Dietary Protein 101

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(Pinch-hitting for Vernon Young who would have given this talk were he still alive)

Disclosure Statement

- I have consulted for, and sometimes received payment from, several governments, various NGOs, academic societies, disease-oriented associations & wide variety of food and drug companies. I am completely conflicted.
- Besides, I won't mention any commercial products and my only firm stance is "Maybe".

Why Proteins?
(Without Proteins Life Itself Would Be Impossible)

- **Essential Functions**
  - They are the body's structural components
  - As enzymes, they catalyze essentially all metabolic reactions
    - Only macronutrient class capable of doing so
  - As hormones, they serve as interorgan messengers
  - As carrier proteins, they serve as interorgan transporters
  - As antibodies, they constitute the adaptive immune system
- **Amount present is not related to importance**
  - TRH, GHRH, Glucagon, Insulin, et al.
- **Absorbed as amino acids or di-/tri-peptides**
  - Does enterocyte know if they are of animal, plant or of alternative protein origin?
- **There is no storage reservoir for amino acids**
  - Unlike carbohydrate and fat
  - Every A.A. has unique function(s); otherwise there would be only one.

No method can measure protein requirements in the free-living state

- **Nitrogen Balance**
  - Biased to the positive
    - Intake is routinely overestimated
    - Losses are invariably underestimated
  - Influenced by energy intake
  - Days of adaptation required to reach new steady state

- **Labelled Nitrogen or Amino Acid Kinetics**
  - Models are imperfect
    - One can’t prove a model, only disprove one.
  - Semi-Synthetic Diets; crystalline amino acid mixtures
  - Calculated requirements are greater than balance estimates
- **Reconciliations are hypotheses, not evidence**

The Problem of Non-Protein Nitrogen*

(Non-Bioavailability of Milk Urea N#)

Patient	Sex	Age (day)	Body weight (g)	Dose of di-^{15}N-urea (mg/kg)	^{15}N excreted (% of dose) As di-^{15}N-urea 0-8 hr	0-24 hr	0-48 hr	0-72 hr
1	M	60	5105	17.8	44.4	73.6	80.9	83.1
2	F	87	5690	17.1	37.3	67.0	73.6	75.3
3	M	147	8365	17.0	36.0	65.0	70.4	71.6
4	M	153	6605	17.5	46.7	77.0	82.9	84.4
5	M	222	7795	17.4	48.7	83.8	91.7	93.9
6	F	267	8135	17.6	51.1	77.1	84.5	86.8
7	F	286	7615	17.3	39.9	70.9	78.6	80.1
8	M	286	7555	17.2	50.3	76.6	86.0	88.4
Mean					44.3	73.9	81.1	83.0
SD					5.9	6.1	6.8	7.2

***Varies widely among foods, 5-10% of total nitrogen is common, but can be as high as 50%**

#Fomon, Matthews, Bier et al. *J. Pediatr*. 111:221, 1987

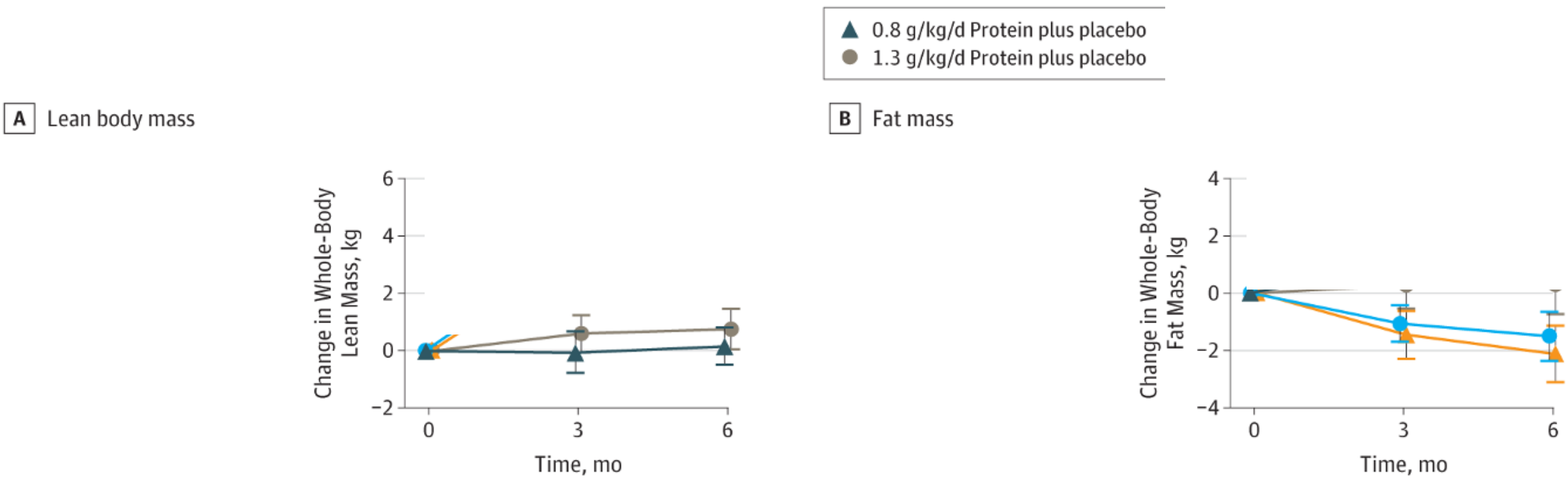
Dietary Protein Requirements Calculated from Obligatory Nitrogen Losses

	Historical (19th Century)	FAO/WHO/UNU 1981	Rand et al. 2003*	NAS/IOM/FNB 2002
Nitrogen Loss (mg/kg/d)	~100	54	105	
Protein Equivalent EAR		0.34 g/kg/d	0.65 g/kg/d	
Protein Equivalent RDA		0.44 g/kg/d	0.83 g/kg/d	
Protein EAR				0.66
Protein RDA				0.80

*235 subjects studied at three or more levels of dietary protein intake.
+2SD for RDI were measured by Rand et al.; not estimated as by FAO/WHO/UNU.

Rand, Pellett & Young. *AJCN* 77:109-127, 2003.
FAO/WHO/UNU. *World Health Organ Tech Rep Ser* 724:1–206, 1985.

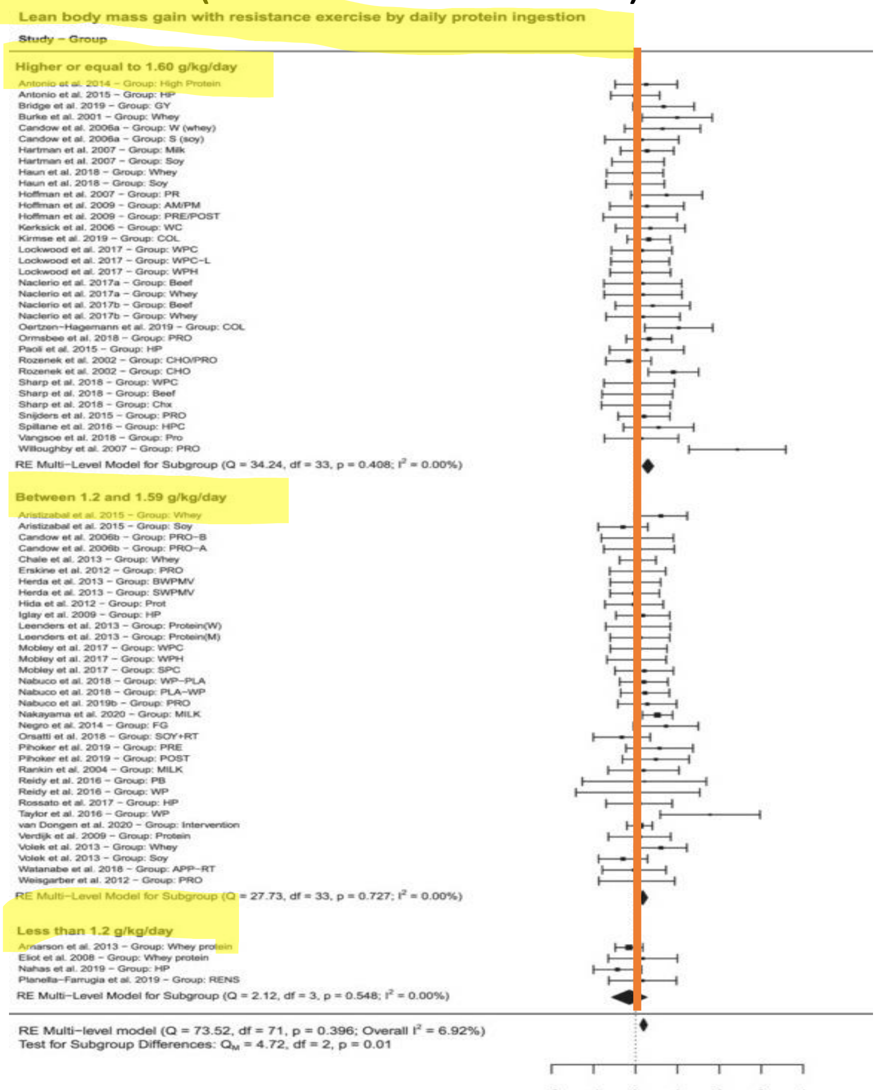
IS More Better? (Elderly)



Bhasin et al. Effect of protein intake on Lean Body Mass in functionally limited older men *JAMA Intern Med* 178:530-541, 2018.

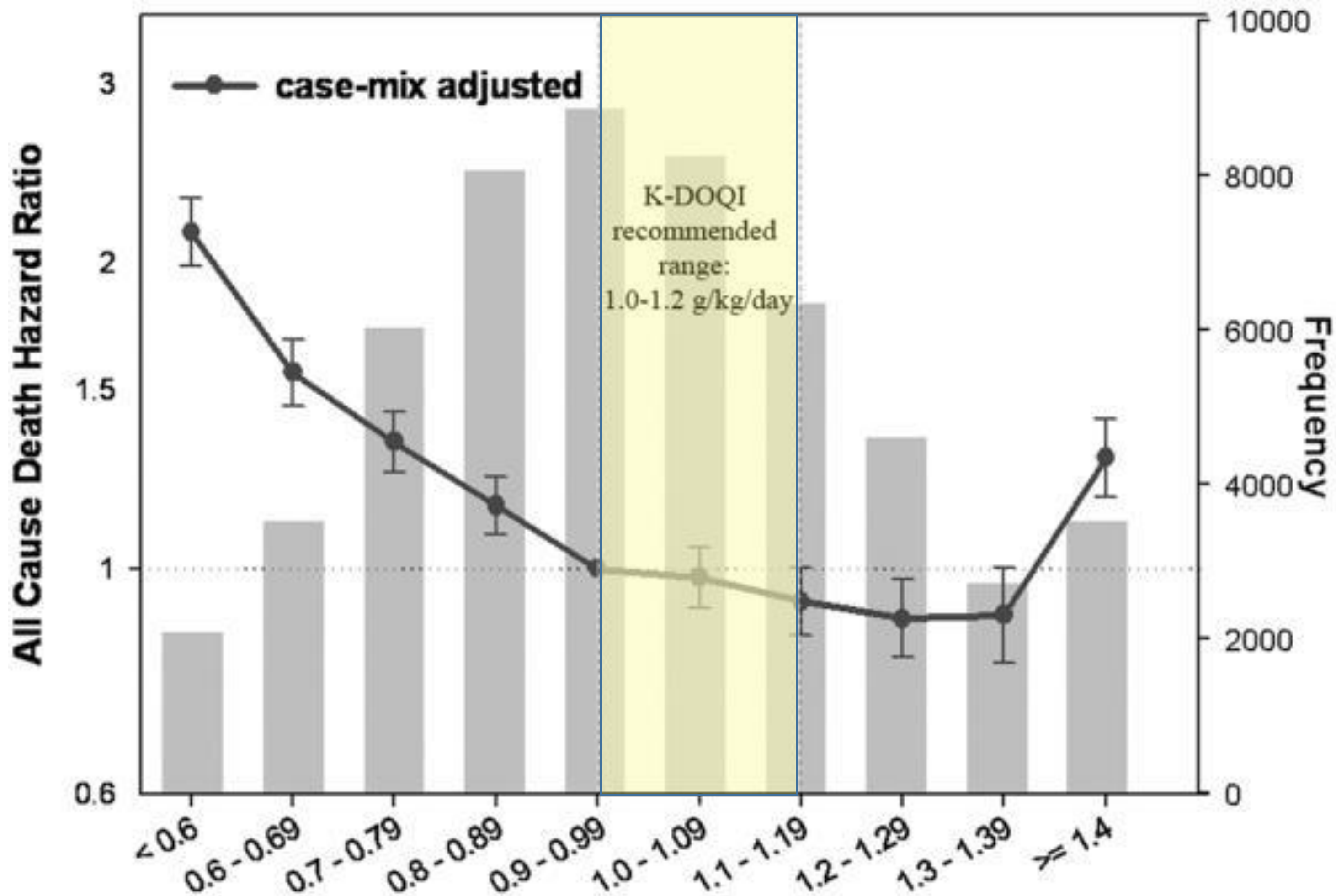
Is More Better?

(Resistance Exercise)



Nunes et al. *J of Cachexia, Sarcopenia and Muscle* 13:795-810. 2022

Is More Better?
(End-Stage Renal Disease)



Kovesdy et al. *Seminars in Dialysis* 23:353-358,2010

Incomplete Proteins and Amino Acid Competition

- Incomplete proteins are abundant
  - Plant proteins are the classical example
- Competition among certain amino acids for absorption from the GI tract surely exists
  - Large body of supporting literature
- These issues are potential considerations:
  - When protein types and overall supply are limited
  - When the host is compromised as in certain inborn errors of metabolism or gastrointestinal disease
  - When excess individual AA are taken as supplements
- In environments where protein availability is abundant, I know of no known issues related to protein amino acid content and/or amino acid competition that have been shown to impair human health.

Plant Amino Acid Digestibility (%)

[Original FAO Estimates Were 70%]

Mung Beans

IAA	MB	MB-^{13}C AA
Methionine	52.2 ± 7.2	48.7 ± 6.3
Phenylalanine	73.4 ± 6.3	74.6 ± 1.4
Threonine	42.5 ± 1.2	42.7 ± 3.2
Lysine	63.0 ± 5.4	69.3 ± 3.4
Leucine	67.5 ± 3.2	69.3 ± 5.0
Iso-leucine	75.8 ± 2.6	76.6 ± 5.0
Valine	67.8 ± 6.0	66.7 ± 5.1
Mean IAA	63.2 ± 1.5	64.0 ± 2.4

Sunflower Isolate

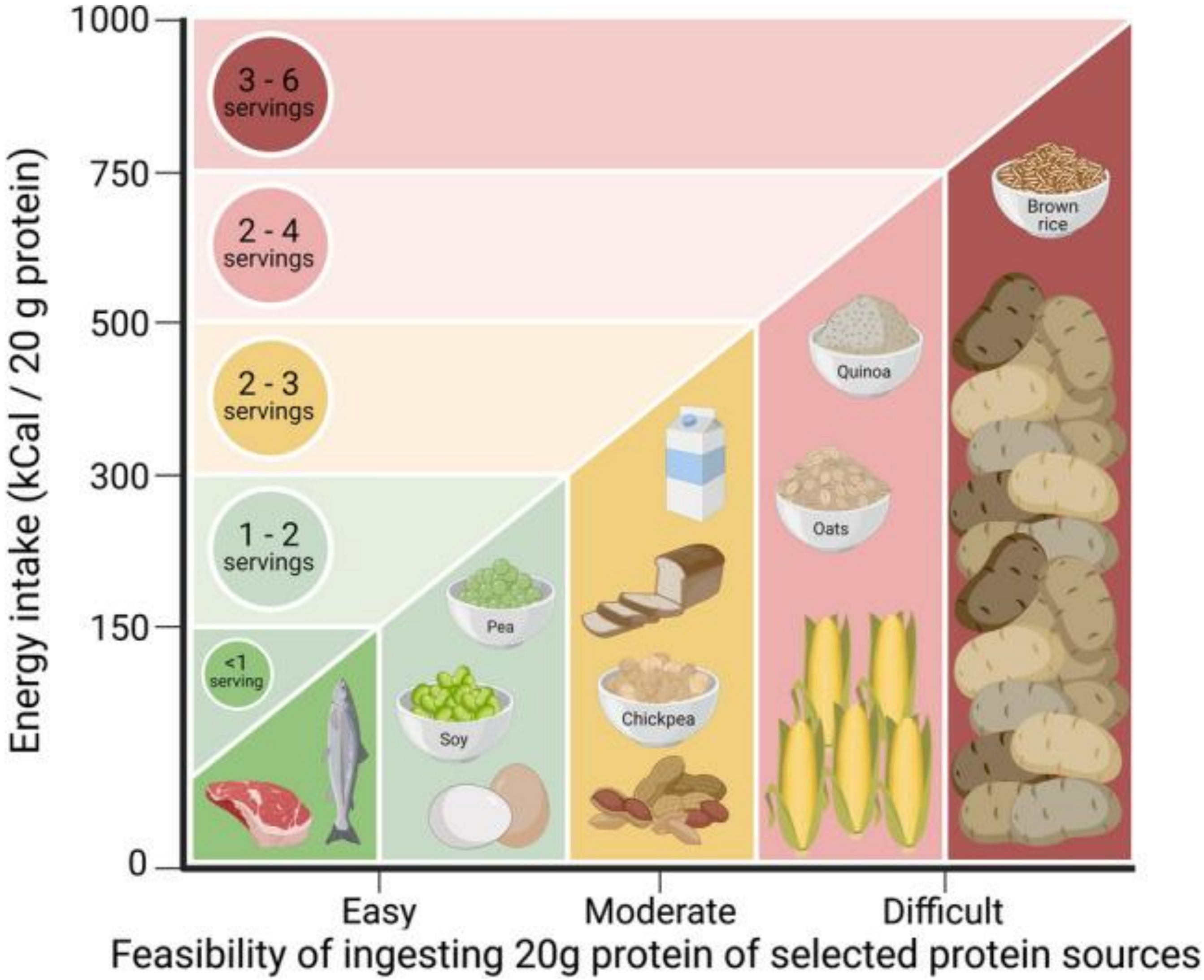
	SUN + Ch	SUN + P
IAA digestibility, %		
Isoleucine	87.7 ± 5.0	90.7 ± 6.0
Leucine	89.9 ± 4.5	92.7 ± 5.2
Lysine	86.4 ± 4.3	88.4 ± 4.8
Methionine	91.1 ± 5.8	95.4 ± 2.6
Phenylalanine	90.3 ± 4.9	92.6 ± 6.7
Threonine	85.8 ± 5.1	89.3 ± 5.5
Valine	88.3 ± 4.7	91.2 ± 6.1
Mean IAA	88.5 ± 5.0	91.5 ± 5.4
DAA digestibility, %		
Alanine	88.4 ± 4.5	91.0 ± 5.6
Glycine	68.3 ± 9.5	73.4 ± 10.0
Glx	92.2 ± 3.1	94.3 ± 3.8
Proline	81.4 ± 6.4	85.9 ± 6.6
Serine	82.1 ± 7.0	81.9 ± 7.1
Mean DAA	82.5 ± 10.6	85.4 ± 9.8
Mean, all AAs	85.2 ± 4.7	88.2 ± 5.6

Bandyopadhyay et al. *Adv Nutr* 13:1131-1143, 2022 and Tessier et al. *J Nutr* 152:698-706, 2022

Can one achieve protein adequacy from plant or alternative protein sources?

Confirmed Vegan

Satisfying Requirements with Plant Proteins (A Fundamental Constraint)



Pinckaers et al. *Sports Med* 51 (Suppl 1) S59-S74, 2021.

Reductionism

- **Confession:** I am a card-carrying reductionist.
- **Admission:** Reductionism will inform, but will not answer, the questions before us.
  - There are far too many confounding environmental exosome co-variates to control for
  - Propagated methodological noise and other uncertainties are greater than the precision required
- **Recommendation:** Outcome variables should include both a reliable estimate of LBM and an appropriate measurement of function (remember, water is LBM)

Closing Observation

- Nutrition Study Section 1978 - 1982
- Study Section members, me included, reviewed grants on the value of alternative protein sources
  - All related to protein availability in the developing world
  - Global sustainability was not a visible issue then
  - Insect protein grants were discussed
- Public adaptation has been slow since then.
- Human behavior is always the rate-limiting step.
- I look forward to the presentations and discussions to come later in this meeting.