How much protein in the ICU:
New data, new ideas

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Faculty Disclosures
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Relevant financial relationships with a commercial interest:

- Fresenius Kabi, Academic Research Grants (Past), Consultant and Speaker's Honoraria (Current)
- Baxter Healthcare, Academic Research Grant (Current), Consultant and Speaker's Honoraria (Current)
- Nestle Healthcare, Academic Research Grant (Current), Consultant and Speaker's Honoraria (Current)

Overview of Talk

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

Editorials, Expert Opinion

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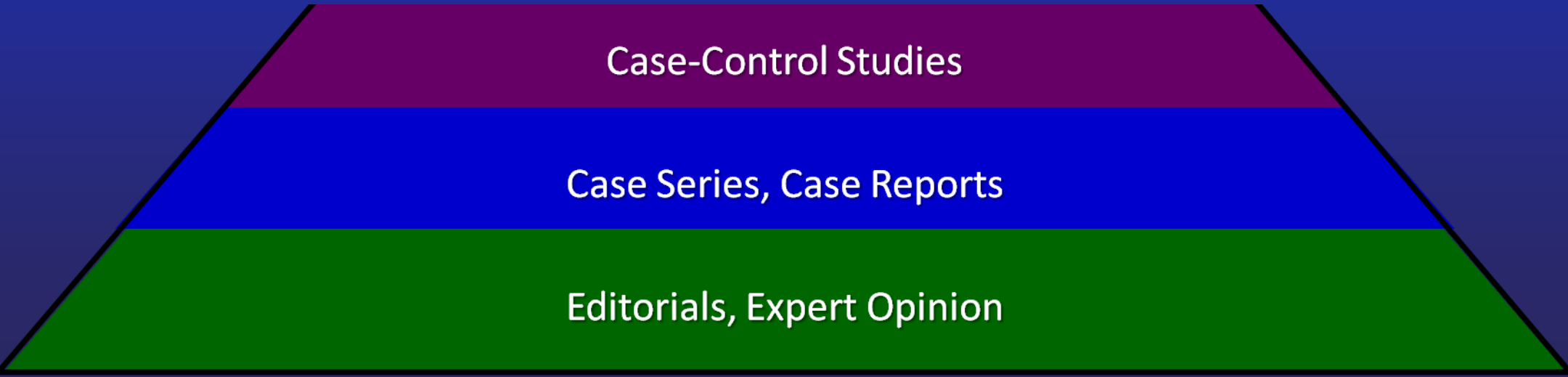

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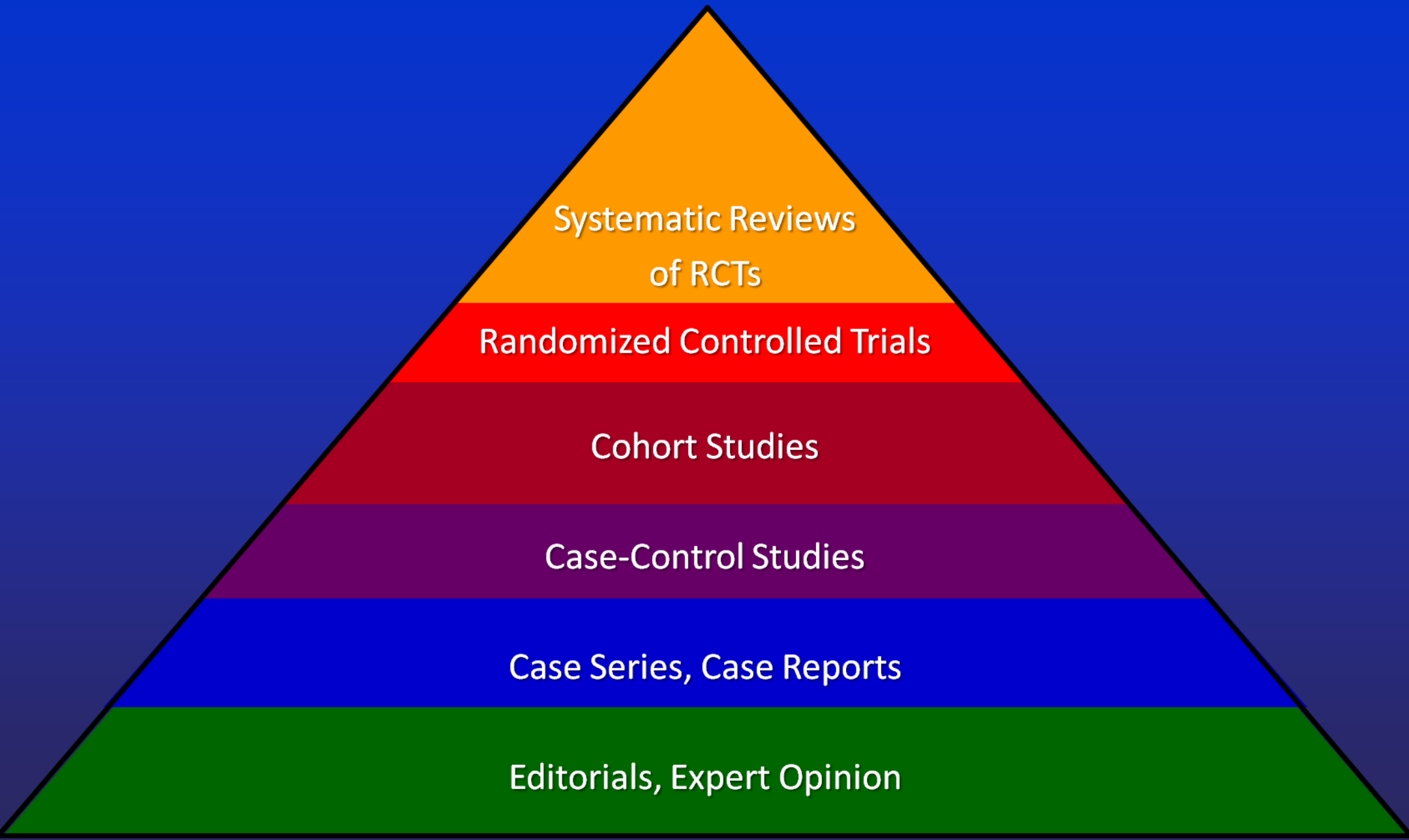

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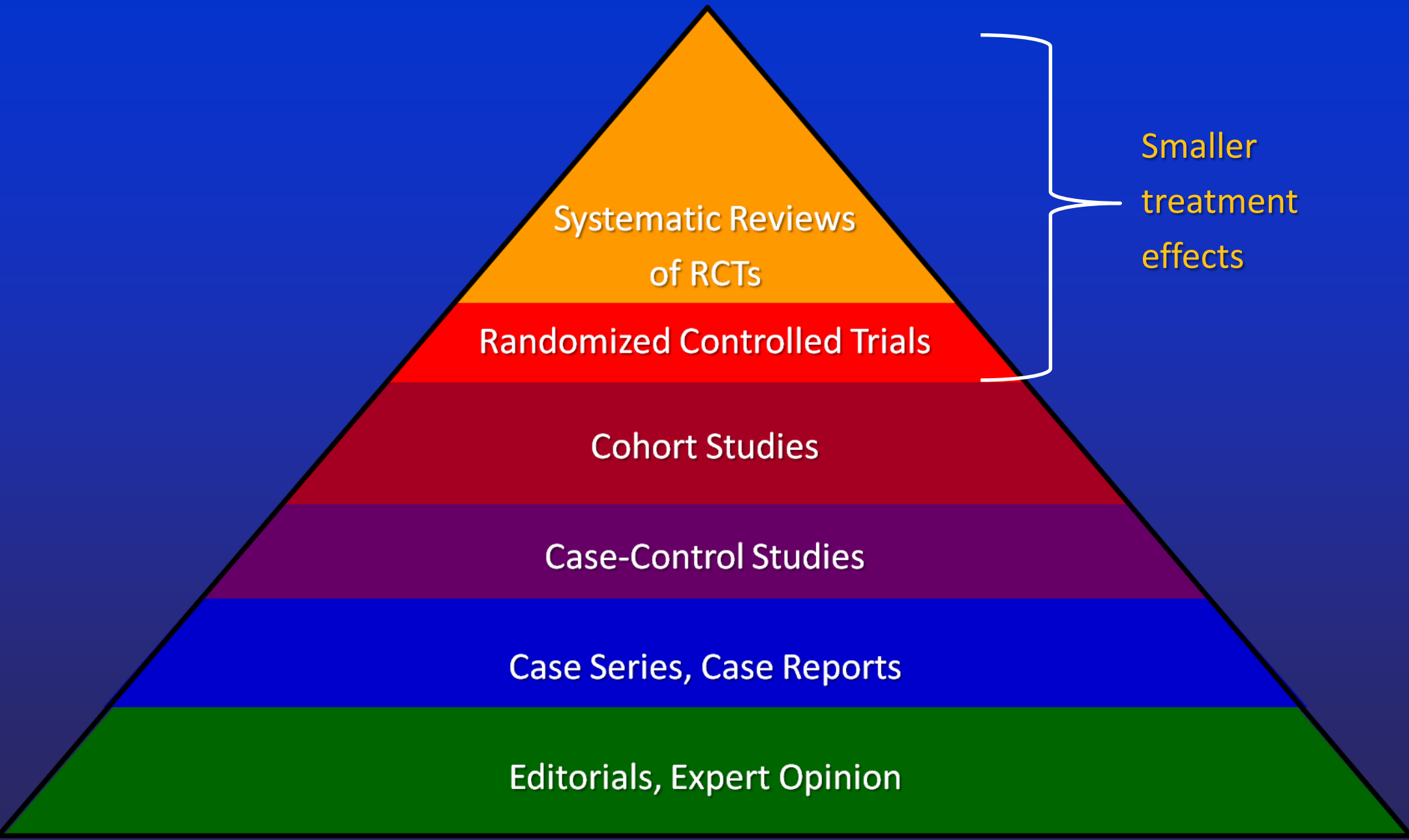

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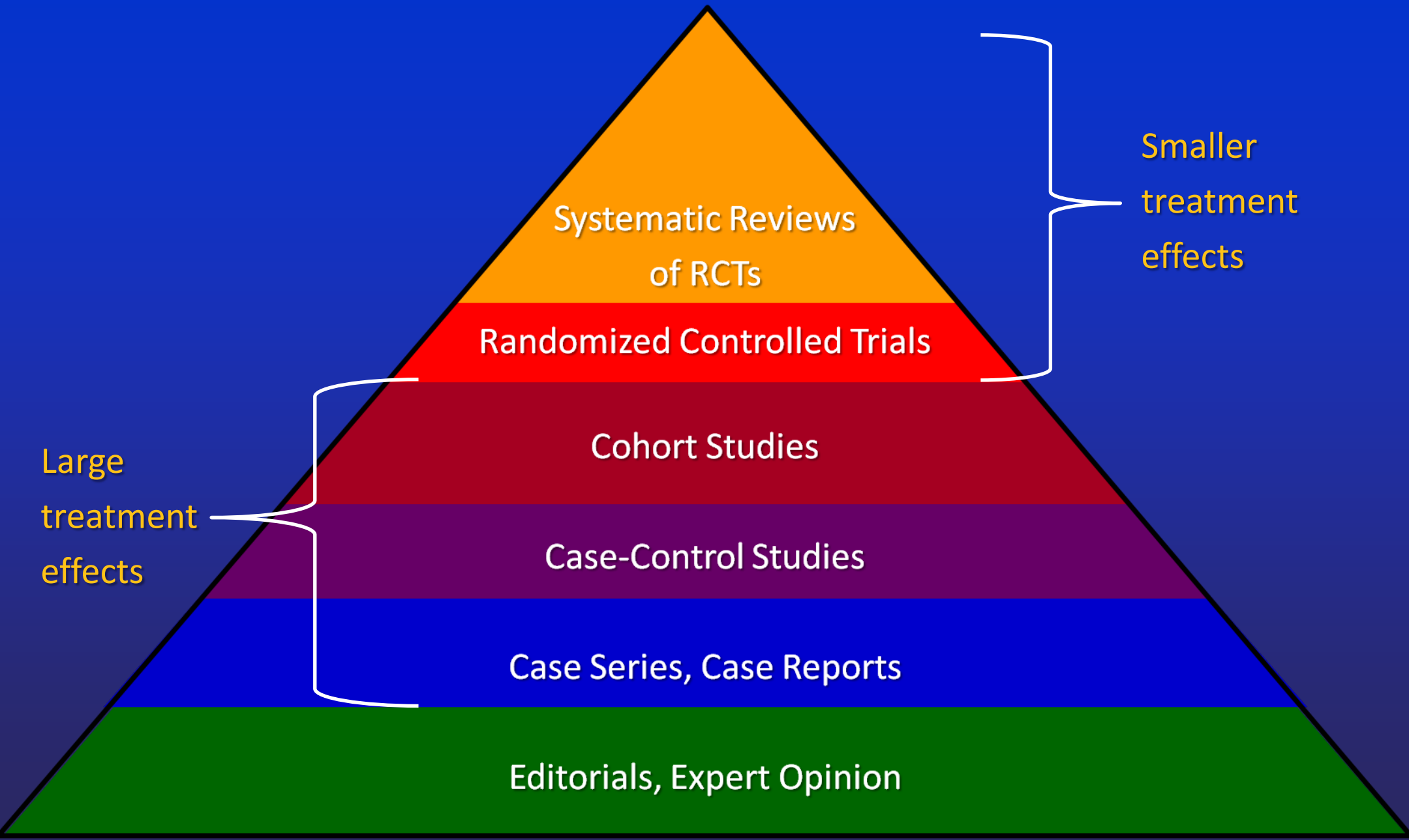

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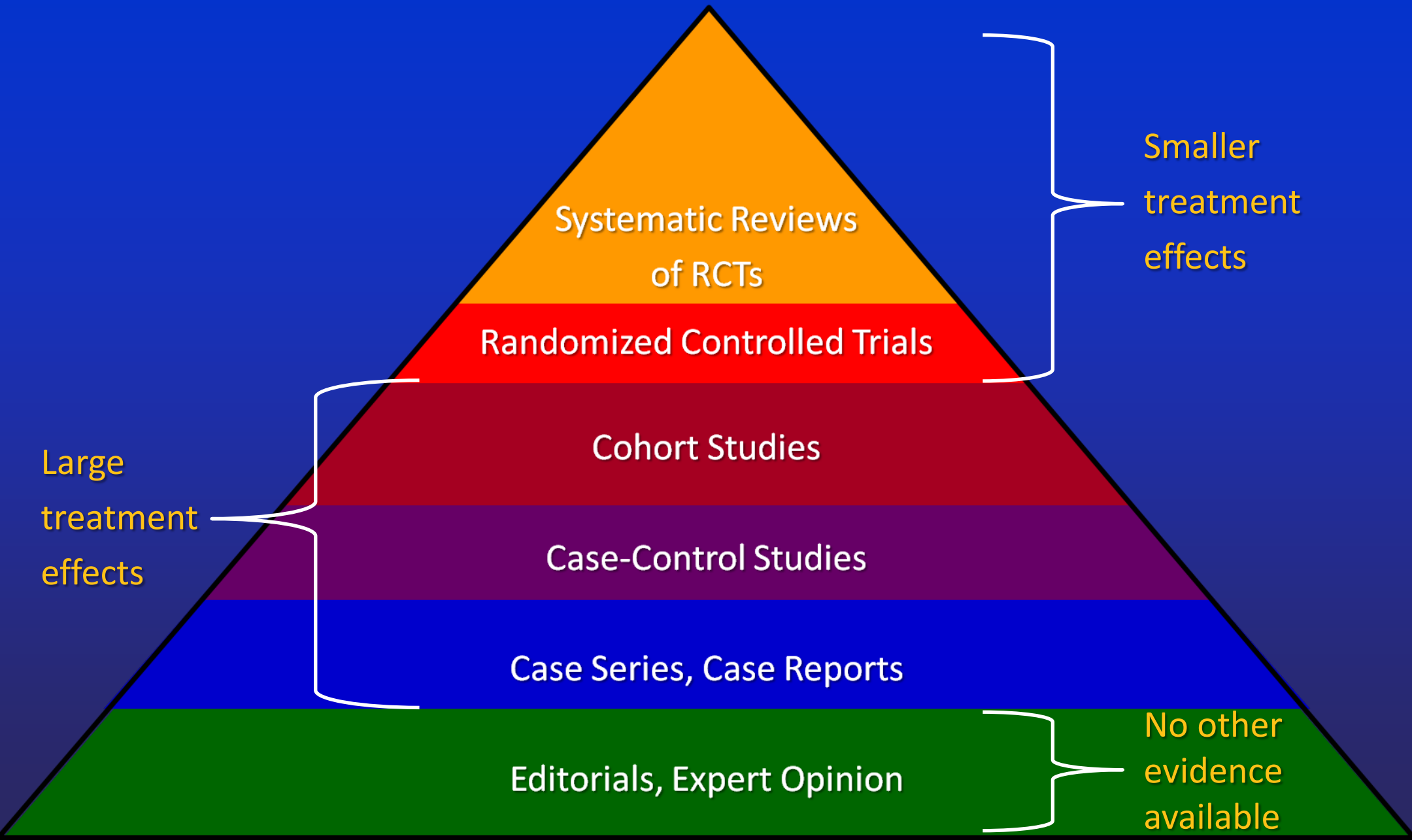

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Allen F Shaughnessy, David C Slawson

BMJ VOLUME 327 2 AUGUST 2003 bmj.com

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Disease and intervention	Disease oriented evidence	Patient oriented evidence
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Heart failure and use of digoxin	Increase in exercise tolerance	No effect on mortality
Heart failure and milrinone	Improved cardiac output and exercise tolerance	Increased mortality
Blood lipid lowering and clofibrate	Lowered lipid concentration	Increased non-cardiac mortality
Blood pressure lowering with doxazosin	Lowered blood pressure	Increased heart failure
Tumour response and drug treatment	Reduction or elimination of tumour	No effect on survival
Postmenopausal osteoporosis treatment with fluoride therapy	Increased bone mineral density	Increase in non-vertebral fractures

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

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Guideline recommendations

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Clinical Nutrition 28 (2009) 387–400

Contents lists available at ScienceDirect

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ESPEN Guidelines on Parenteral Nutrition: Intensive care

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

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

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RCTs

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Food and Nutrition Sciences, 2013, 4, 201-214
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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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New data

- Observational study conducted in 167 ICUs across 21 countries

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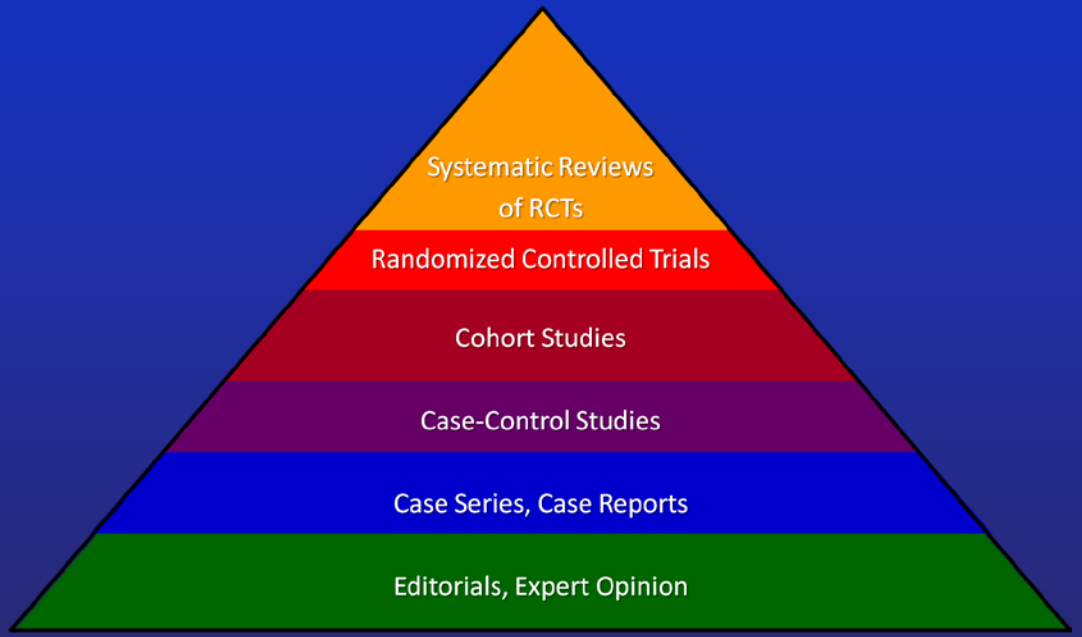

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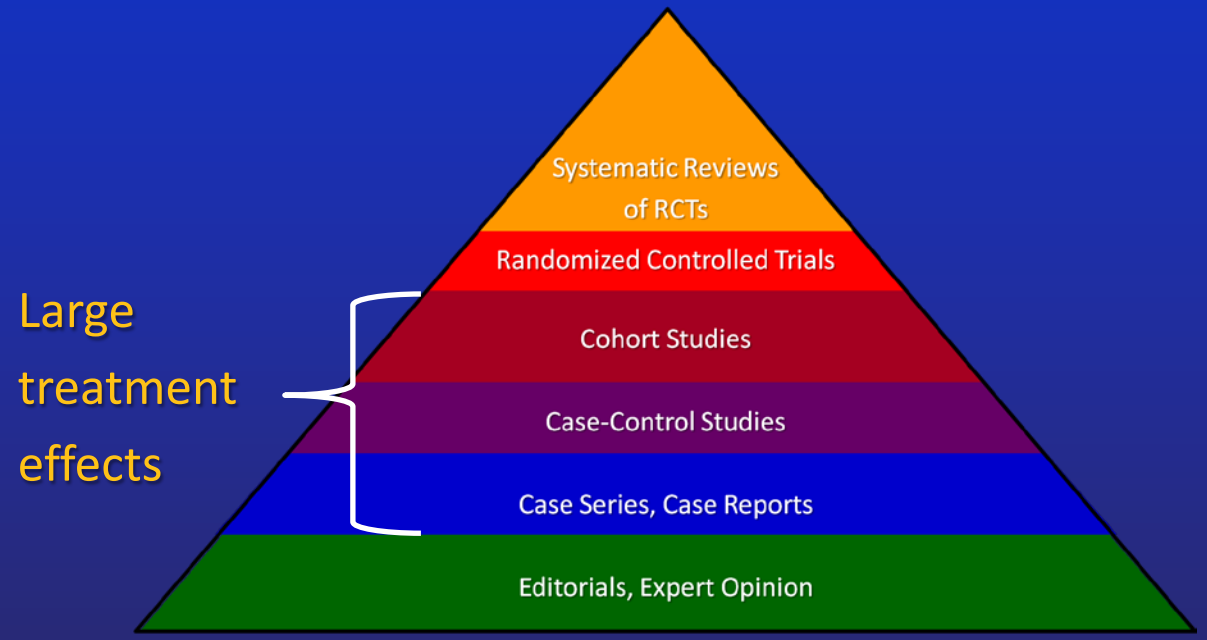

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New data

(b) Increased protein intake

BMI group	Unadjusted (n = 2,771[b])			
	Odds ratio	95% CI		p value
		LCL	UCL	
Overall	0.83	0.75	0.92	<0.001
<20	0.60	0.43	0.84	0.003
20 to <25	0.79	0.66	0.94	0.008
25 to <30	0.95	0.80	1.14	0.609
30 to <35	0.92	0.72	1.19	0.533
35 to <40	0.70	0.47	1.04	0.075
≥40	0.82	0.59	1.14	0.237

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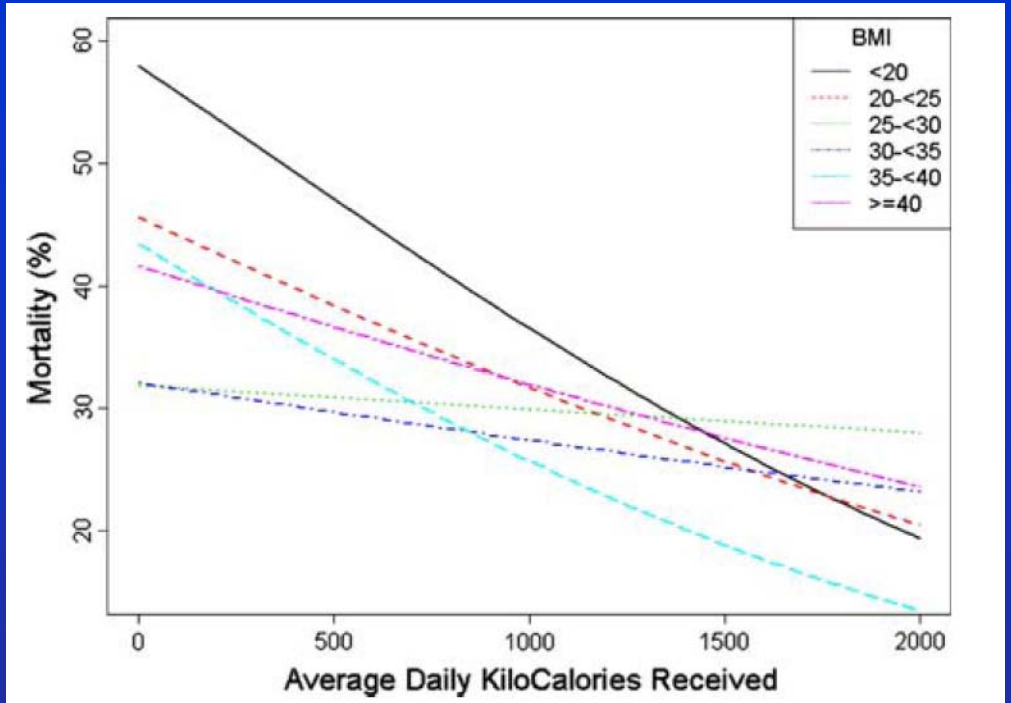

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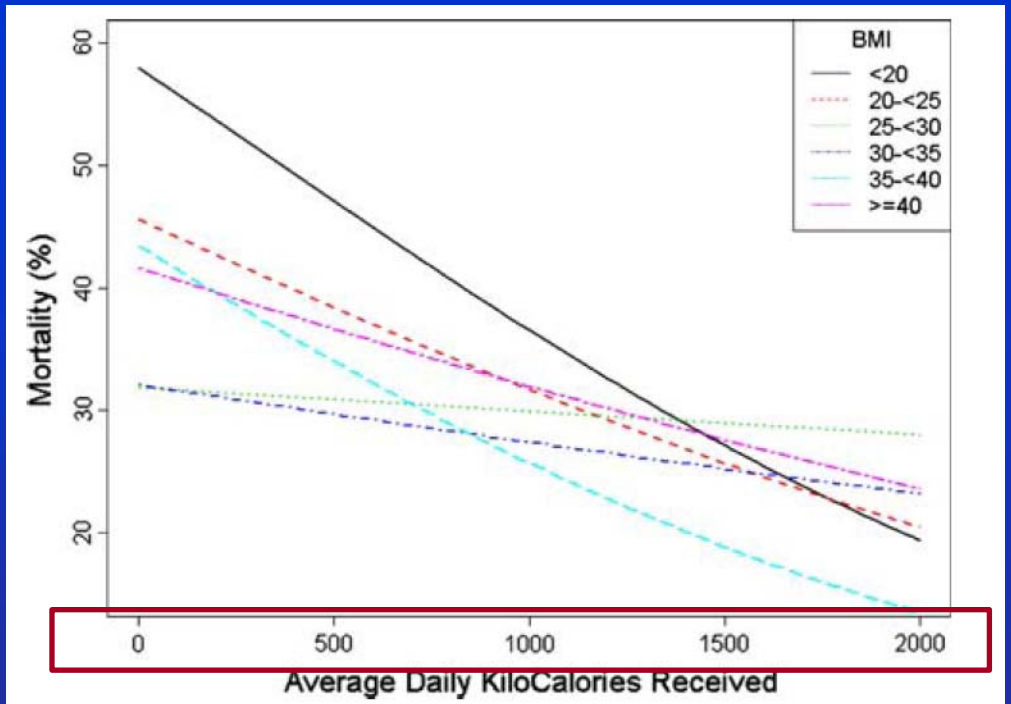

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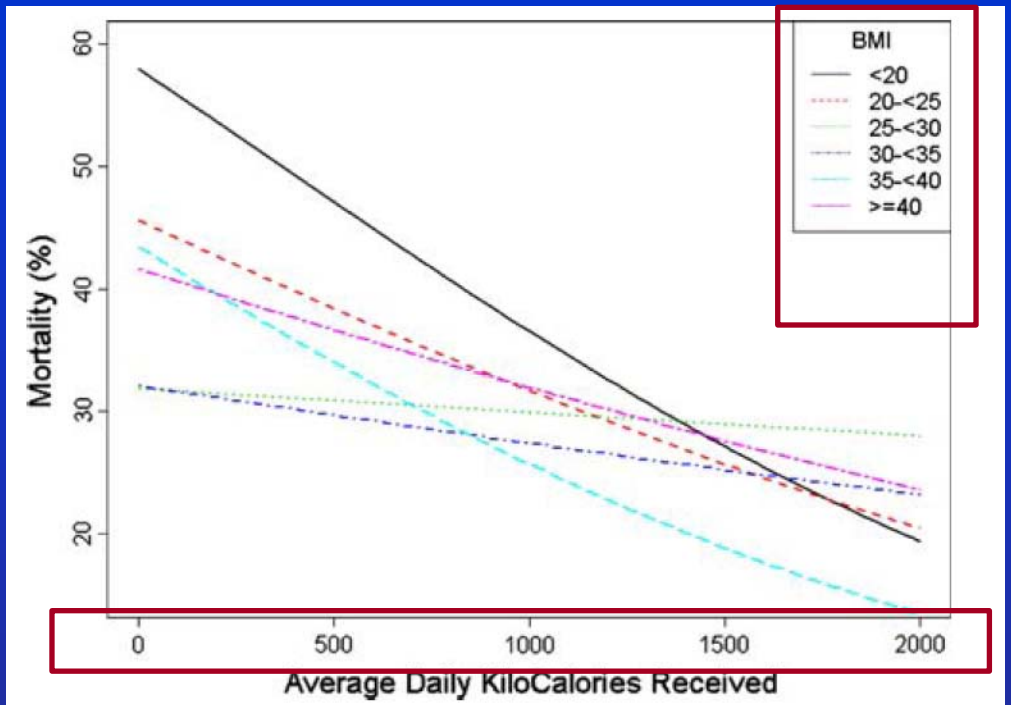

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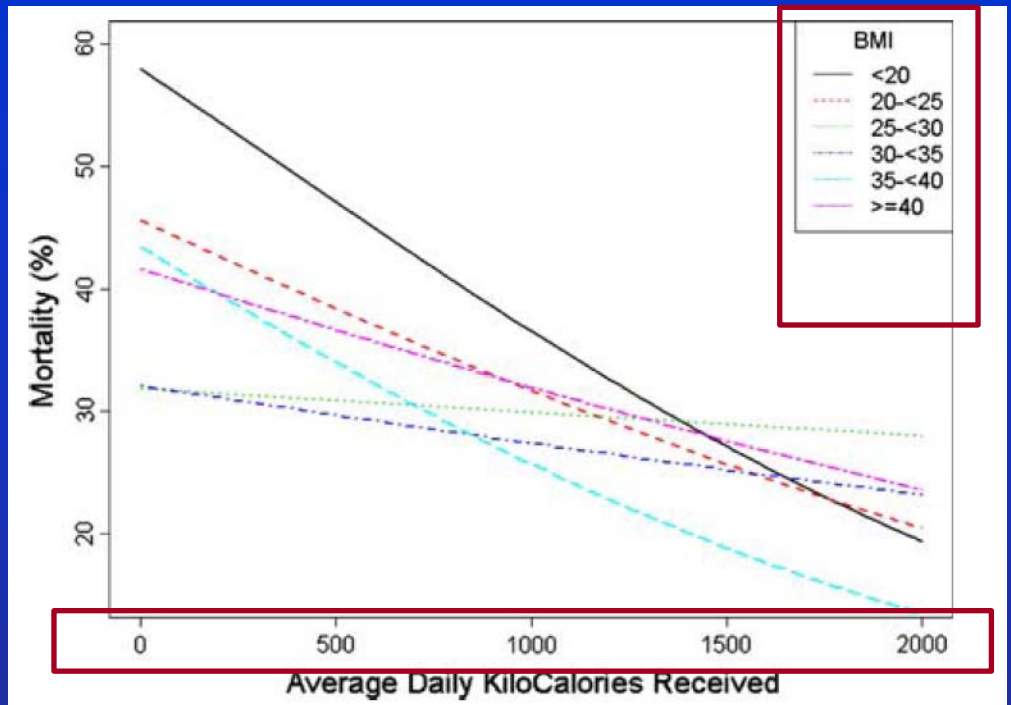

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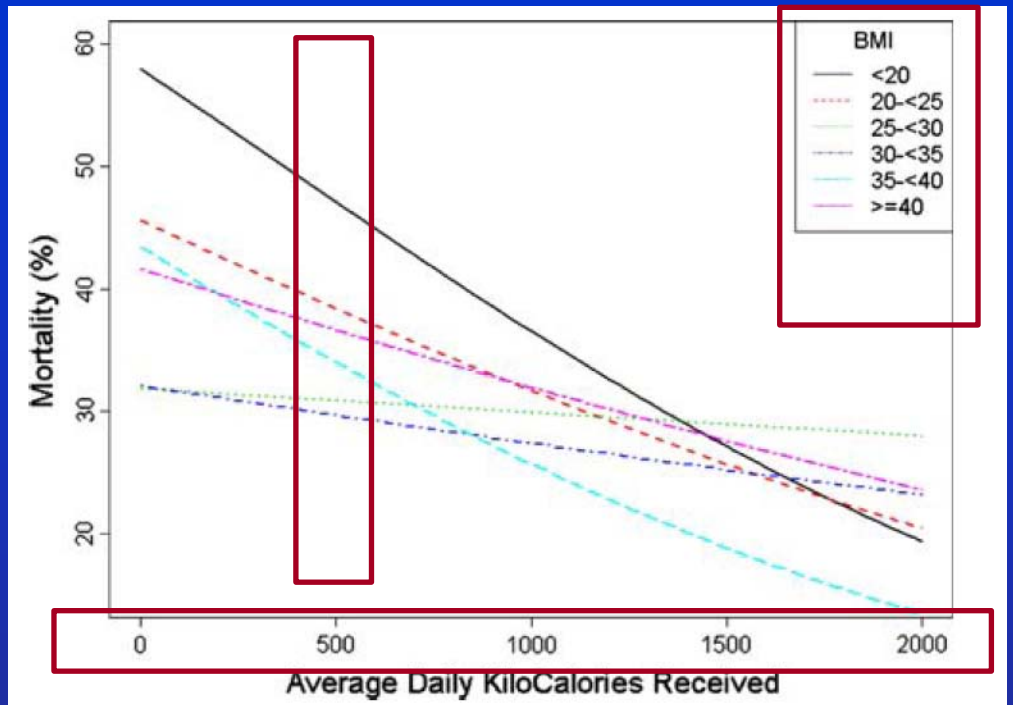

Fig. 1 The relationship between increasing calories/day and 60-day mortality by BMI. *BMI* body mass index

(a) Increased energy intake

BMI group	Unadjusted (n = 2,772)			
	Odds ratio	95% CI		p 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

- 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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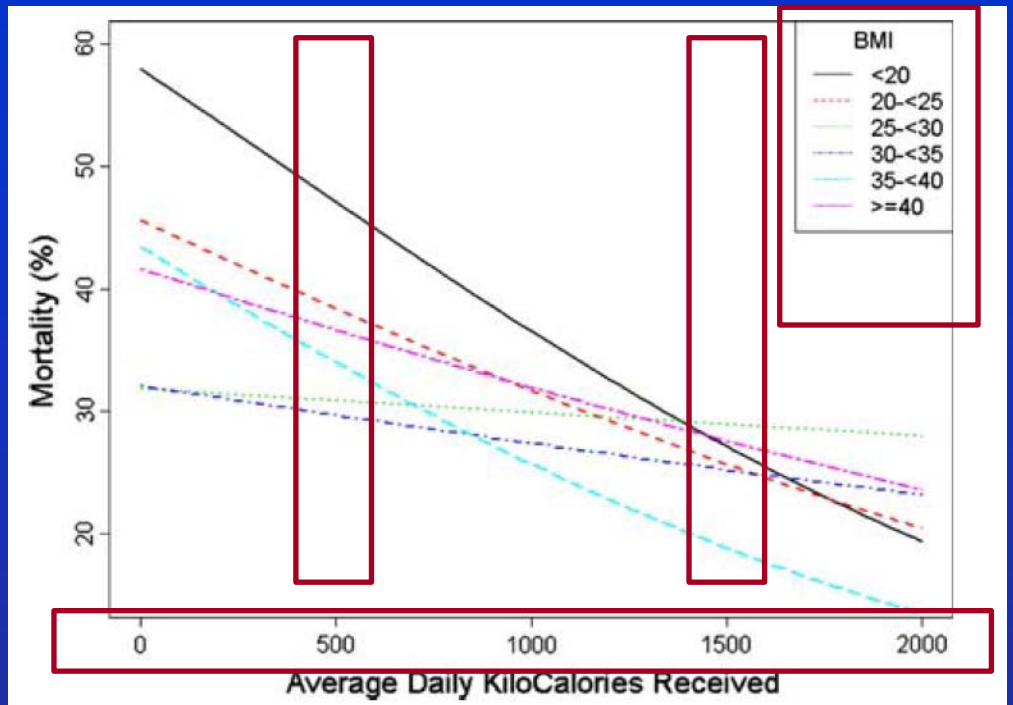

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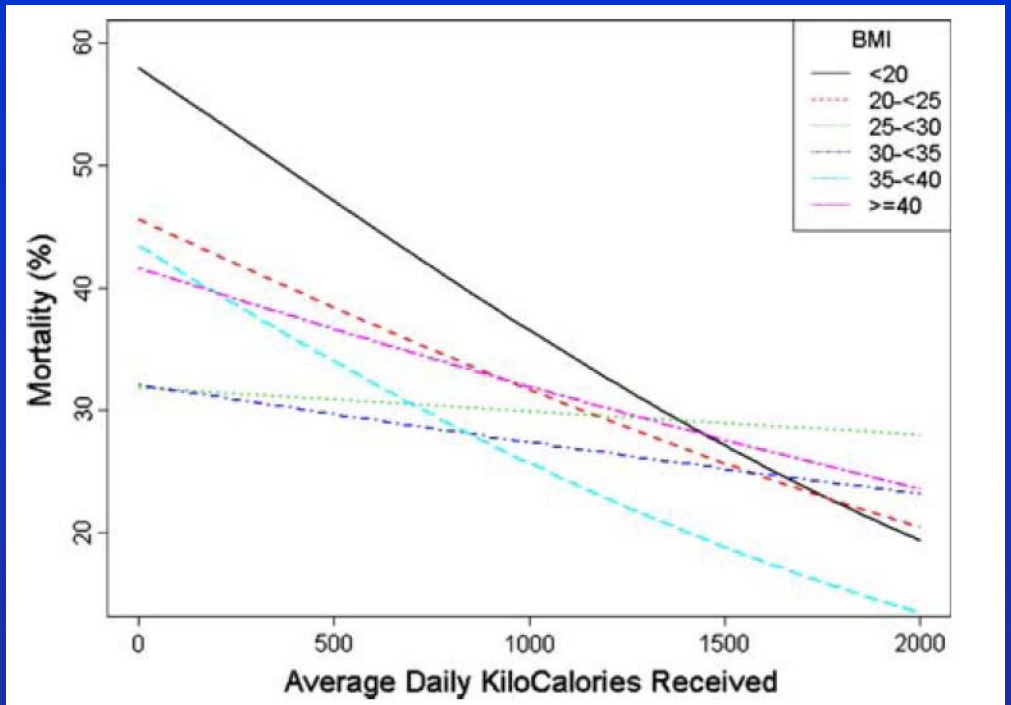

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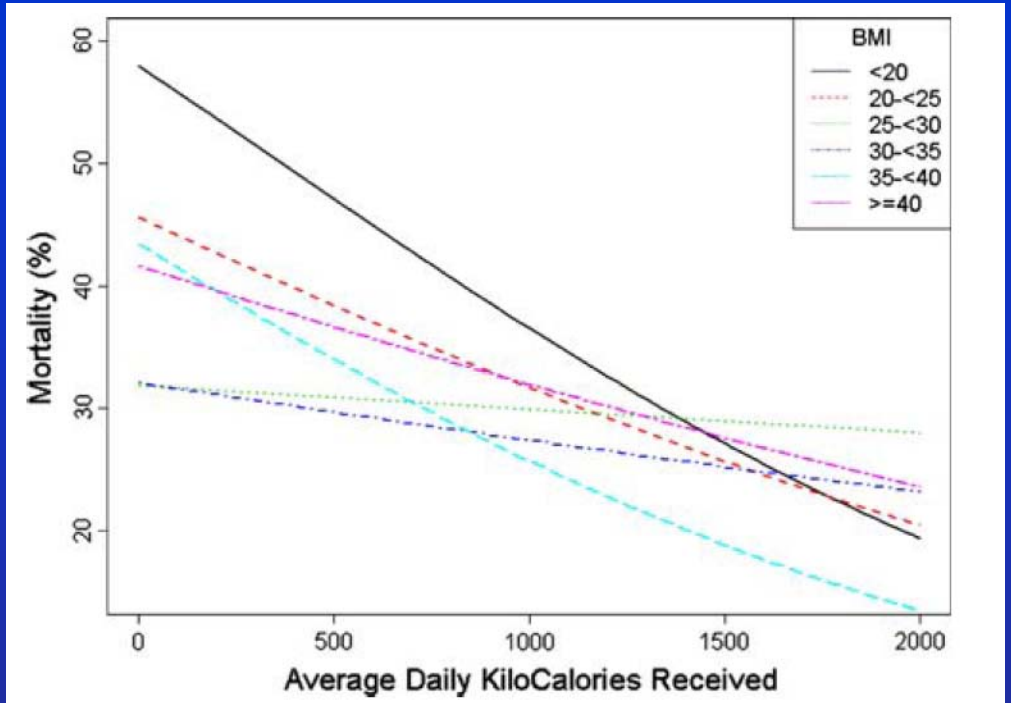

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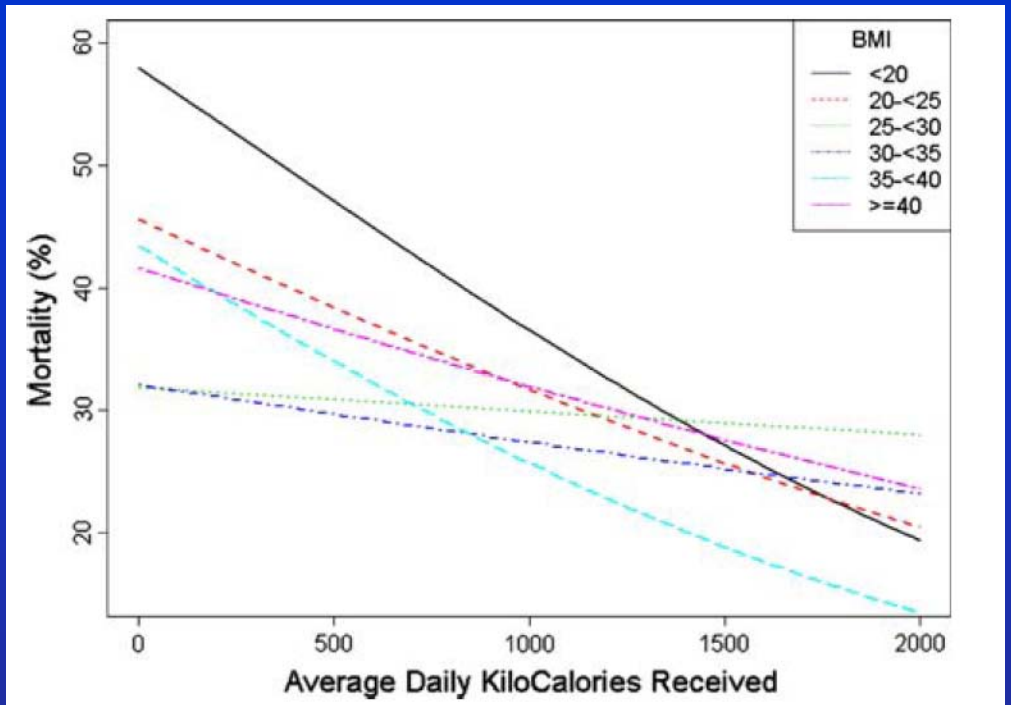

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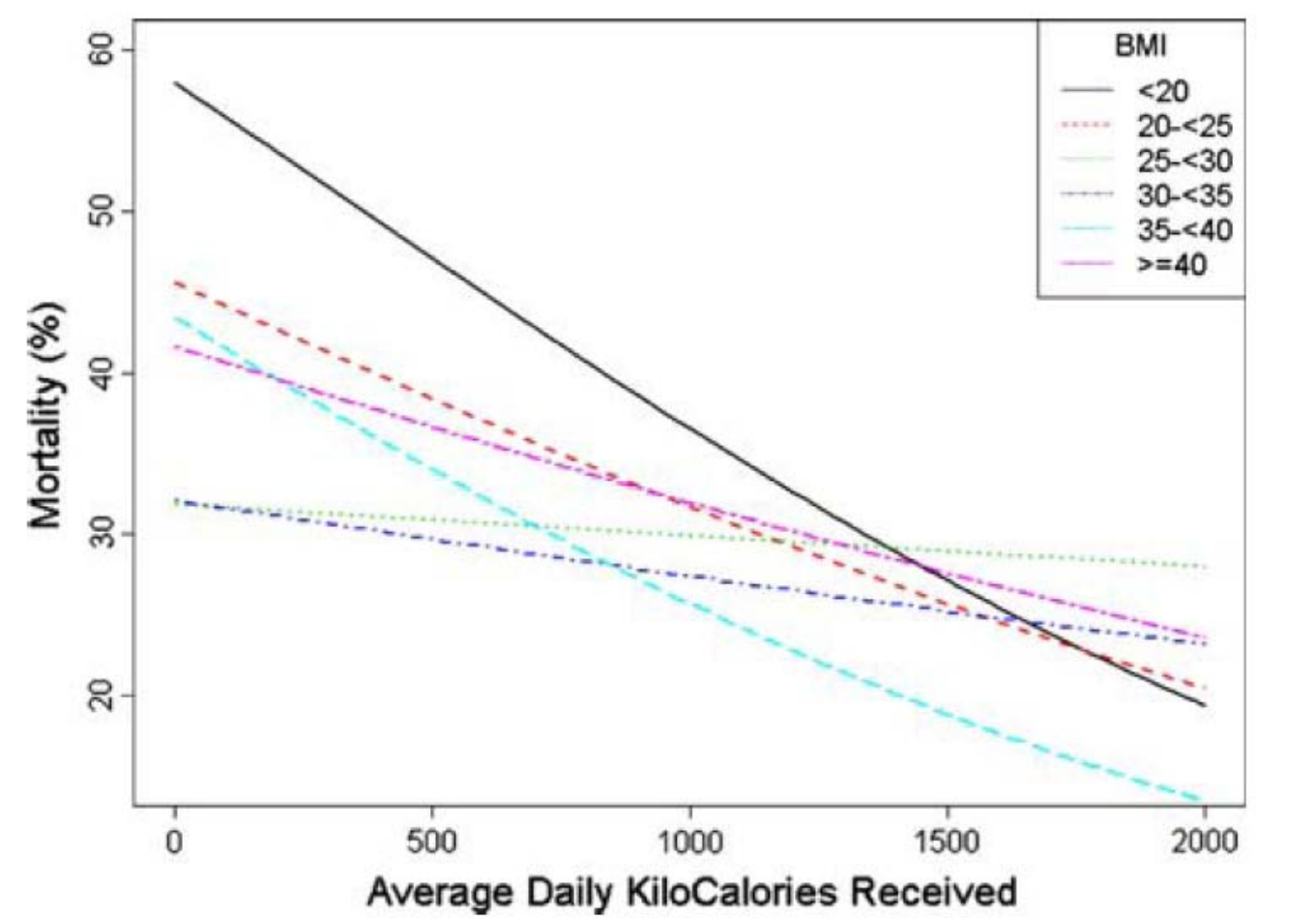

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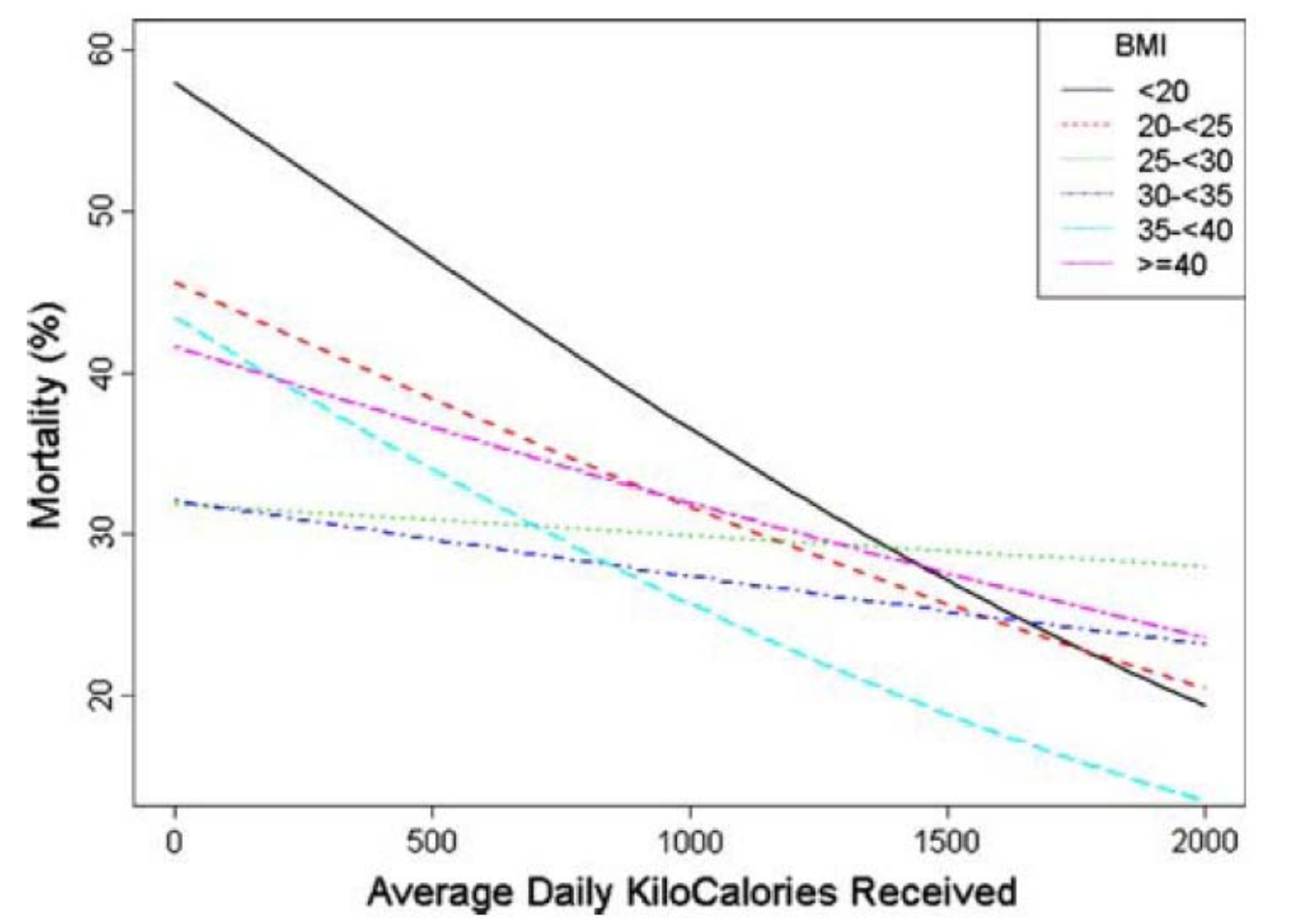

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All lines slope down and to the right (decreased mortality as energy increases), we should conclude that ALL classes of BMI benefit, however some benefit more than others.

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New data

- Observational study conducted in 167 ICUs across 21 countries
- 2,772 mechanically ventilated critically ill patients
- Patients with a BMI < 20 demonstrated a significant reduction in mortality with increasing caloric intake (OR 0.52, 95% CI 0.29 to 0.95, P = 0.033) and protein intake (OR 0.60, 95% CI 0.41 to 0.87, P = 0.007)
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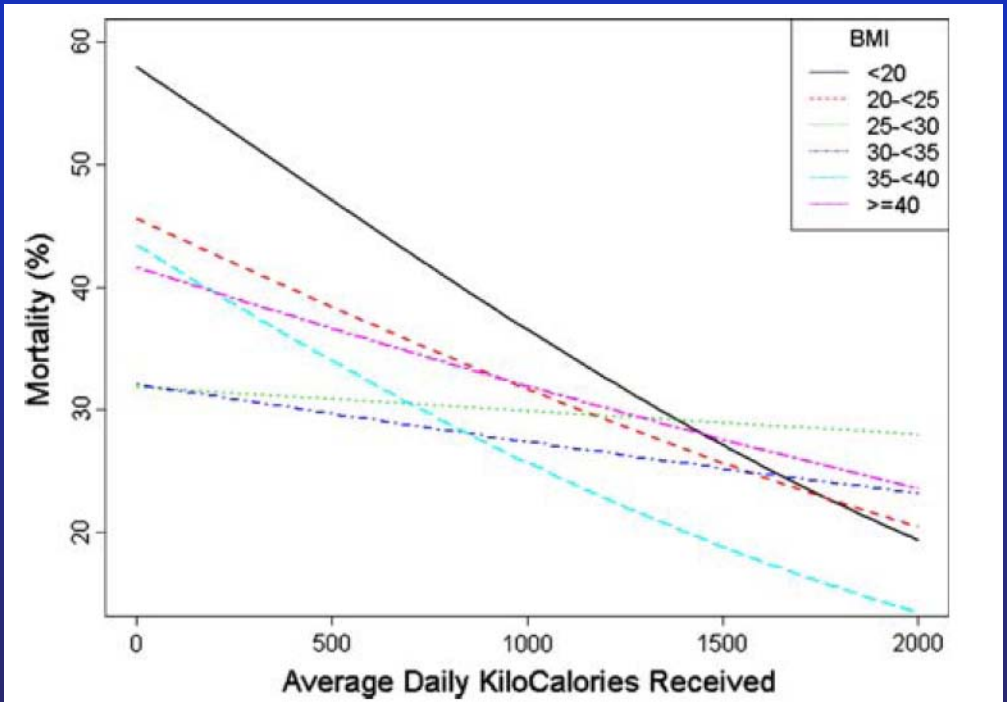

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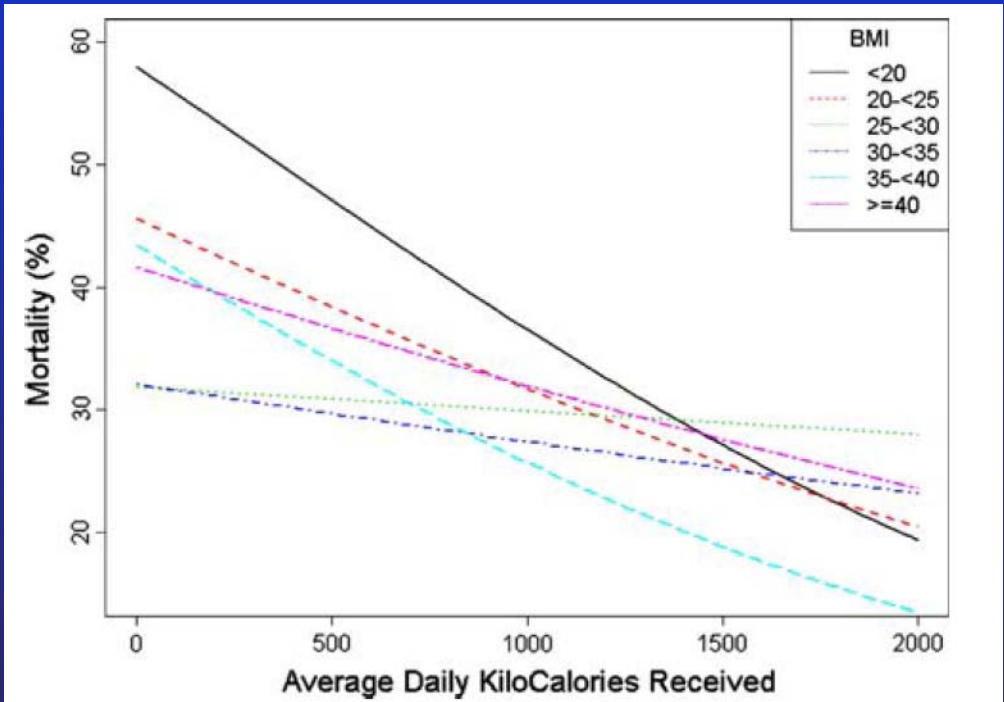

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Protein dosing is a hot topic and may lead to reduced mortality. We need more well done multi-centre RCTs focussed on patient oriented outcomes to refine our target range.

www.EvidenceBased.net

Interactions in covariate adjusted logistic regression

See this page for more details: http://www.ats.ucla.edu/stat/stata/faq/logit2by2.htm

Interactions in covariate adjusted logistic regression

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Logistic regression                                     Number of obs   =        200
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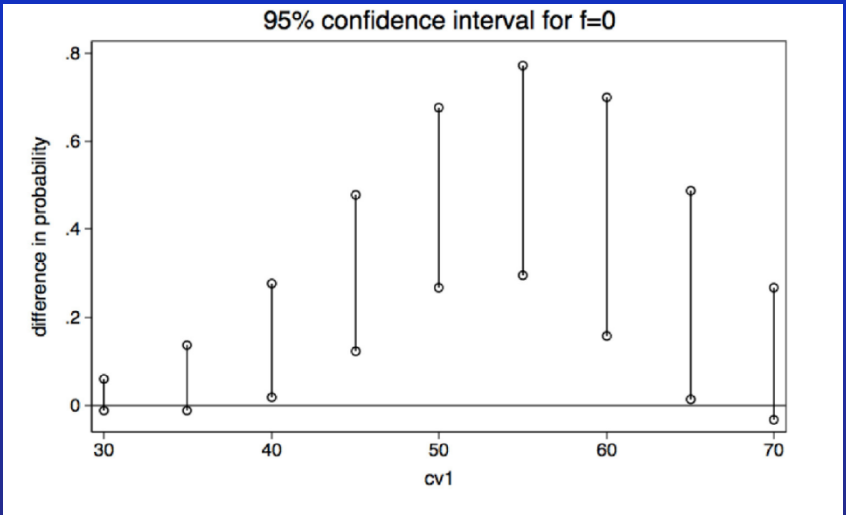

Figure A: effect of h on f=0 for all values of cv1

See this page for more details: http://www.ats.ucla.edu/stat/stata/faq/logit2by2.htm

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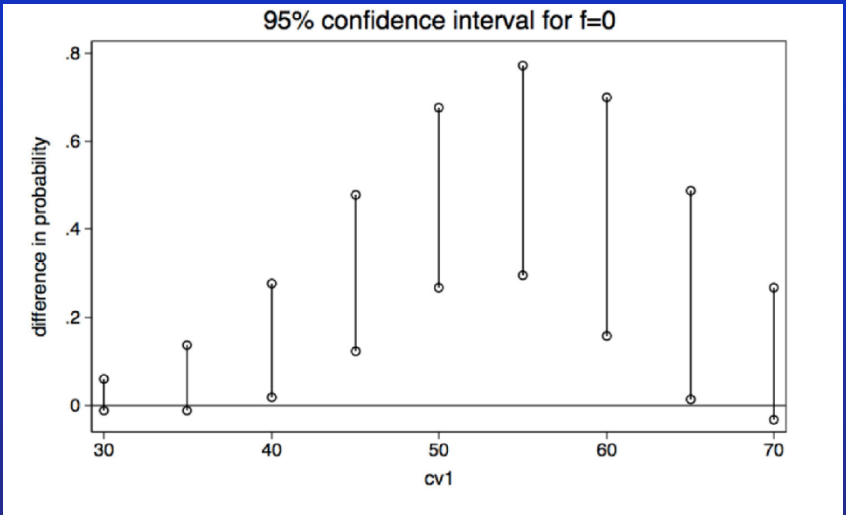

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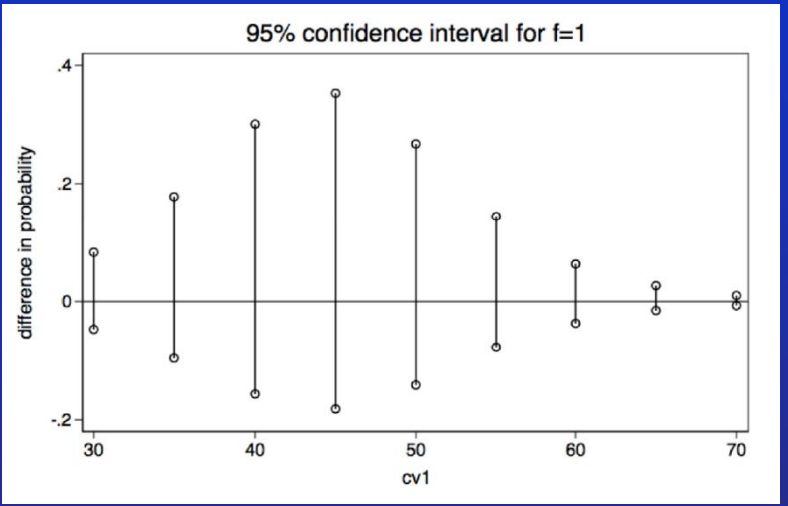

Figure B: effect of h on f=1 for all values of cv1

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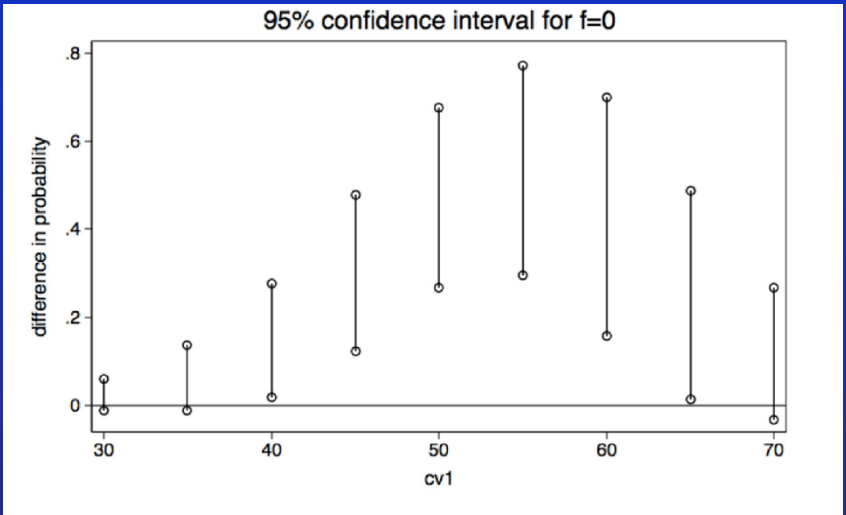

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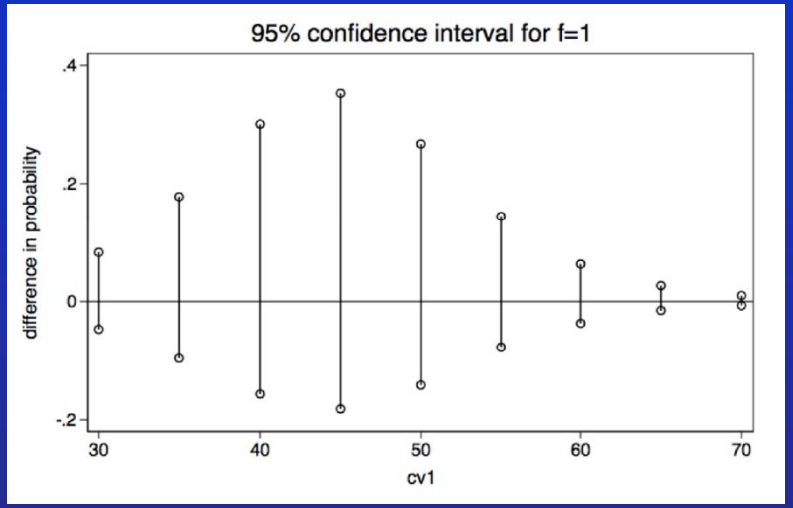

Figure B: effect of h on f=1 for all values of cv1

The magnitude of the interaction may change drastically at each value of the covariate *and* at each level of each interaction term.

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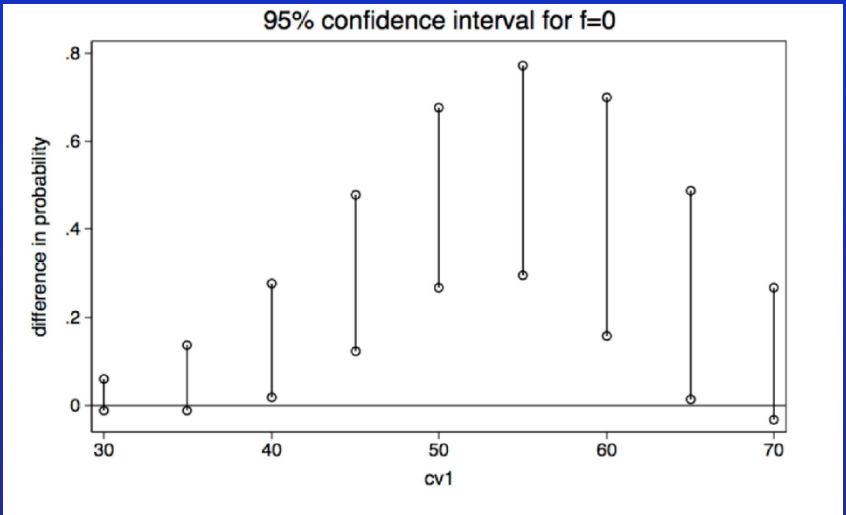

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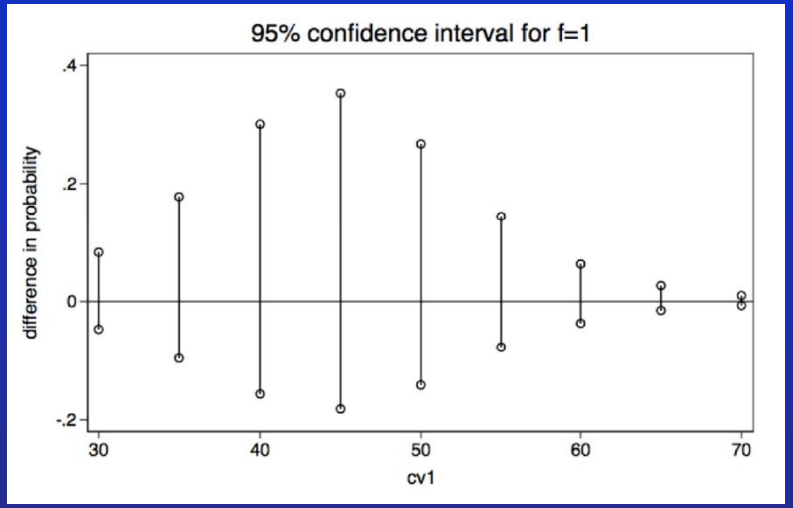

Figure B: effect of h on f=1 for all values of cv1

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Interpretation requires visual inspection of all levels of covariates and all levels of the interacting terms.

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