Protein and Amino Acid Requirements in Pregnancy & Lactation: New Evidence Challenge Current Recommendations

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Outline

- Need for protein and amino acids during pregnancy and lactation
- Current recommendations
- Novel stable isotope based estimation of protein and amino acid needs in pregnancy
- New estimates of protein requirements in pregnancy within the context of overall dietary pattern
- Protein supplements during pregnancy – necessary/beneficial?
- Protein in the context of popular dieting trends
- Summary & Research next steps

- Dietary protein forms an essential component of a healthy diet in humans to support either:
  - growth + maintenance during stages of development
  - or maintenance alone during all other life-stages

Current Definition for Protein Requirements

- "*the lowest level of dietary protein intake that will balance the losses of nitrogen from the body, and thus maintain the body protein mass, in persons at energy balance with modest levels of physical activity, plus, in children or in pregnant or lactating women, the needs associated with the deposition of tissues or secretion of milk at rates consistent with good health*"

WHO/FAO/UNU 2007

Current Recommendations – Pregnancy & Lactation

	Estimated Average Requirement, EAR	Recommended Dietary Allowance, RDA
	g/kg/d	
Pregnancy (all stages)	0.88	1.1
Lactation (1-6 months)	1.05	1.3

- Based on factorial calculations

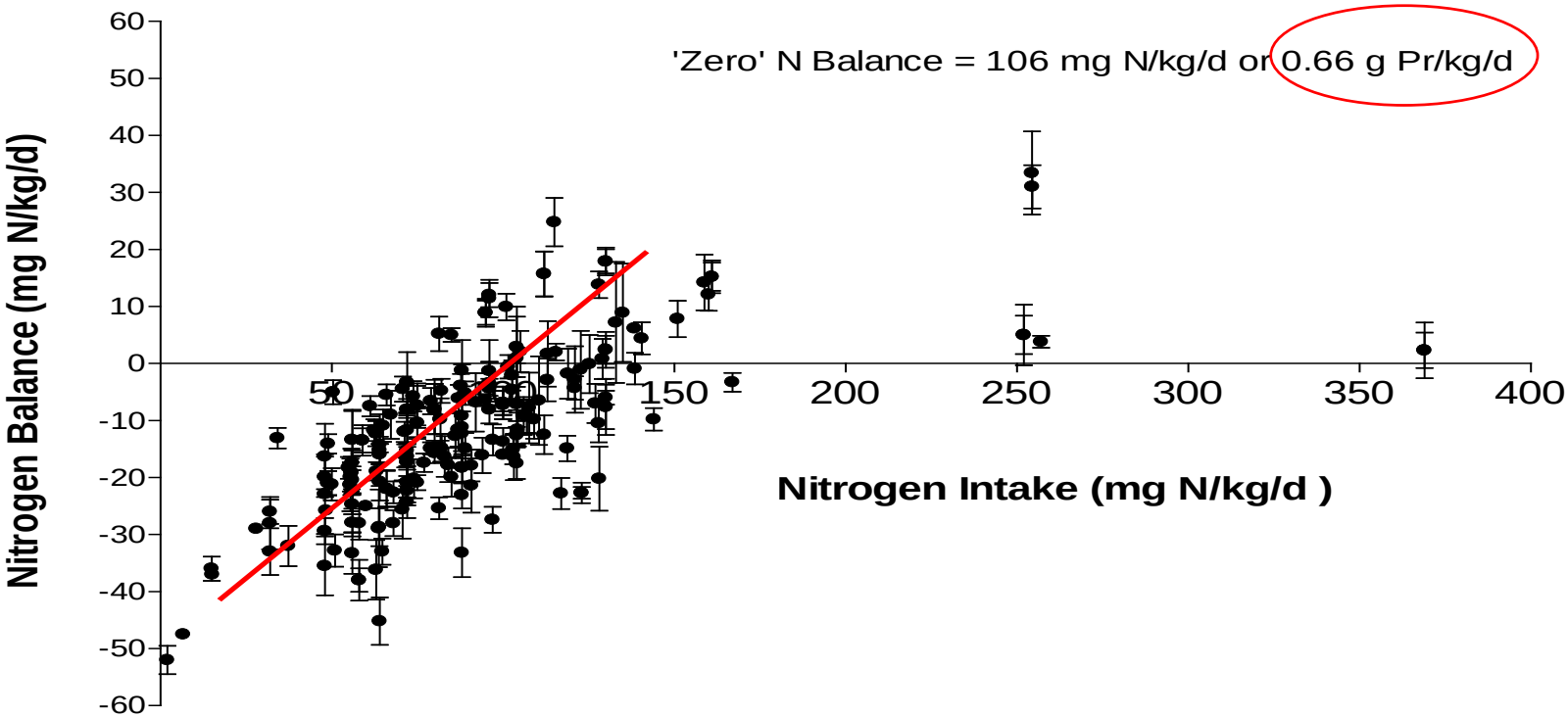
Dietary Reference Intakes (DRI) 2005

Factorial Estimations

	Estimated Average Requirement, EAR	Recommended Dietary Allowance, RDA
	g/kg/d	
Pregnancy (all stages)	0.22 + 0.66 = 0.88	1.1
	(Average tissue protein deposition * efficiency) + maintenance needs	EAR + 24%
Lactation (1-6 mo)	0.39 + 0.66 = 1.05	1.3
	(Average protein equivalent of human milk output * efficiency) + maintenance needs	EAR + 24%

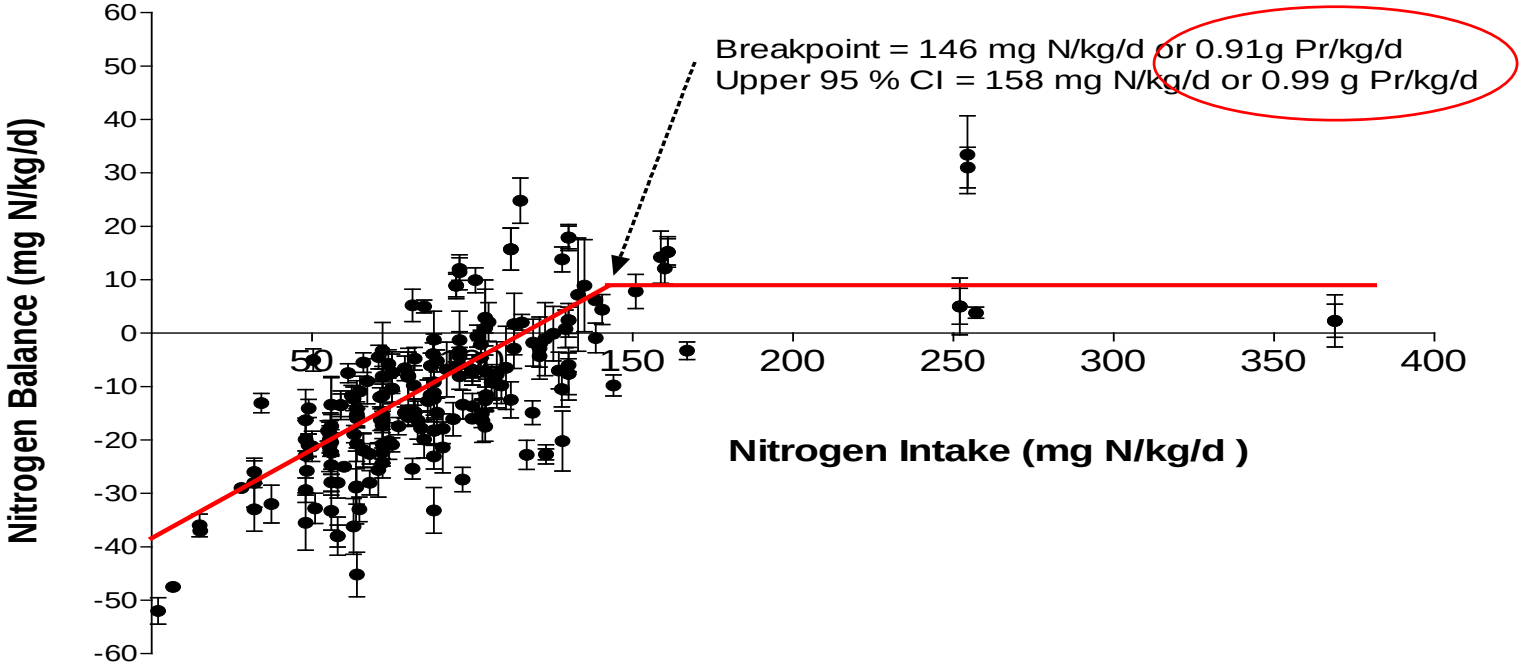
Dietary Reference Intakes (DRI) 2005

Maintenance needs - N Balance Studies in Young Men



Rand et al AJCN;73:109-27, 2003; Dietary Reference Intakes (DRI) 2005

Reanalysis of N Balance Studies in Young Men

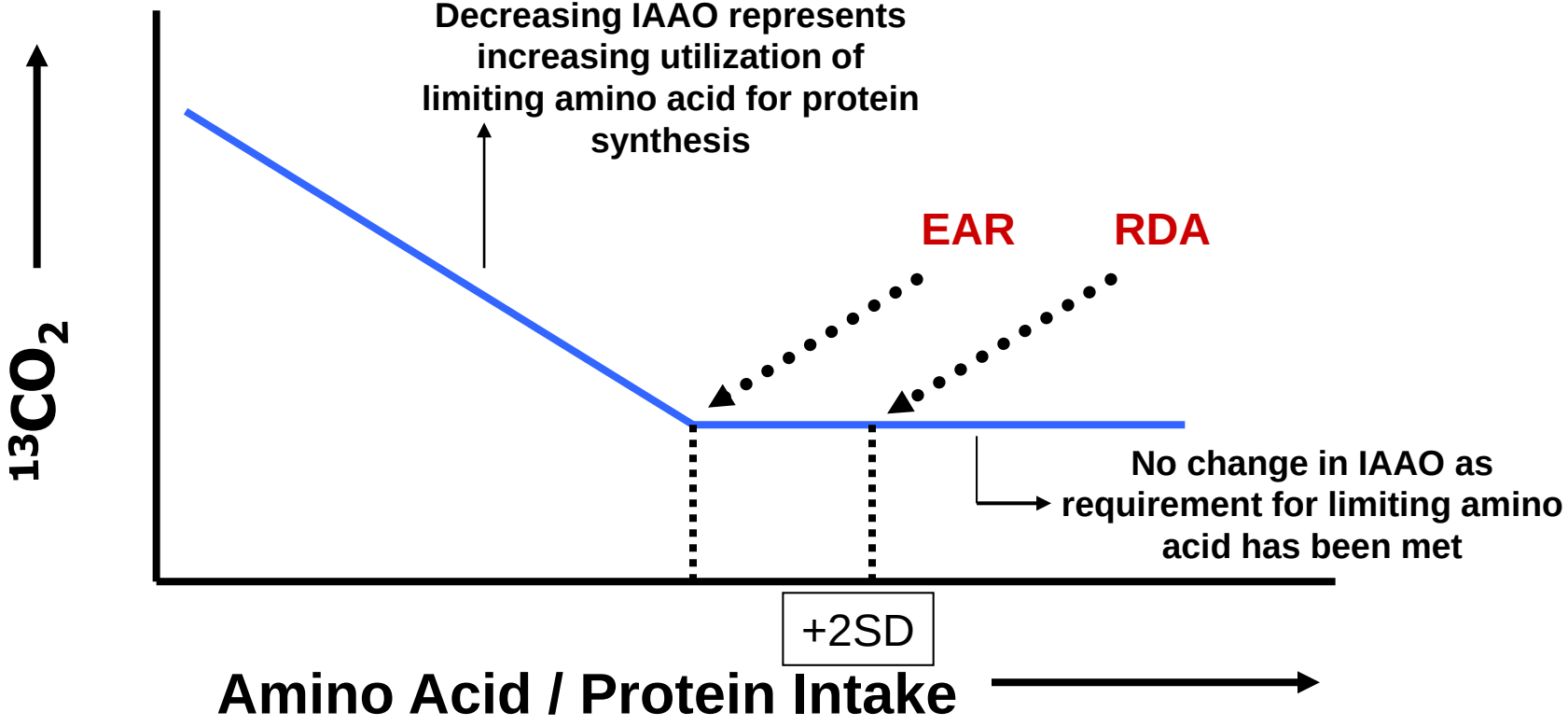


*Humayun, **Elango** et al AJCN;86:995-1012, 2007*

Key Quote from Dietary Reference Intakes 2005

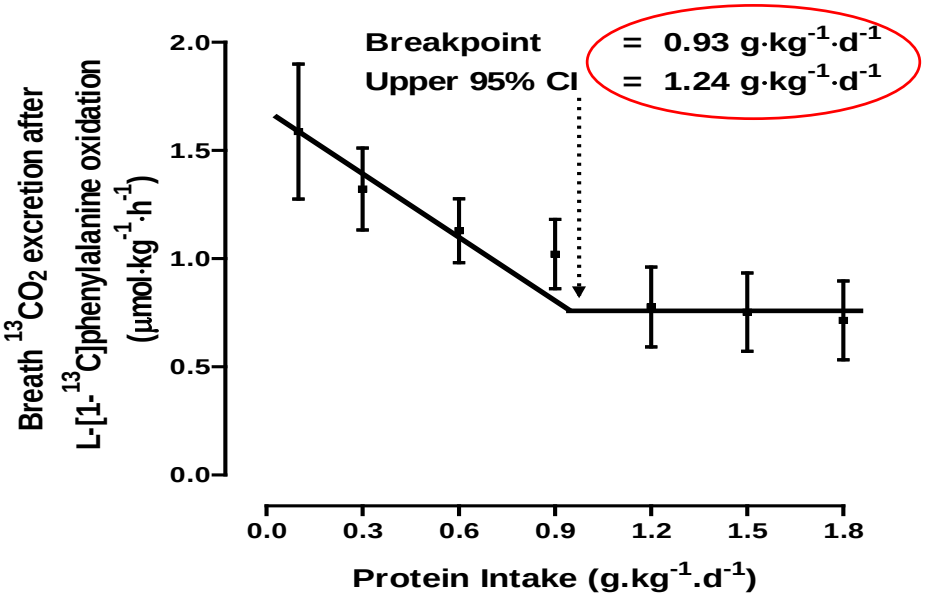
- “However, due to the shortcomings of the nitrogen balance method noted earlier, it is recommended that the use of nitrogen balance should no longer be regarded as the “gold standard” for the assessment of the adequacy of protein intake and that alternative means should be sought.”
  - DRI Macronutrients 2005, pg 643

Indicator Amino Acid Oxidation: Concept



Elango et al. J Nutr 138:243-246, 2008

Protein Requirements – Adult Men



Current DRI (2005)

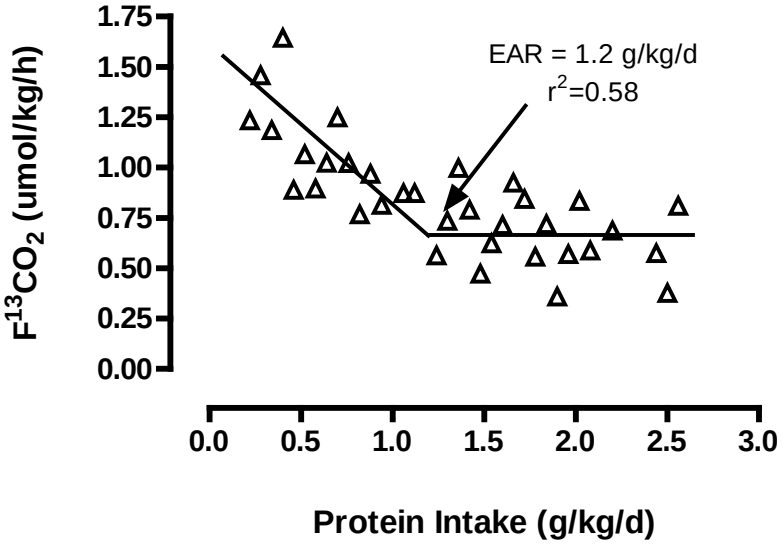
EAR = 0.66 g/kg/d
RDA = 0.8 g/kg/d

Current recommendations are ~30% underestimated

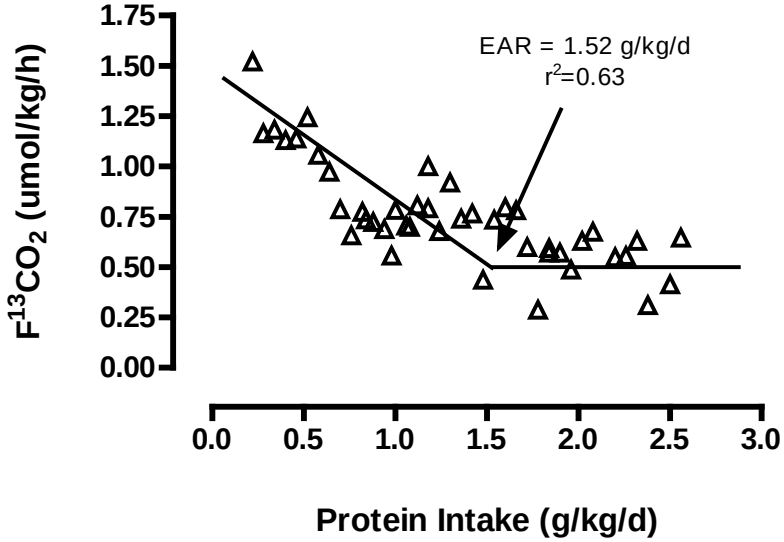
*Humayun, **Elango,** et al Am J Clin Nutr;86:995-1012, 2007*

Protein Requirements in Pregnancy

- *11-20 wk Gestation*



- *30-38 wk Gestation*



Requirements are ~27% higher during later stages of pregnancy

*Stephens, **Elango** et al, J Nutr. 2015;145:73-8*

Summary - Protein Requirements - Pregnancy

	DRI 2005	IAAO Early Pregnancy	IAAO Late Pregnancy	IAAO (% calories)
	g/kg/d			
EAR	0.88	1.2	1.5	~13 – 15%
RDA	1.1	1.6	1.7	~15 - 17%

Current DRI (2005)
Protein % kcal

Range ~6-8%

Thus IAAO estimates
Within Acceptable Macronutrient Distribution Ranges (AMDR)

- Current recommendations are underestimates

*Stephens, **Elango** et al J Nutr. 2015;145:73-8.*

Points to Note

- DRI estimates are a minimum, and does not represent a ‘ceiling’ or ‘maximum’ recommendation

- Protein recommendations are provided based on ‘high quality’ protein food sources

Protein intakes in Vancouver, Canada

n = 212 Healthy pregnant women

	16 wk	**36wk**
	Median (25th, 75th percentiles)	
g/kg/d	1.5 (1.18, 1.79)	1.3 (1.04, 1.60)
% of energy	17.1 (15.2, 18.6)	17.3 (15.2, 19.3)
g/d	99.4 (85.3, 119.4)	100.4 (82.9, 119.4

Women	**Median (25th, 75th percentiles)**
Prepregnancy weight (kg)	63.2 (56.8, 70.5)
Height (cm)	165.1 (160.0, 170.2)
Prepregnancy BMI (kg/m2)	23.0 (21.0, 25.3)
16-Wk weight gain (kg)	4.3 (2.3, 6.1)
36-Wk weight gain (kg)	14.4 (11.6, 17.3)
Infant weight (g)	3457 (3170, 3772)

*Stephens, **Elango** et al Nutr Res 2014;34:569-576*

Dietary Intake / Interventions in Pregnancy - Controversial

2014 Editorials

- High-protein diets during pregnancy: healthy or harmful for offspring? *Blumfield & Collins, AJCN 2014;100:993-5*
- Eating for two? The unresolved question of optimal diet in pregnancy. *Robinson et al, AJCN 2014;100:1220-1*

Articles

- Maternal protein intake during pregnancy and offspring overweight 20y later. *Maslova et al, AJCN 2014;100:1139-48*
  - 1:1g substitution of animal protein for CHO increased risk of BMI>25
  - But, observational study, no measure of body composition, and no data on offspring dietary and lifestyle
- Effects of dietary interventions on neonatal and infant outcomes: a systematic review and meta-analysis. *Gresham et al, AJCN 2014;100:1298-321*
  - Dietary macronutrient interventions based on food and fortified food increased infant size
  - But, interventions varied significantly across studies

Protein Interventions in Pregnancy – Controversy Partly Explained

Protein Supplementation and Energy

- Interventions vary in macronutrient balance

- **Balanced protein/energy supplementation**
  - protein provides <25% of total energy content

- **High protein**
  - protein provides ≥ 25% of the total energy content

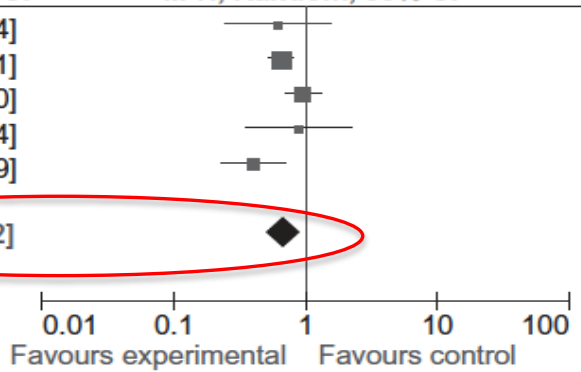
- **Isocaloric protein supplementation**
  - protein replaces an equal quantity of non-protein energy

Imdad and Bhutta, BMC Public Health 2011;11:S17

Effect of Balanced Protein-Energy Supplementation and Low Birth Weight

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Blackwell 1973[31]	7	143	11	138	8.5%	0.61 [0.25, 1.54]
Ceesay 1997[35]	112	1010	176	1037	35.8%	0.65 [0.52, 0.81]
Huybregts 2009[40]	67	523	67	497	29.7%	0.95 [0.69, 1.30]
Mardones-Santander 1988[23]	24	391	5	72	8.3%	0.88 [0.35, 2.24]
Prentice 1987[38]	16	200	37	185	17.6%	0.40 [0.23, 0.69]
Total (95% CI)		2267		1929	100.0%	0.68 [0.51, 0.92]
Total events	226		296			

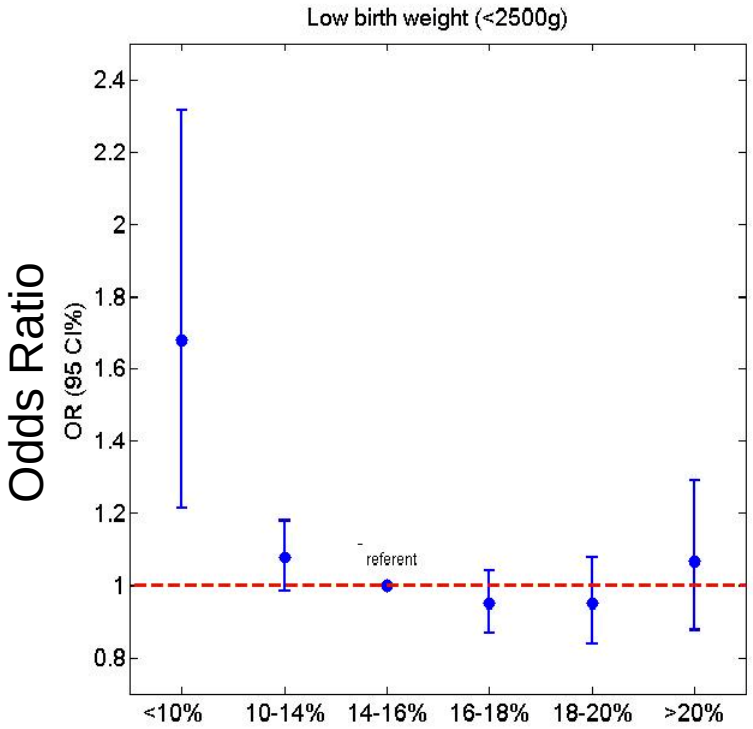
Heterogeneity: Tau² = 0.05; Chi² = 8.26, df = 4 (P = 0.08); I² = 52%
Test for overall effect: Z = 2.51 (P = 0.01)



- Balanced protein-energy supplementation resulted in a 32% reduction in low birthweight prevalence

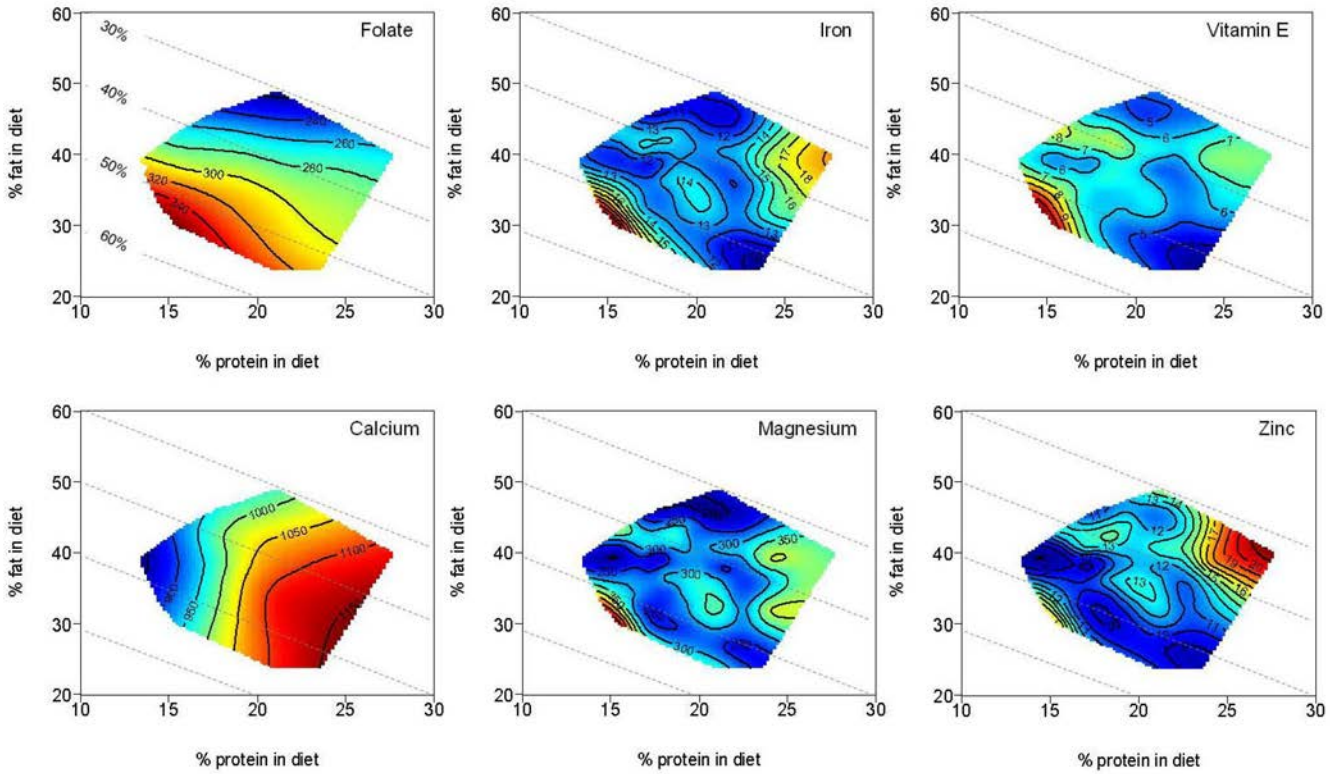
Imdad and Bhutta, Paediatr Perinat Epidemiol 2012;26:178-190

Protein Supplements in Pregnancy



(Olsen SF et al 2012, Danish National Birth (DNBC) and the Norwegian Mother-Child (MoBa) Cohorts)

- **Gambia Trial:** 22 g protein and 1017 kcal, starting at 20-24wks, resulted in 39-42% reduction in LBW
- ~8% of energy
- *Ceesay et al: Effects on birth weight and perinatal mortality of maternal dietary supplements in rural Gambia: 5 year randomised controlled trial. BMJ 1997*
- **New York Trial:** 40 g protein and 470 kcal, small, non-significantly higher weight gain, and a higher, non-significant increase in neonatal death, and no difference in fetal growth
- ~34% of energy
- *Rush et al: A randomized controlled trial of prenatal nutritional supplementation in New York City. Pediatrics 1980; 65: 683-697*



Women and Their Children's Health (WATCH) Study

Right-angled mixture triangles

-high micronutrient intakes in the red shading

Results suggest a **moderate protein intake** may support pregnant women to consume the largest variety of nutrients across all food groups.

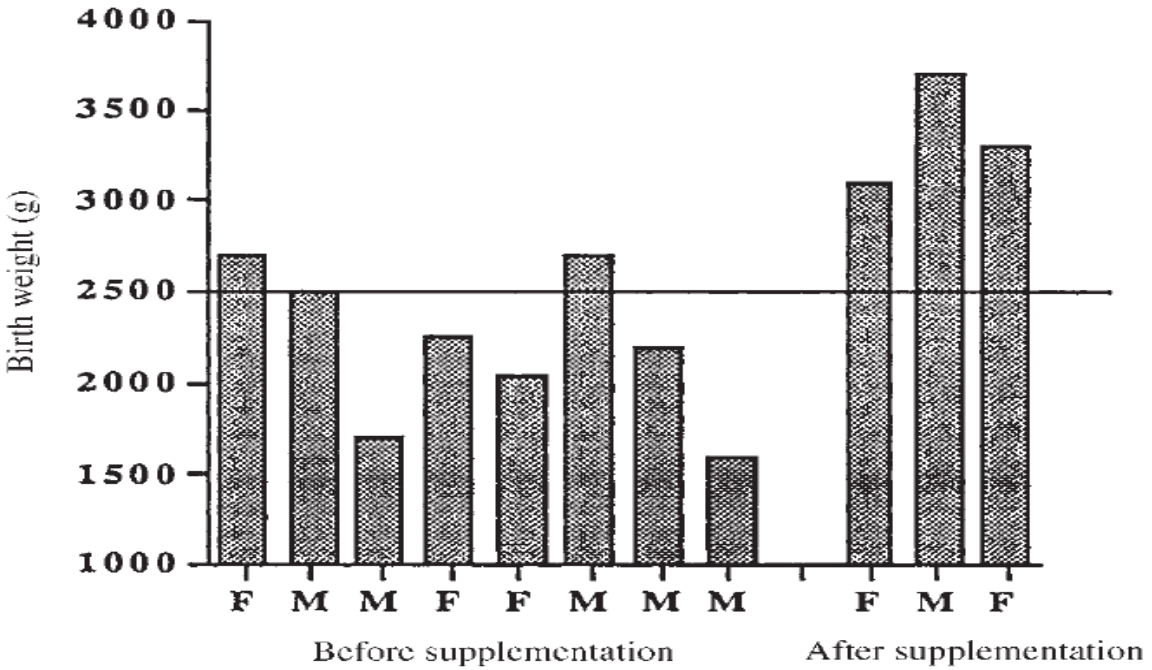
The association between the macronutrient content of maternal diet and the adequacy of micronutrients during pregnancy in the Women and Their Children's Health (WATCH) study. Blumfiled et al 2012; Nutrients 4(12):1958-76.

Role of Protein in Birth Weight

Montreal Diet Dispensary (1963 – 72)

Food supplements added 35g protein and ~525kcal/d

- Nutrition counseling and food supplements to women below poverty level
- **Additional milk, eggs and oranges**
- Case of a 29y woman who had 11 children
- 8 before being part of program
- 3 after enrolling
- All 3 children after supplementation were healthy and >3kg at birth



Agnes C. Higgins, JADA,1989, 89:1097–1103

King JC, Am J Clin Nutr 2000; 71:1218S-25S

Body Protein Needs are for Amino Acids

Essential
Lysine, Methionine, Threonine
Tryptophan, Phenylalanine, Histidine
Leucine, Isoleucine, Valine
Conditionally-Essential
Tyrosine, Cysteine, Arginine
Glycine, Proline, Glutamine
Non-Essential
Alanine, Asparagine, Serine
Aspartate, Glutamate

- Nutritional importance of protein is because of their constituent 20 amino acids
- Dietary amino acids be considered as individual nutrients (FAO/WHO 2011)

Protein Quality

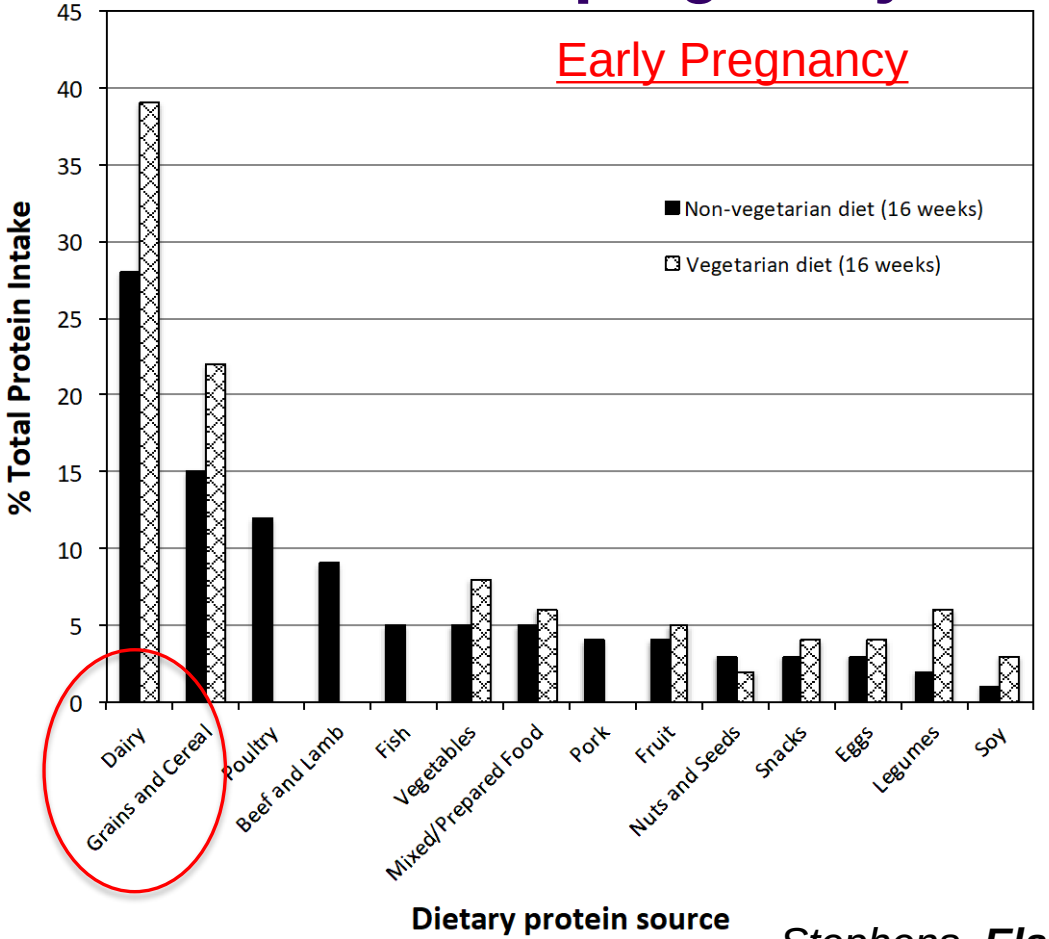
- Not all protein sources are equal

Protein Source	Lysine	Methionine	Threonine
mg/g protein			
Milk	77	25	44
Egg	72	30	44
Beef	83	26	40
Soy	67	14	44
Wheat	28	16	29

- Balance of essential/nonessential amino acids

Elango R *et al. Br J Nutr 2012;108:S306-14.*

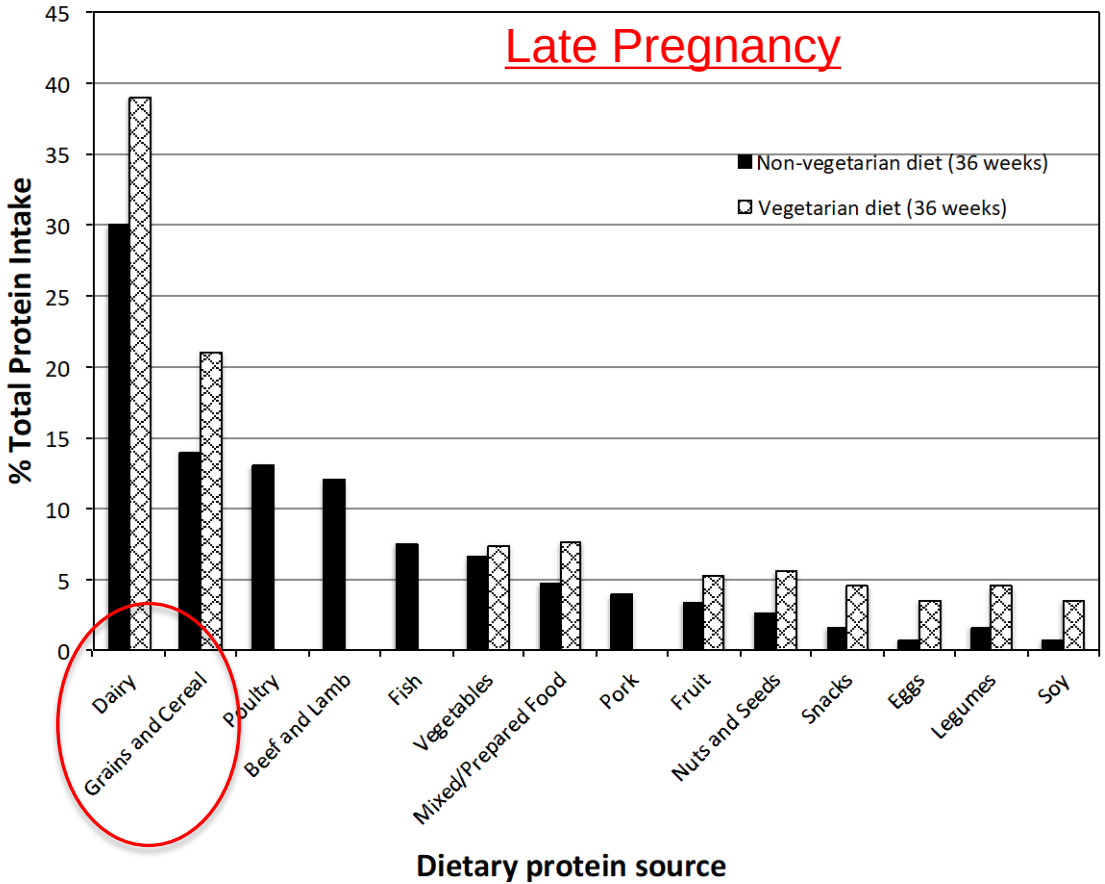
Protein sources in pregnancy – Vancouver, Canada



Dairy as primary source

*Stephens, **Elango** et al Nutr Res 2014;34:569-576*

Protein sources in pregnancy - Canada



Dairy as primary source

*Stephens, **Elango** et al Nutr Res 2014;34:569-576*

Pregnancy Protein needs vs Amino Acid needs

Nutrient	Non-Pregnant Needs	Early Stage Pregnancy	Late Stage Pregnancy	Reference
Protein (g/kg/d)	0.9	1.2	1.52	Stephens et al, J Nutr;145:73-8, 2015
Lysine (mg/kg/d)	36	37	50	Payne et al, J Nutr;148:94–99, 2018
Phenylalanine (mg/kg/d)	9	15	21	Ennis et al, Am J Clin Nutr 2019

Not proportional – While protein needs are increased early, not all amino acid needs are simultaneously increased

Popular Diets and Pregnancy

- Plant-based diets
  - While this is hugely popular right now, it is unknown what impact products that are processed, such as Beyond Meat®, has on human pregnancy (because protein quality may not be sufficient)

- Vegan/Vegetarian diets
  - Vegan–vegetarian diets in pregnancy: danger or panacea? A systematic narrative review, BJOG 2015 (***Piccoli GB et al***)
  - Is a vegetarian diet safe to follow during pregnancy? A systematic review andmeta-analysis of observational studies, Critical Reviews In Food Science And Nutrition 2019 (***Tan C et al***)
  - Both had few observational studies to analyze (~19 studies), with large heterogeneity, and no conclusive evidence for harm/good

Popular Diets and Pregnancy

- Keto Diet
  - Very popular now, however origins of the diet are for seizure management
  - Has been beneficial for pregnant mothers who suffer from seizures
  - But very high fat, low carbohydrates and **moderate-high protein**, is very unnatural for pregnancy
  - Glucose and amino acids are the primary fuel for fetus
- The ketogenic diet in disease and development, Int J of Develop Neuroscience 68 (2018) 53–58 (***Barry D et al***)

- Position of the Academy of Nutrition and Dietetics: Nutrition and Lifestyle for a Healthy Pregnancy Outcome
  - Journal of the Academy of Nutrition and Dietetics July 2014 Volume 114 No. 7
  - No position statement on ‘protein’ or on any ‘popular diets’ during pregnancy

Summary

- Maternal protein intake recommendations by DRI (2005) are underestimates
- Protein in the diet must be balanced considering:
  - % of calories
  - Mother's pre-pregnancy nutritional status
- Protein quality matters
  - Within the context of overall dietary pattern
- Individual amino acid needs may increase in some vulnerable women, and must be supplied from food sources
- *Protein needs in lactation* – needs to be determined using state-of-the-art stable isotope techniques

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