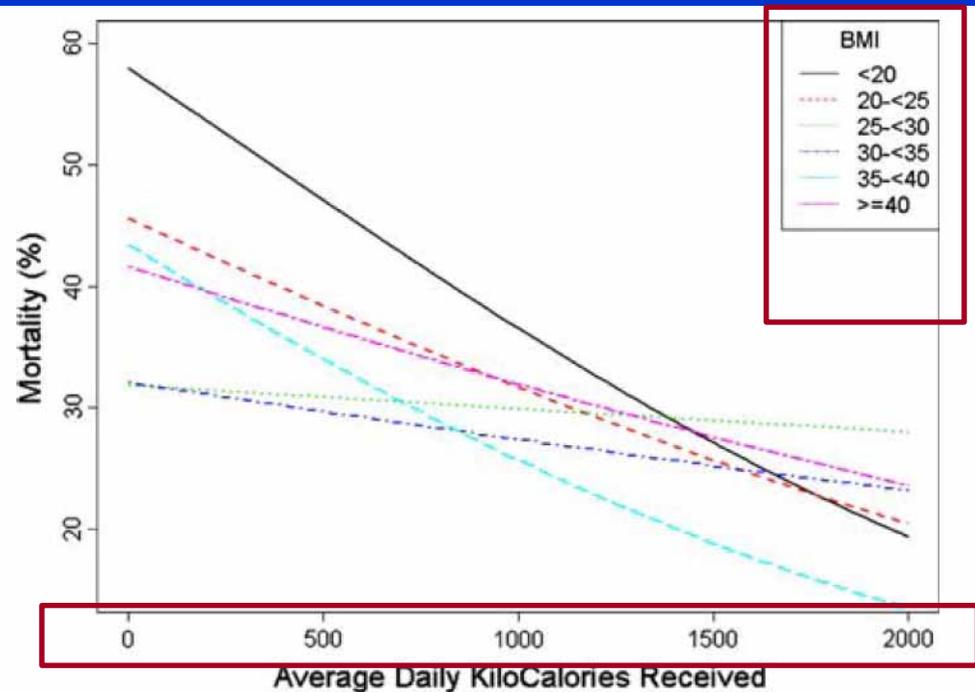
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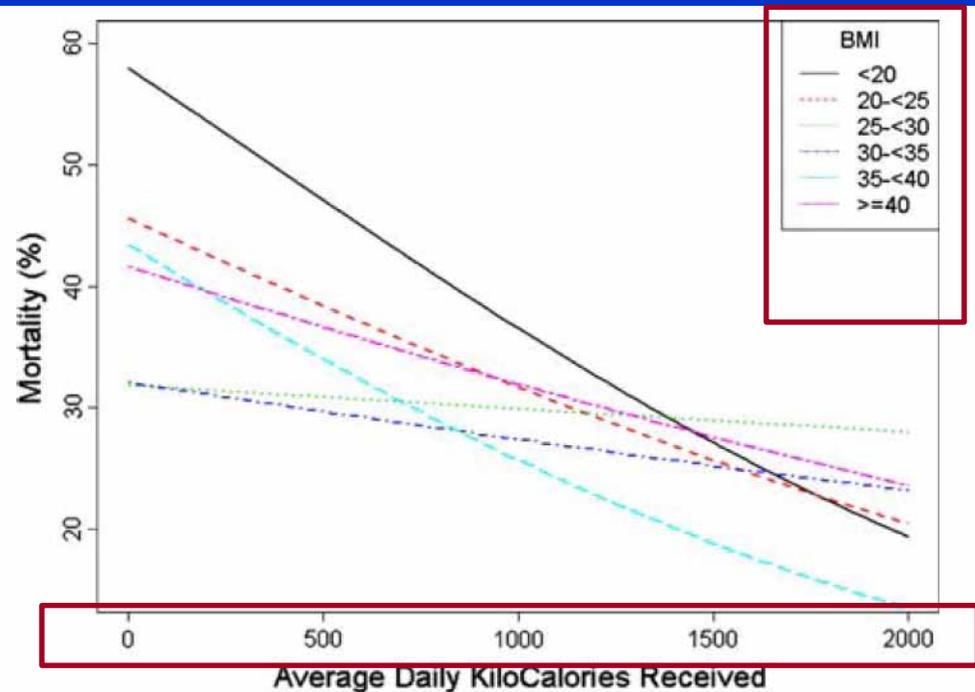
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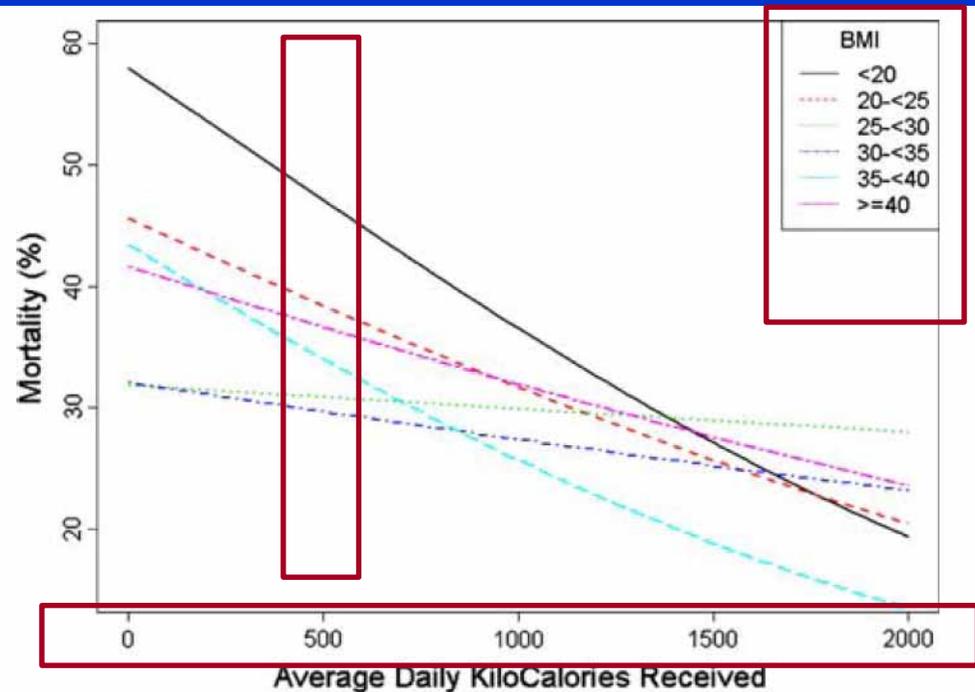
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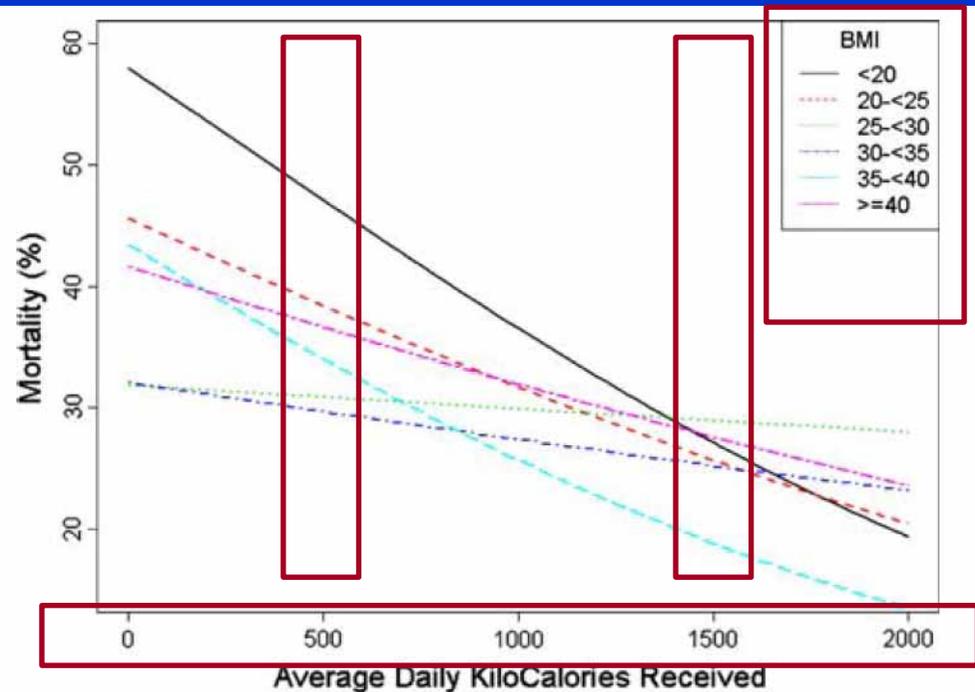
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