Nutrition in Human Pregnancy: New and Old Discoveries

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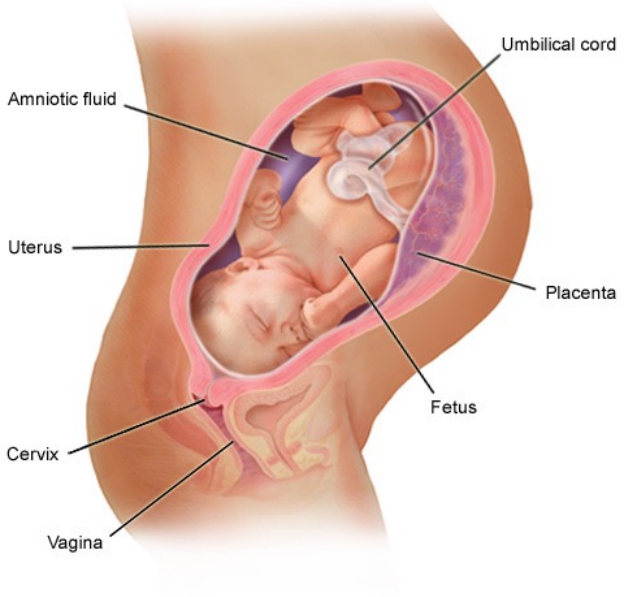
Outline

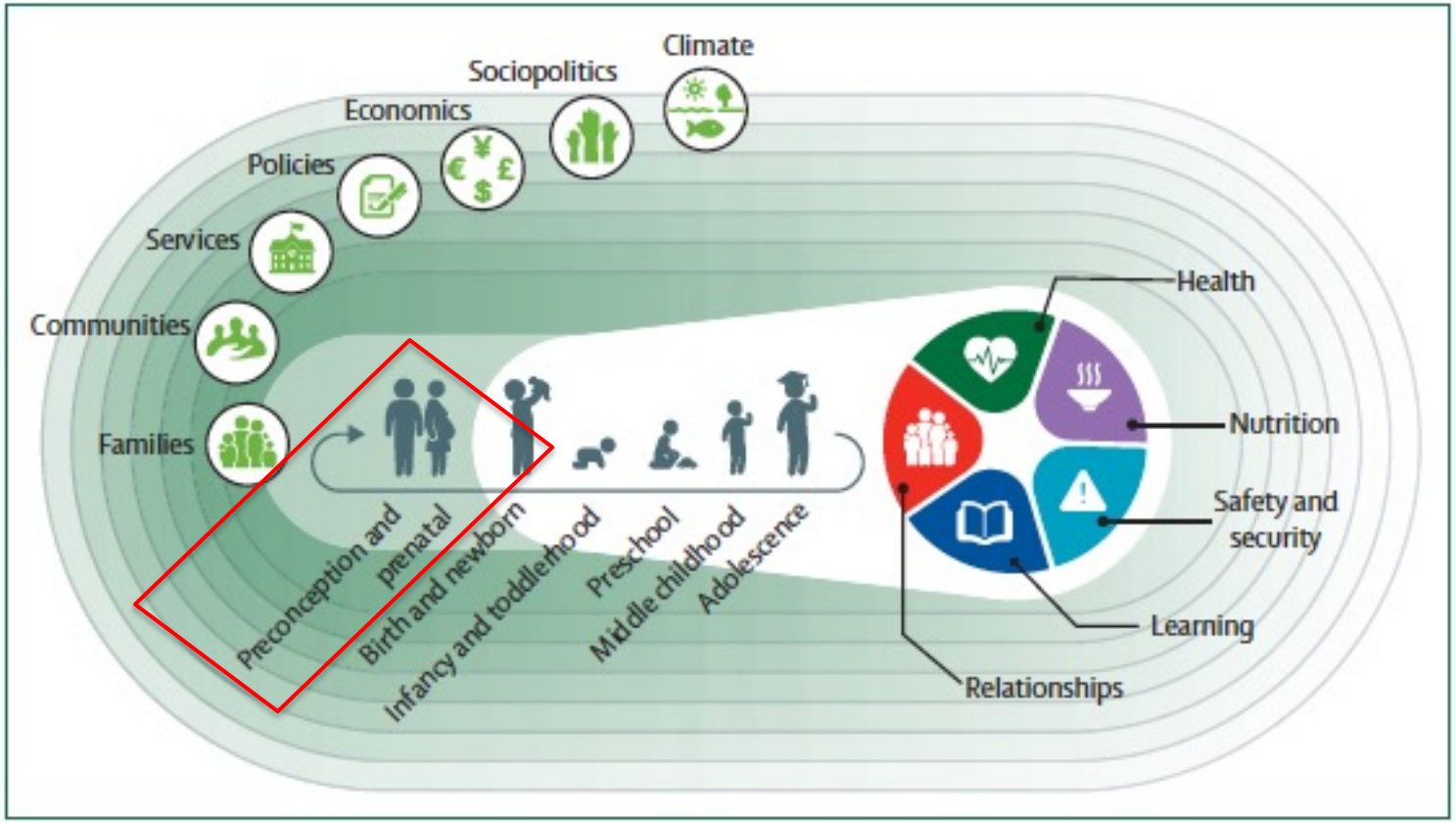
- Understand the importance of nutrition as the basis of life
- Understand how nutrient intake recommendations, and dietary guidelines in pregnancy are set
- Understand the role of macronutrients, specifically protein and interaction with energy
- Understand key micronutrients in pregnancy
- Understand whether nutrients can play a role in pregnancy disorders, with pre-eclampsia as an example

Quote: "You are what you eat"

Perhaps: "You are what your mother ate"



Nurturing Care Framework from Preconception through Adolescence

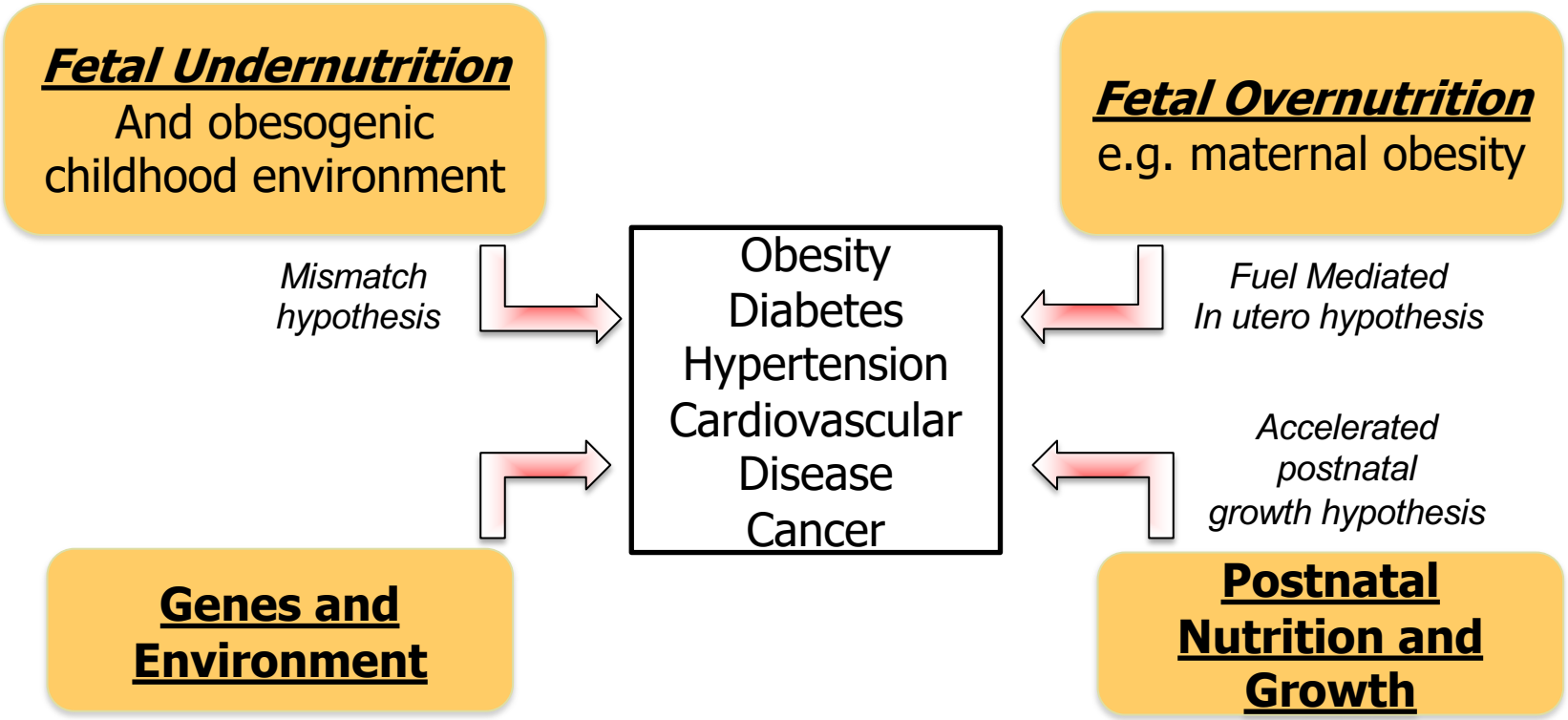


Prenatal care at the heart of all 'Maternal and child Nutrition' Programs

Impacts can be wide ranging

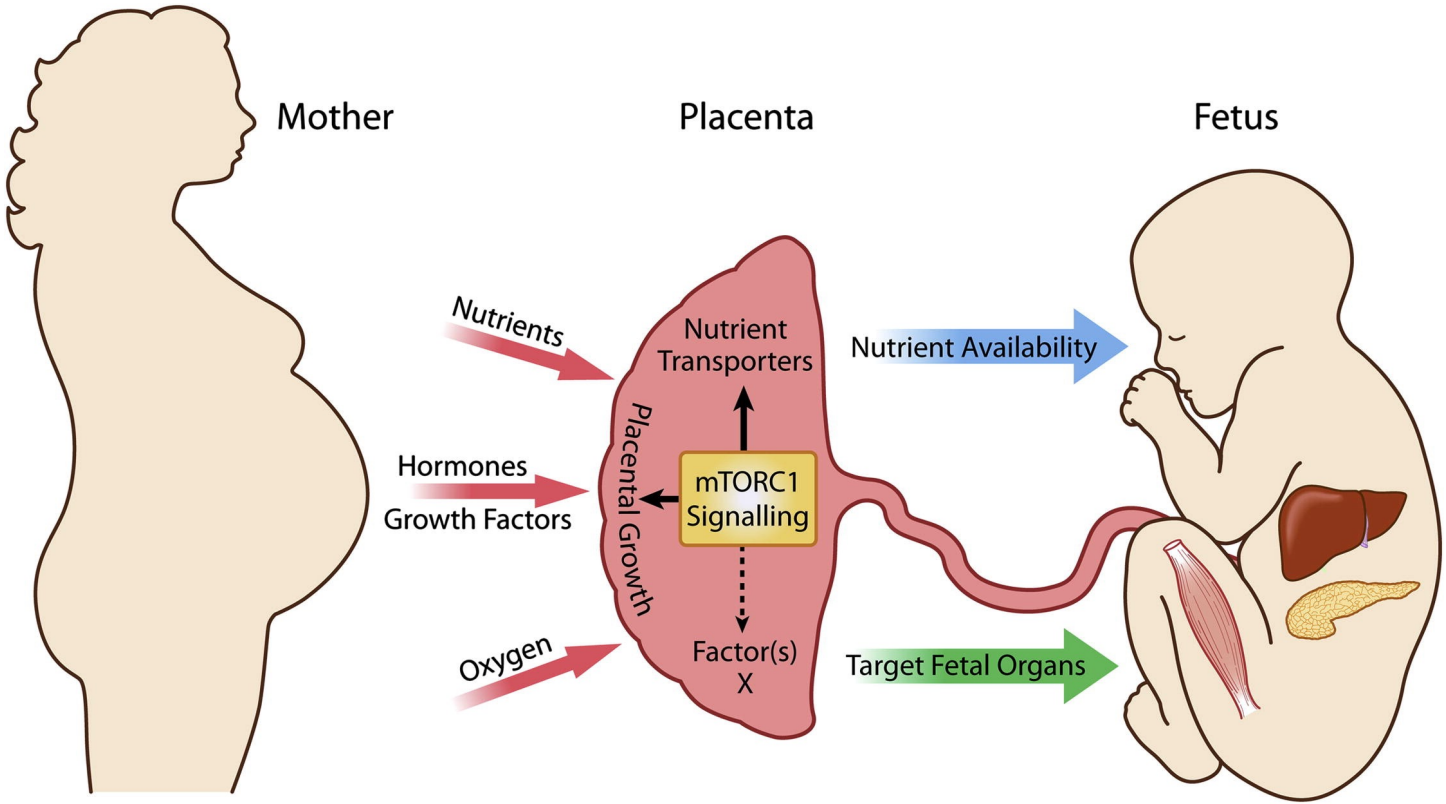
Black MM, et al. BMJ Global Health 2021

Developmental Origins of Health and Disease [DOHAD]



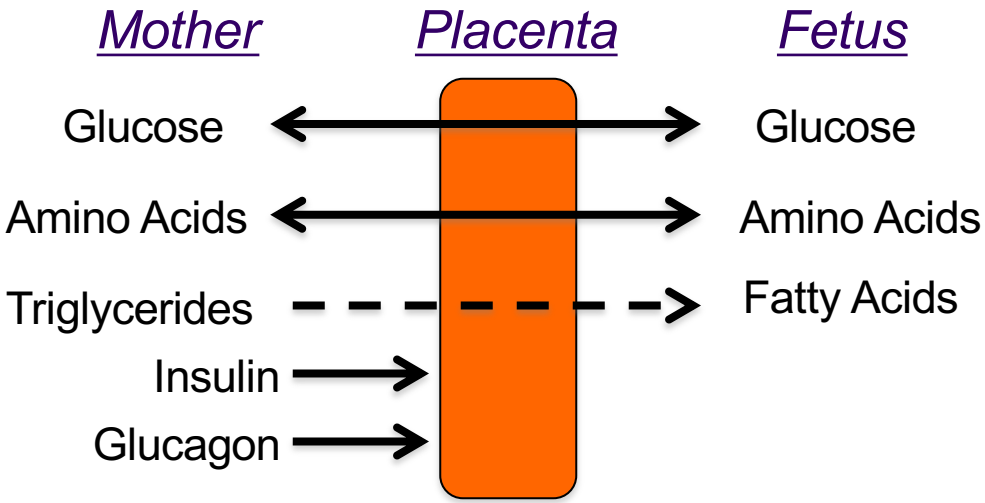
Koletzko et al, Ann Nutr Metab 2017;70:161–169

Maternal – Fetal Relationship, A Triad



The placenta, as a key regulator of nutrient transport, interconversion, and metabolism

Maternal – Fetal Nutrition



Canada's Food Guide 2019

https://food-guide.canada.ca/en/

Canada's food guide

Healthy eating when pregnant and breastfeeding

https://food-guide.canada.ca/en/tips-for-healthy-eating/pregnant-breastfeeding/#section-3

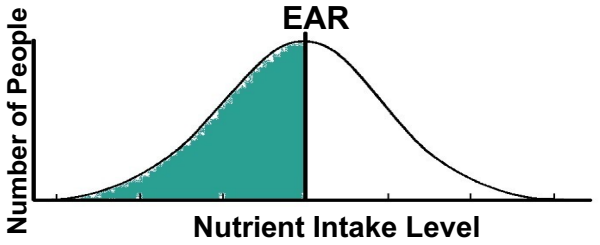
On this page

1) Concerns are that the guidelines are not specific enough
2) Not adaptable for all individuals
3) Does not provide much support to clinical care and management

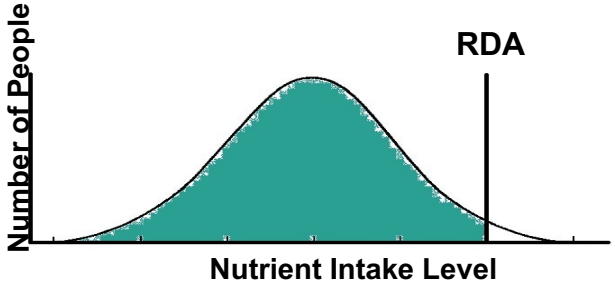
Recommendations for Nutrient Intake in Humans

Dietary Reference Intakes (DRI) – set by National Academies of Science, Engineering and Medicine

- Estimated Average Requirement (EAR) = meets needs for 50% of population



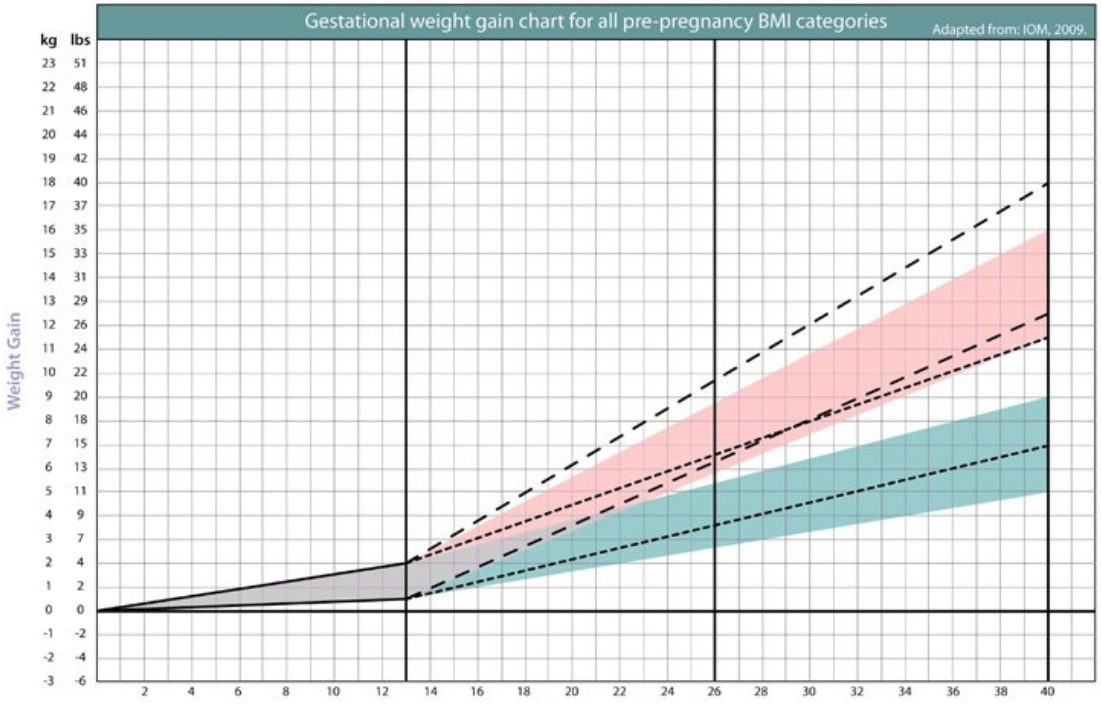
- Recommended Dietary Allowance (RDA) = meets needs of 97.5% of population



WHO/FAO provides global nutrient intake recommendations as ‘Average’ and ‘Safe’

Dietary Reference Intakes (DRI) 2005; FAO/WHO/UNU 2007

National Academies & Health Canada Guidelines – Gestational Weight Gain



Legend	Pre-pregnancy BMI	Recommended range of total weight gain
— — — — — —	< 18.5	12.5 – 18 kg (28 – 40 lbs)
	18.5 – 24.9	11.5 – 16 kg (25 – 35 lbs)
- - - - - - - - - - - -	25.0 – 29.9	7 – 11.5 kg (15 – 25 lbs)
	≥ 30	5 – 9 kg (11 – 20 lbs)

- *Rate of gestational weight gain (GWG), is dependent on pre-pregnancy body status*
- *GWG shown to be principal determinant in neonatal birth outcome*
- *Understood that BMI as a form of classification has flaws*
- *However, the relative rate of GWG is a powerful tool for objective week-to-week assessment*

https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/healthy-weights/prenatal-guidelines-professionals-gestational-weight-gain.html

Suboptimal gestational weight gain and neonatal outcomes in low and middle income countries: individual participant data meta-analysis

Nandita Perumal,[1,2] Dongqing Wang,[3] Anne Marie Darling,[2] Enju Liu,[4,5] Molin Wang,[6,7] Tahmeed Ahmed,[8] Parul Christian,[9] Kathryn G Dewey,[10] Gilberto Kac,[11] Stephen H Kennedy,[12] Vishak Subramoney,[13] Brittany Briggs,[14] Wafaie W Fawzi,[2,6,15] on behalf of the GWG Pooling Project Consortium

BMJ 2023;382:e072249

WHAT THIS STUDY ADDS

Suboptimal weight gain (inadequate or excessive) was associated with an increased risk of low birthweight, small for gestational age, large for gestational age, macrosomia, low head circumference, and short for gestational age at birth

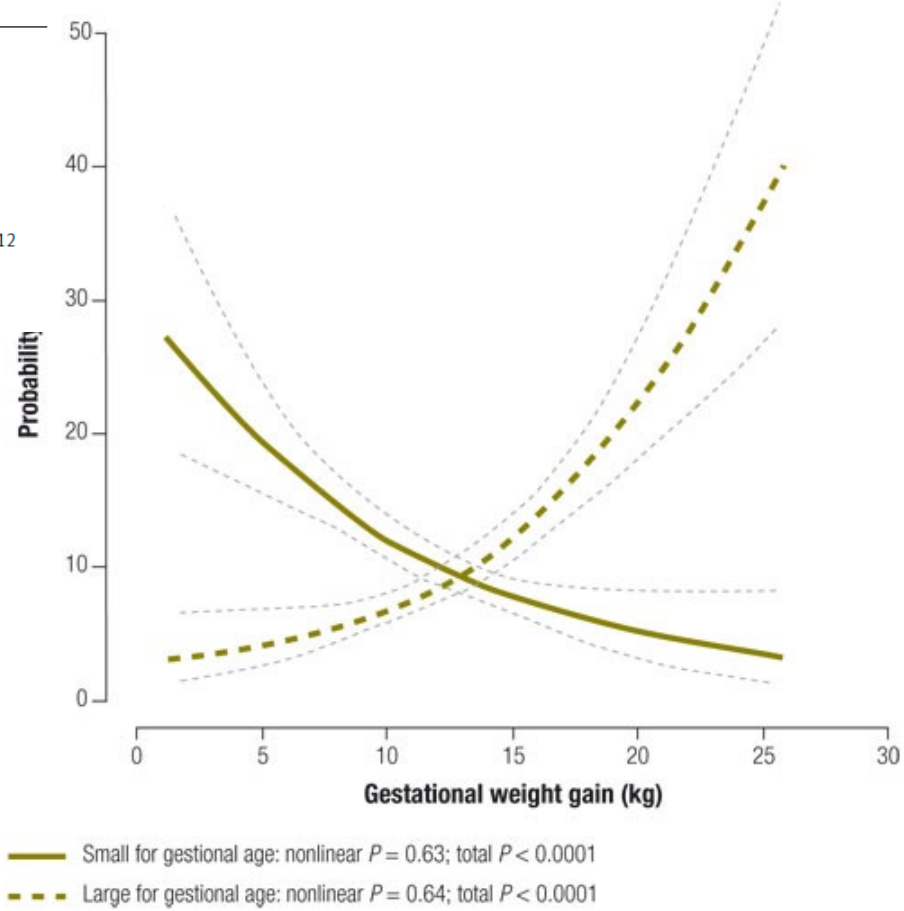
Women who were underweight, overweight or had obesity had a higher risk of adverse neonatal outcomes associated with suboptimal GWG compared with women of normal weight

Adolescent women younger than 20 years had a higher risk of some adverse neonatal outcomes associated with suboptimal GWG compared with women aged 20-29 years

53 Studies from 24 different countries

55% of participants had severely inadequate (<70%) or moderately inadequate (70% to <90%) GWG, 22% had adequate GWG (90-125%), and 23% had excessive GWG (≥125%).

GWG and Probability of SGA vs LGA



Erica et al Bulletin of the World Health Organization 2011;89:127-136

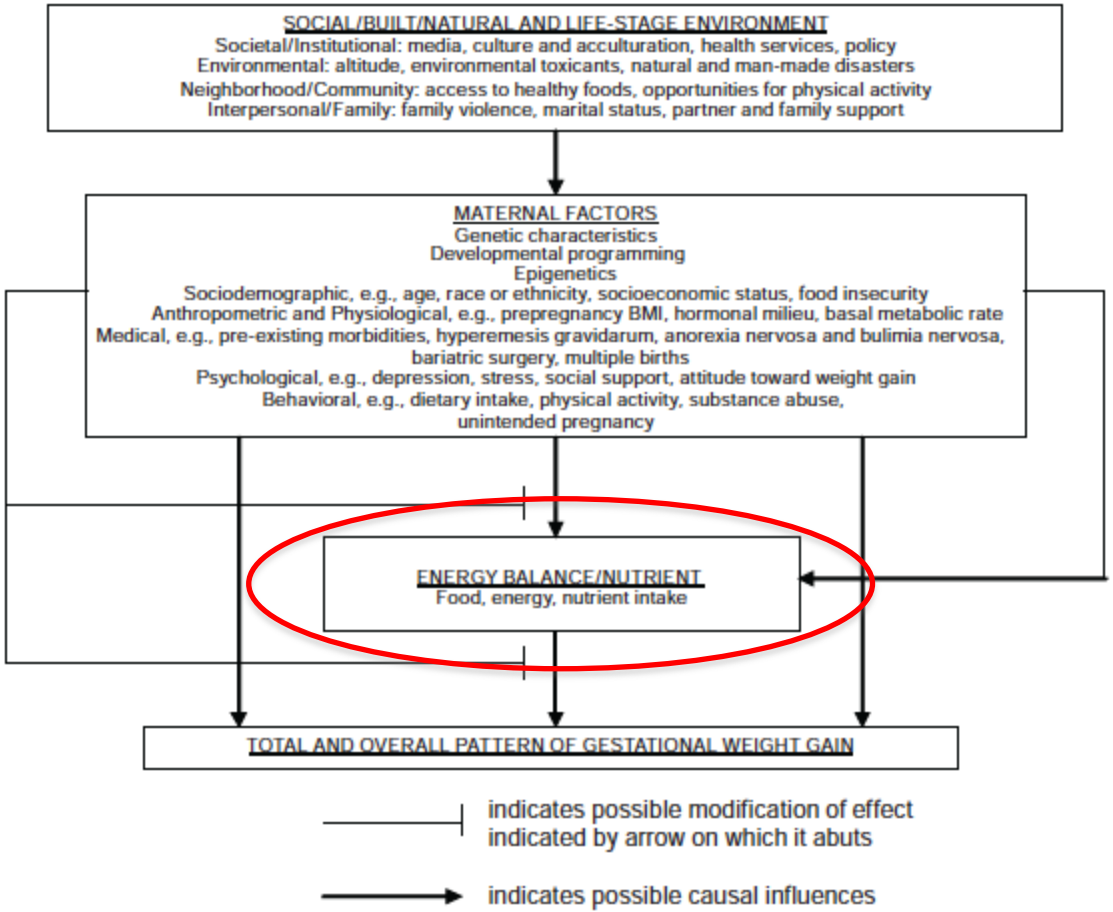
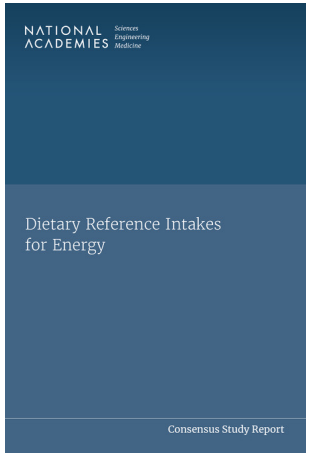


FIGURE 4-1 Schematic summary of determinants associated with GWG.

Estimated Energy Requirement, Recommendations: DRI 2023

Life Stage	PAL Category	EER Equation (kcal/day)
2nd and 3rd trimester of pregnancy[a]	Inactive	EER = 1,131.20 – (2.04 × age) + 0.34 × height) + (12.15 × weight) + (9.16 × gestation) + energy deposition
	Low active	EER = 693.35 – (2.04 × age) + (5.73 × height) + (10.20 × weight) + (9.16 × gestation) + energy deposition
	Active	EER = -223.84 – (2.04 × age) + (13.23 × height) + (8.15 × weight) + (9.16 × gestation) + energy deposition
	Very active	EER = -779.72 – (2.04 × age) + (18.45 × height) + (8.73 × weight) + (9.16 × gestation) + energy deposition



- Doubly Labeled Water based study data used, to derive predictive equations
- Physical Activity based equations
- With stage of pregnancy taken into account
- **Energy deposition:** for underweight = +300kcal/d,
  - for normal weight = +200kcal/d,
  - for overweight = +150kcal/d
  - For obese = -50kcal/d

Dietary Reference Intakes for Energy (2023)

Protein Requirements - Pregnancy

	DRI 2005	New Study Early Pregnancy	New Study Late Pregnancy	New Study (% 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 new estimates
Within Acceptable Macronutrient Distribution Ranges (AMDR)

- Current recommendations are underestimates

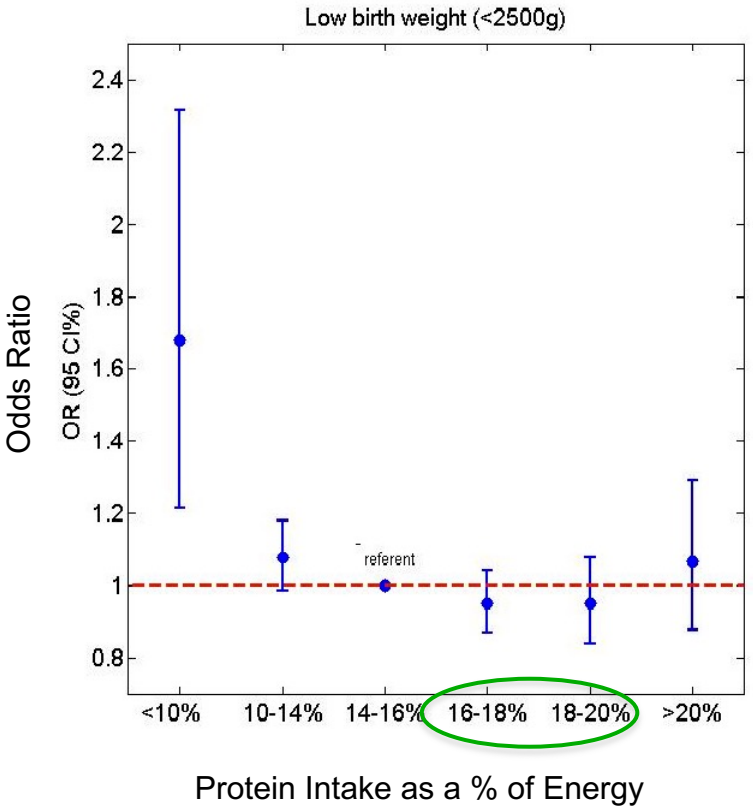
*Stephens, **Elango** et al J Nutr. 2015;145:73-8.*

Article

Old Question Revisited: Are High-Protein Diets Safe in Pregnancy?

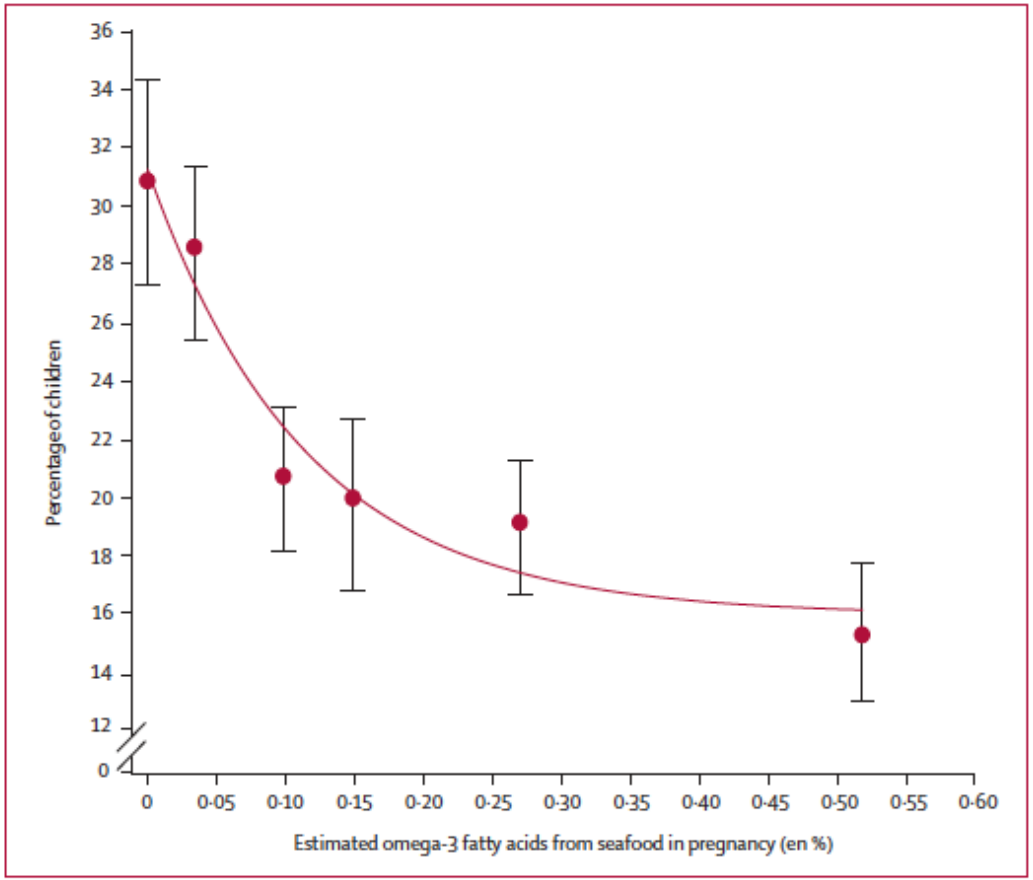
Thorhallur I. Halldorsson [1,2,*], Bryndis E. Birgisdottir [1], Anne L. Brantsæter [3], Helle Margrete Meltzer [3], Margaretha Haugen [3], Inga Thorsdottir [1], Anna S. Olafsdottir [4] and Sjurdur F. Olsen [2,5]

- Danish National Birth Cohort (DNBC) (n = 60,141); Norwegian Mother, Father and Child Cohort Study (MoBa) (n = 66,302) were merged through harmonization process
- Protein intake as a % of energy (16-20%) with choice of all (variety) food groups ideal
- Protein rich foods are also rich in various other essential nutrients and has the ability to improve maternal-child health



Halldorsson et al, Nutrients 2021, 13, 440.

Prevalence of children with low verbal IQ, based on mother's Omega-3 fatty acid from seafood



- A very influential figure, which led to several studies since!!
- *However, observational studies do not relate to causality*
- Led to multiple RCT's on Fish Oil Supplements/DHA supplements in pregnancy and lactation

Hibblen et al, Lancet. 2007; 369: 578–85

Editorial

See corresponding articles on pages 115, 128, and 268.

Fish-oil supplementation: the controversy continues

*Karen Simmer**

King Edward and Princess Margaret Hospitals and Centre for Neonatal Research and Education, University of Western Australia, Perth, Australia

Am J Clin Nutr 2016;103:1–2. Printed in USA.

- The above Editorial was published in 2016, in response to new series of DHA RCT's
- As yet unresolved
- Concern with seafood is with mercury/contaminants
- Supplements of omega-3 may not improve IQ, but may have immunological benefits/reduction in allergic disease
- Supplements need to be balanced with omega-3's: Eicosapentanoic Acid (EPA) + Docosahexanoic Acid (DHA)
  - EPA = 100 mg + DHA = 200 mg

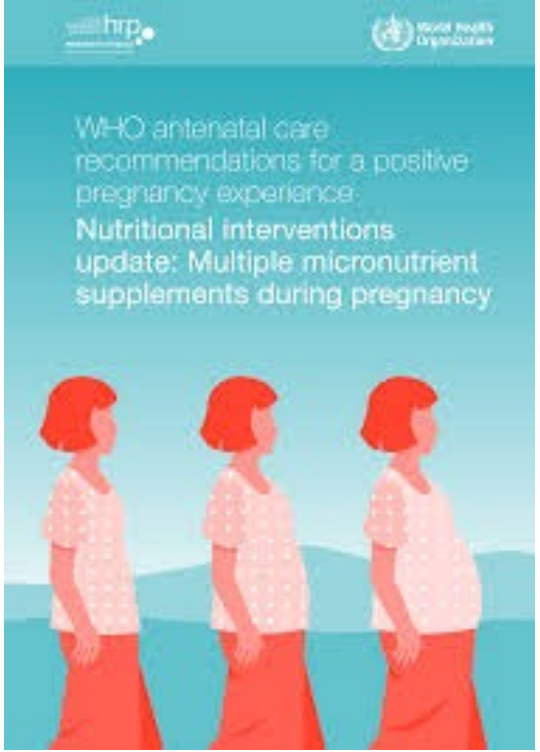
Multiple Micronutrients and Pregnancy

- It is clear that many micronutrients play key roles in maternal-fetal nutrition
- Individual micronutrient effects on pregnancy are inconsistent - we need intervention trials in large scale
- More relevant in conditions of overall poor diets. Hard to determine 'marginal deficiency' effects
- Developed countries have availability of 'Prenatal' supplements
- Not all supplements are equal!!

Prenatal Supplements
(some are not on market anymore)

	RDA*	Materna	Jamieson	Progressive	GNC	Natural Factors	AOR
Vitamin A (IU) beta-carotene	n/a†	2500	1800	2500	4500	30,000	9990
Vitamin B6 (mg)	1.9	1.9	10	35	10	60	80
Vitamin B12 (µg)	2.6	2.6	10	400	8	800	647
Calcium (mg)	1000	250	200	300	1200	1000	25
Vitamin D (IU)	600	400	200	400	400	200	1000
DHA (mg)	n/a	--	--	50	200	--	--
Folic Acid (µg)	600	1000	1000	1000	1000	800	800
Iodine (µg)	220	220	150	221	290	300	290
Iron (mg)	27	27	28	18	18	30	35
Selenium (µg)	60	30	--	100	70	100	55
Zinc (mg)	11	7.5	20	15	15	30	13

•Food and Nutrition Board, Institute of Medicine, National Academies (2004). Dietary reference intakes (DRIs): For individuals, elements. Available: http://www.iom.edu/Object.File/Master/21/372/0.pdf
•† RDA for vitamin A is not specific to beta-carotene.



World Health Organization 2020

WHO recommendation on antenatal multiple micronutrient supplements (MMS)

"Antenatal multiple micronutrient supplements that include **iron and folic acid** are recommended in the context of rigorous research. *(Context-specific recommendation – research)"*

MMS or Multiple Micro Nutrient, the UNICEF/WHO/UNU international MMN preparation (UNIMMAP) supplement: Folic Acid (400 µg), iron (ferrous fumarate, 30 mg), vitamin A (800 µg), vitamin E (10 mg), vitamin D (5 µg), vitamin C (70 mg), thiamine (1.4 mg), riboflavin (1.4 mg), vitamin B6 (1.9 mg), vitamin B12 (2.6 µg), niacin (18 mg), zinc (15 mg), copper (2 mg), iodine (150µg), and selenium (65 µg).

Public Health Nutrition: 24(6), 1526–1530 doi:10.1017/S1368980020003894

Commentary

The missing focus on women's health in the First 1,000 days approach to nutrition

The First 1,000 Days (time between conception and a child's second birthday) is a critical period where adequate nutrition is essential for development and growth

While nutrition interventions are facilitated with pregnant and lactating mothers, the focus is often on child health and there is a gap in measuring outcomes in women

Kinshella, Moore, Elango 2020

A gap in measuring women's health and nutritional status

- Maternal Child Health interventions are facilitated through the 'mother', but maternal outcomes are often overlooked

Multiple-micronutrient supplementation for women during pregnancy (Review)

Haider BA, Bhutta ZA 2017 Cochrane Review

- 16 trials reported effects on preterm births and Low Birthweight (LBW)
- 15 trials reported small-for-gestational age (SGA)
- *5 trials reported maternal anaemia,*
- *4 trials reporting caesarean section rates,*
- *3 that reported maternal mortality rates,*
- *1 trial reported pre-eclampsia*

Hypertensive disorders & Pre-eclampsia

- Nearly half of all maternal deaths are associated with 3 leading direct causes:
  - maternal hemorrhage (27%)
  - Hypertensive disorders (14%)
  - sepsis (11%)

- Pre-eclampsia – pregnancy specific inflammatory & **hypertensive disorder**, multifactorial etiology, including improper placental development

Maternal Dietary Patterns and Pregnancy Hypertension in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis

Kinshella, Elango et al Adv Nutr 2021

Advances in Nutrition
AN INTERNATIONAL REVIEW JOURNAL

nutrients

Kinshella, Elango et al 2021

MDPI

Review

Effects of Maternal Nutritional Supplements and Dietary Interventions on Placental Complications: An Umbrella Review, Meta-Analysis and Evidence Map

British Journal of Nutrition

Accepted manuscript

An evidence review and nutritional concept framework for pre-eclampsia prevention

Published online by Cambridge University Press: **09 December 2022**

Mai-Lei Woo Kinshella, Kelly Pickerill, Jeffrey N Bone, Sarina Prasad, Olivia Campbell, Marianne Vidler, Rachel Craik, Marie-Laure Volvert, Hiten D. Mistry, Eleni Tsigas, Laura A. Magee, Peter von Dadelszen, Sophie E. Moore, Rajavel Elango and The PRECISE Conceptual Framework Working Group

Kinshella et al. Reproductive Health (2022) 19:188
https://doi.org/10.1186/s12978-022-01485-9

Reproductive Health

REVIEW Open Access

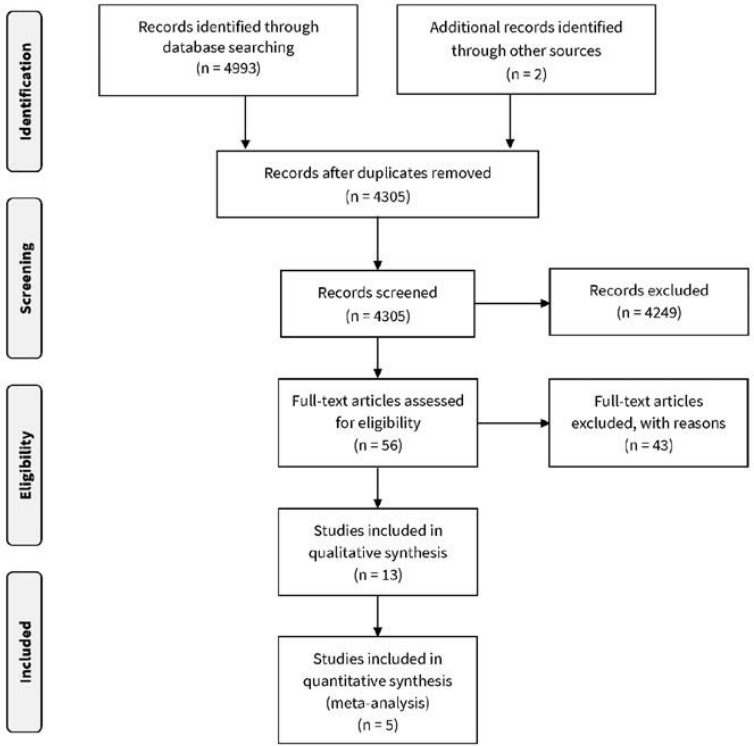
Maternal nutritional risk factors for pre-eclampsia incidence: findings from a narrative scoping review

Mai-Lei Woo Kinshella[1], Shazmeen Omar[1], Kerri Scherbinsky[1,2], Marianne Vidler[1], Laura A. Magee[1,3], Peter von Dadelszen[1,3], Sophie E. Moore[3,4], Rajavel Elango[2,5*] and The PRECISE Conceptual Framework Working Group

PRECISE Cohort – Gambia, Kenya and Mozambique: Data collection complete in ~6000 women

Maternal Dietary Patterns and Pregnancy Hypertension in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis

Advances in Nutrition
AN INTERNATIONAL REVIEW JOURNAL



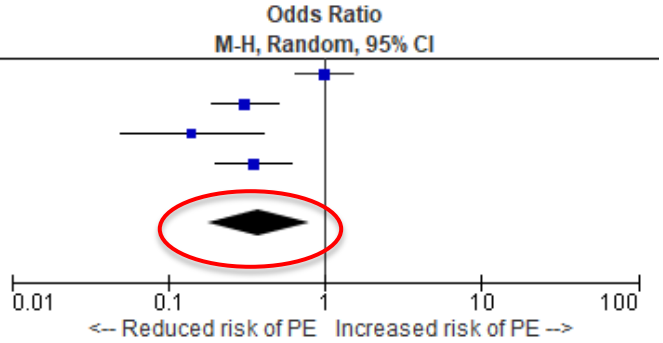
Evaluate the association between maternal dietary patterns and pregnancy hypertension in low-and middle-income (LMIC) countries where there is a current research gap

Kinshella, Elango et al Adv Nutr 2021

Adequate vegetable consumption and risk of pre-eclampsia (PE)

Study or Subgroup	Cases (PE) Events	Total	Control (Normotensive) Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Atkinson et al 1998	122	180	132	194	27.7%	0.99 [0.64, 1.53]
Endeshaw et al 2015	105	151	266	302	27.0%	0.31 [0.19, 0.50]
Grum et al 2018	66	81	157	162	19.1%	0.14 [0.05, 0.40]
Mekie et al 2020	73	107	184	214	26.1%	0.35 [0.20, 0.61]
Total (95% CI)		**519**		**872**	**100.0%**	**0.38 [0.18, 0.80]**
Total events	366		739			

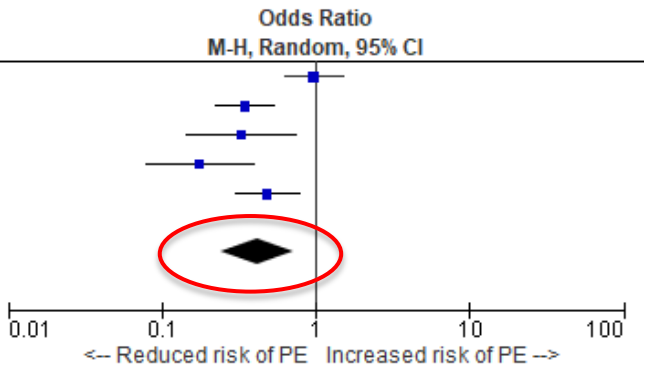
Heterogeneity: Tau² = 0.48; Chi² = 20.17, df = 3 (P = 0.0002); I² = 85%
Test for overall effect: Z = 2.54 (P = 0.01)



Adequate fruit consumption and risk of pre-eclampsia (PE)

Study or Subgroup	Cases (PE) Events	Total	Control (Normotensive) Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Atkinson et al 1998	124	180	135	194	22.5%	0.97 [0.62, 1.50]
Endeshaw et al 2015	92	151	247	302	22.5%	0.35 [0.22, 0.54]
Grum et al 2017	80	95	179	190	16.3%	0.33 [0.14, 0.75]
Grum et al 2018	59	81	152	162	16.6%	0.18 [0.08, 0.39]
Mekie et al 2020	50	107	138	214	22.0%	0.48 [0.30, 0.77]
Total (95% CI)		**614**		**1062**	**100.0%**	**0.42 [0.24, 0.71]**
Total events	405		851			

Heterogeneity: Tau² = 0.28; Chi² = 18.63, df = 4 (P = 0.0009); I² = 79%
Test for overall effect: Z = 3.20 (P = 0.001)



Suggests importance of dietary diversity

Kinshella, Elango et al Adv Nutr 2021

SYSTEMATIC REVIEW

Calcium for pre-eclampsia prevention: A systematic review and network meta-analysis to guide personalised antenatal care

Mai-Lei Woo Kinshella[1] | Catherine Sarr[2] | Akshdeep Sandhu[1] | Jeffrey N. Bone[1] | Marianne Vidler[1] | Sophie E. Moore[2,3] | Rajavel Elango[4] | Gabriela Cormick[5] | José M. Belizan[5] | G. Justus Hofmeyr[6,7] | Laura A. Magee[1,2] | Peter von Dadelszen[1,2] | On behalf of the PRECISE Network

BJOG. 2022;129:1833–1843.

- A systematic review, with network meta-analysis

- Prevention of preeclampsia, is calcium a viable option? And at what dose?

- Low dose (500mg/d) and high dose (>1000mg/d) calcium were effective in the meta-analysis in reducing preeclampsia
  - especially in low calcium intake populations

- Has cost implications and practical implications >1000mg dose requires multiple large calcium pills/d

Vegetarian/Vegan Diets in Pregnancy

- "Well-planned vegan and other types of vegetarian diets are appropriate for all stages of the life cycle, including during pregnancy, lactation, infancy…"

- Position of Dietitians of Canada & American Dietetics Association

- Adequacy depends on
  - Type of vegetarian, e.g. Lacto-ovo, vegan, etc
  - Length of diet adherence
  - Other foods excluded, e.g. Wheat, legumes, etc

Craig WJ, Mangels AR. Position of the American Dietetic Association: vegetarian diets. J Am Diet Assoc 2009;109: 1266–82.

Example of habitual diets low in calcium

nutrients

Systematic Review

The Association of a Vegan Diet during Pregnancy with Maternal and Child Outcomes: A Systematic Review

Deidre Meulenbroeks [1,*], Eline Otten [2], Sophie Smeets [2], Luuk Groeneveld [1], Daisy Jonkers [3], Simone Eussen [4], Hubertina Scheepers [1] and Jessica Gubbels [2]

Nutrients **2024**, *16*, 3329. https://doi.org/10.3390/nu16193329

- N=6 articles selected, after searches from 2,211 articles
- **Maternal outcomes**
  - Vegan diets had women with lower than adequate gestational weight gain
  - Protein intake low
  - 2 studies found higher incidence of hypertensive disorders
  - No other impact on anemia, Gestational Diabetes Mellitus (GDM), child birth hemorrhage
- **Fetal outcomes**
  - Higher incidence of low birth weight
  - Higher number of SGA babies

Adherence to different forms of plant-based diets and pregnancy outcomes in the Danish National Birth Cohort: A prospective observational study

Signe Hedegaard[1] | Ellen Aagaard Nohr[2] | Sjurdur Frodi Olsen[3] | Thorhallur Ingvi Halldorsson[3,4] | Kristina Martha Renault[1,5]

Acta Obstet Gynecol Scand. 2024;103:1046–1053.

Key message

Women adhering to vegan diets during pregnancy had offspring with lower mean birthweight compared to omnivorous mothers. Further research is needed regarding possible causality between plant-based diets and pregnancy and birth outcomes to strengthen the basis for dietary recommendations.

TABLE 2 Dietary nutrient intake as recorded in gestation week 25 according to adherence to omnivorous or plant-based diets.

	Omnivorous ($n = 65\,872$)	Vegetarian fish/poultry ($n = 666$)	Vegetarian lacto/ovo ($n = 182$)	Vegan ($n = 18$)
Macronutrients	Mean (standard deviation)			
Energy, MJ/day	10.4 (2.8)	9.9[2] (2.7)	10.1 (3.2)	9.7 (2.5)
Protein, %E	15.4 (2.4)	14.7[2] (2.5)	13.3[2] (2.3)	10.4[1] (2.6)
Fat, %E	32.3 (6.1)	29.9[2] (6.6)	29.7[2] (6.7)	32.7 (5.7)
Carbohydrates, %E	51.8 (5.9)	55.1[2] (6.4)	56.7[2] (6.5)	56.7 (6.1)
Fiber, g/day	27 (9)	29[2] (11)	30[2] (12)	30 (11)
GDM, % [no. cases/N]	0.8% [512/65872]	0.5% [3/666]	0.6% [1/182]	0% [0/18]
Preeclampsia, % [no. cases/N]	2.6% [1680/65872]	3.0% [20/666]	2.2% [4/182]	11.1%[1] [2/666]

Summary

- To improve pregnancy nutrition, importance must be placed in 'maternal' impacts
- Intergenerational transfer of benefit to health
  - Developmental origins of Health & Disease (DOHAD)
- Gestation Weight Gain (GWG) must be monitored with a focus on overall energy balance
- Protein intake recommendations are not adequate, and protein must be provided at a more concentrated level (16-20% of energy)
- Omega-3 supplements must be balanced with EPA + DHA
- Iron and folic acid supplements are recommended, MMN/MMS needs are unclear.
- Pre-eclampsia, a leading cause of morbidity in women during pregnancy can be reduced by improving overall diet diversity & quality
- Vegetarian diets are safe during pregnancy, if well-planned
- Vegan diets appear to increase low birthweight prevalence and increased risk for pre-eclampsia
- Nutrition in women could potentially be a key modulator of future health for generations, but also important in the present

Final Takeaway

Public Health Nutrition: 24(6), 1526–1530 doi:10.1017/S1368980020003894

Commentary

The missing focus on women's health in the First 1,000 days approach to nutrition

"There is a great hope and potential for nutrition to strengthen infant growth and the society they will live in, but our vast dreams for the future cannot neglect the potential for benefits for women and her own life in the here and now."

Kinshella, Moore, Elango 2020

Acknowledgements

- Collaborators
  - Dr. Sophie Moore, Kings' College London
  - Dr. Glenda Courtney-Martin, SickKids, Toronto

- Elango Lab
- Noof Al-Mansoori
- Arati Swaminadan
- Kaitlin Berris
- Taylor Bailey
- Kerri Scherbinsky
- Maggie-Woo Kinshella
- Kendall Plant

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BC Children's Hospital Research Institute

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