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Prenatal Supplements and Their Role in Reducing Stunting

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Prevalence of Stunting

- Globally 1 in 4 children stunted; ~209 mln in developing world
- Stunting linked to reduced cognitive development, productivity and chronic disease in later life
- UN Sustainable Development Goal #2
- Large impact on individuals, also on countries' GDP (up to 20%)

Source: The Borgen Project; Onis & Branca, 2016

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WHA Global Nutrition Targets 2025

"..reducing the rate of infants born with low birth weight … associated with a decreased risk of stunting."

"Actions focused on prevention such as ensuring pregnant mothers…are adequately nourished…can help address both stunting and wasting."

DEFINITION:
Low birth weight (LBW) is birth weight <2500g regardless of gestational age

WHA Global Nutrition Targets 2025: Stunting Policy Brief, WHO, 2012

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Low birth weight is a predictor of stunting - Indonesian study

Table 3 Multivariate regression analysis of risk factors for stunting

	Estimated				
Factor	Regression Coefficient (β)	SE of (β)	*p*-value	Odds Ratio Exp (β)	95% CI for Exp (β)
Constant	−0.606	0.085	0.000	0.545	
Low Birth weight	0.554	0.119	0.000	1.740	1.378–2.197
Boys	0.245	0.075	0.001	1.278	1.103–1.481
Ill at age 0–28 days	0.203	0.104	0.052	1.225	0.998–1.503
Poor	0.263	0.075	0.000	1.301	1.123–1.508

- LBW was the most dominant predictor associated with stunting among children aged 12-23 months in Indonesia
- Prevalence of stunting was >40%
- LBW infants were 1.74 times more likely to be stunted
- Also Zimbabwe – LBW is a major contributing factor to stunting among children 0-59 months (Marazika et al., 2016)

Arystami et al., 2017 BMC Nutrition

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Term and SGA is leading risk cluster for stunting globally

- 5 risk clusters
  - Maternal nutrition and infection
  - Teenage motherhood and short birth intervals
  - Term and SGA
  - Child nutrition and infection
  - Environmental factors
- Prevalence for each risk cluster estimated per country (137) along with stunting for 2010
- Term and SGA estimated to account for 10.8mln cases of stunting out of 44.1 mln in 2010

Risk Factors for Childhood Stunting in 137 Developing Countries: A Comparative Risk Assessment Analysis at Global, Regional, and Country Levels

Goodarz Danaei[1,2]*, Kathryn G. Andrews[1], Christopher R. Sudfeld[1], Günther Fink[1], Dana Charles McCoy[3], Evan Peet[1,4], Ayesha Sania[1], Mary C. Smith Fawzi[5], Majid Ezzati[6,7], Wafaie W. Fawzi[1,2,8]

1 Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, United States of America, 2 Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, United States of America, 3 Harvard Graduate School of Education, Cambridge, Massachusetts, United States of America, 4 RAND Corporation, Pittsburgh, Pennsylvania, United States of America, 5 Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts, United States of America, 6 MRC-PHE Centre for Environment and Health, School of Public Health, Imperial College London, London, United Kingdom, 7 Wellcome Trust Centre for Global Health Research, Imperial College London, London, United Kingdom, 8 Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, Massachusetts, United States of America

DEFINITION:
Small for Gestational Age (SGA) is newborn with weight below 10th percentile for gestational age

Danaei et al., 2016

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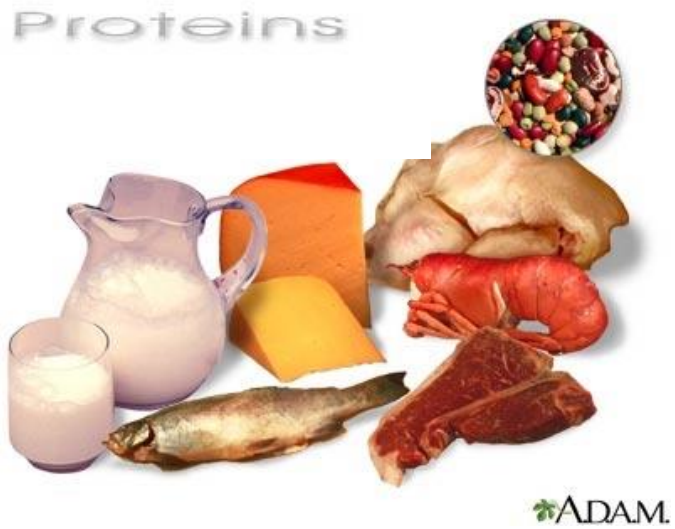
Dietary patterns amongst pregnant women in developed countries



- Dietary pattern studies:
  - Auckland Birthweight Collaborative study, 2008
  - Osaka Maternal and Child Health Study, 2012
  - Generation R study (NL), 2012
  - 2 studies from Spain, 2010, 2012
  - Danish National Birth Cohort, 2008
- High intakes of fish, low fat dairy, lean meat, legumes -> higher BW, lower risk of IUGR
- High intake of refined grains, processed meat, confectionary, soft drinks -> increased risk of SGA/LBW

Source: Grieger & Clifton, 2015; Clark, 2016

DEFINITION:
Intrauterine Growth Retardation (IUGR) is when fetal weight is below 10th percentile for gestational age

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Dietary patterns amongst pregnant women in developed countries

- Literature review 2000-2011 on maternal milk/dairy consumption and birth weight in healthy Western mothers
- Birth Weight: 2 no associations; 4 positive associations with milk/dairy consumption
- Positive effect most pronounced at low-moderate milk intake level
- All papers highlighted importance of inclusion of some milk or dairy in maternal diet

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Source: Brantsaeter et al., 2012; Clark, 2016

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Recent studies: Association between dairy consumption and LBW/SGA

Matern Child Health J (2016) 20:1296–1304
DOI 10.1007/s10995-016-1931-2

CrossMark

Association Between Low Dairy Intake During Pregnancy and Risk of Small-for-Gestational-Age Infants

Rocío Olmedo-Requena[1,2,3] · Carmen Amezcua-Prieto[1,2,3] · Juan de Dios Luna-Del-Castillo[2,4] · Anne-Mary Lewis-Mikhael[1] · Juan Mozas-Moreno[3,5] · Aurora Bueno-Cavanillas[1,2,3] · José Juan Jiménez-Moleón[1,2,3]

- Low dairy product intake associated with higher risk of SGA
- Increasing dairy product intake by 100g/d in early pregnancy decreased risk of SGA by 11%
- Dose dependent response was observed

Table 3 Population attributable fraction (PAF) of SGA from dairy consumption

Dairy consumption (g/day)	Scenario 1: All women in the study		Scenario 2: Women consuming less than the median, 572 g/day	
	PAF (%)	(95 % CI)	PAF (%)	(95 % CI)
600	4.5	[−0.7, 9.1]	19.6	[6.3, 30.9]*
700	13.2	[2.6, 22.6]*	26.8	[8.9, 41.2]*
800	21.1	[5.2, 34.3]*	33.5	[11.4, 50.1]*
900	28.4	[7.8, 44.4]*	39.7	[13.8, 57.8]*

* $P < 0.05$. The models were built using the total simple

Source: Olmeda-Requena et al., 2016

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Nutrient intake of pregnant women in developing world frequently insufficient

British Journal of Nutrition (2016), **116**(S1), S57–S66 doi:10.1017/S000711451600057X

Nutritional status of pre-pregnant and pregnant women residing in Bogor district, Indonesia: a cross-sectional dietary and nutrient intake study

Siti Madanijah[1,2], Dodik Briawan[1,2], Rimbawan Rimbawan[1,2], Zulaikhah Zulaikhah[1], Nuri Andarwulan[1,3], Lilis Nuraida[1,3], Tonny Sundjaya[4], Laksmi Murti[5], Priyali Shah[6] and Jacques Bindels[6]*

- >50% or women or reproductive age unable to meet national nutrient requirements
- 44% pregnant women – inadequate intake of energy and protein
- Observed increased intake of milk/dairy during pregnancy but insufficient to meet nutrient requirements

Source: Madanijah et al., 2016

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Recent studies: Maternal dietary intake during pregnancy - Malawi

- Malawian diet: Deficient in several micro- & macronutrients, animal protein intake low
- C/H negatively associated with birth length and abdominal circumference
- Fat positively associated with birth length and abdominal circumference
- Milk intake positively associated with birth weight
- Each additional day of milk consumption within the 7 measurement days was associated with 75.3g increase in birth weight.

TABLE 2 Proportion of sample eating items from each food group at least once during seven measurement days (n = 203)

Food group	*n* (%)
Cereals	203 (100)
White roots and tubers	135 (66.5)
Vitamin A-rich vegetables and tubers	17 (8.4)
Dark green leafy vegetables	198 (97.5)
Other vegetables	203 (100)
Vitamin A-rich fruits	163 (80.3)
Other fruits	188 (92.6)
Flesh meat	77 (37.9)
Eggs	59 (29.1)
Fish	188 (92.6)
Legume, nuts, and seeds	190 (93.6)
Milk and milk products	40 (19.7)

"..taking into account the effect sizes of the associations between birth size and the different nutrients and food groups, it becomes apparent that milk foods are the most important food to promote."

Hjertholm et al., 2016

Unclear links between dairy intake and gestational weight gain

Steube et al., 2009 Associations of diet and physical activity during pregnancy with risk for excessive weight gain

- Positive association between excessive GWG and dairy consumption
- Result only just significant (OR=1.09)

DEFINITION:
Gestational Weight Gain (GWG) is the amount of weight a woman gains during pregnancy

Abreu et al., in press Relationship between dairy product intake during pregnancy and neonatal and maternal outcomes among Portuguese women

- Associations dairy intake 1st-2nd trimester of pregnancy:
  - Positive Neonatal head circumference
  - Positive placental weight
  - Negative GWG

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Protein:C/H ratio appears critical factor with respect to maternal GWG

BMJ Open **Dietary protein-to-carbohydrate ratio and added sugar as determinants of excessive gestational weight gain: a prospective cohort study**

Ekaterina Maslova,[1] Thorhallur I Halldorsson,[1,2,3] Arne Astrup,[4] Sjurdur F Olsen[1,5]

- High protein:C/H ratio associated with reduced GWG, partly driven by decrease in intake of added sugar
- Analysis by protein source showed lower GWG with high protein from meat and fish but not dairy

Source: Maslova et al, 2015

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Also concerns about maternal diet and fetal programming?

Maslova et al 2014 Maternal protein intake during pregnancy and offspring overweight 20 y later.

"…higher BMI in offspring….driven by protein from meat and meat products rather than fish or milk products."

Jahan-Mihan et al., 2015 The Role of Maternal Dietary Proteins in Development of Metabolic Syndrome in Offspring

"Both low and high protein maternal diets have detrimental effects on body weight and body composition of offspring."

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With correct protein:energy balance, dairy protein positively associated with leanness in neonate

Nutritional Epidemiology

Dietary Composition of Pregnant Women Is Related to Size of the Baby at Birth[1,2]

Vivienne M. Moore,[3] Michael J. Davies,* Kristyn J. Willson, Anthony Worsley,† and Jeffrey S. Robinson*

*Department of Public Health, University of Adelaide, Australia; *Department of Obstetrics & Gynaecology, University of Adelaide, Australia; and †School of Health Sciences, Deakin University, Australia*

- % energy from C/H negatively associated with neonate leanness
- % energy from dairy protein more positively associated with leanness than other sources
- Every 1% increase in dairy protein delivered 24g increase in birth weight

Moore et al., 2004

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…maternal animal protein intake impacts body composition in Asian phenotype

J Nutr. 2016 August ; 146(8): 1571–1579. doi:10.3945/jn.116.230730.

Maternal macronutrient intake during pregnancy is associated with neonatal abdominal adiposity: the Growing Up in Singapore Towards healthy Outcomes (GUSTO) study[1-4]

Ling-Wei Chen[5,c,*], Mya-Thway Tint[6,*], Marielle V. Fortier[7], Izzuddin M. Aris[8], Jonathan Y. Bernard[8], Marjorelee Colega[8], Peter D. Gluckman[8,9], Seang-Mei Saw[10], Yap-Seng Chong[6,8], Fabian Yap[11,12], Keith M. Godfrey[13], Michael S. Kramer[6,14], Rob M. van Dam[10,15,16], Mary Foong-Fong Chong[8,10,17,c], and **Yung Seng Lee[5,8,18,c]**

- Higher protein, lower C/H and fat diet during pregnancy associated with lower abdominal internal adipose tissue (IAT)
- Higher maternal intake of animal protein BUT NOT plant protein associated with lower neonate IAT

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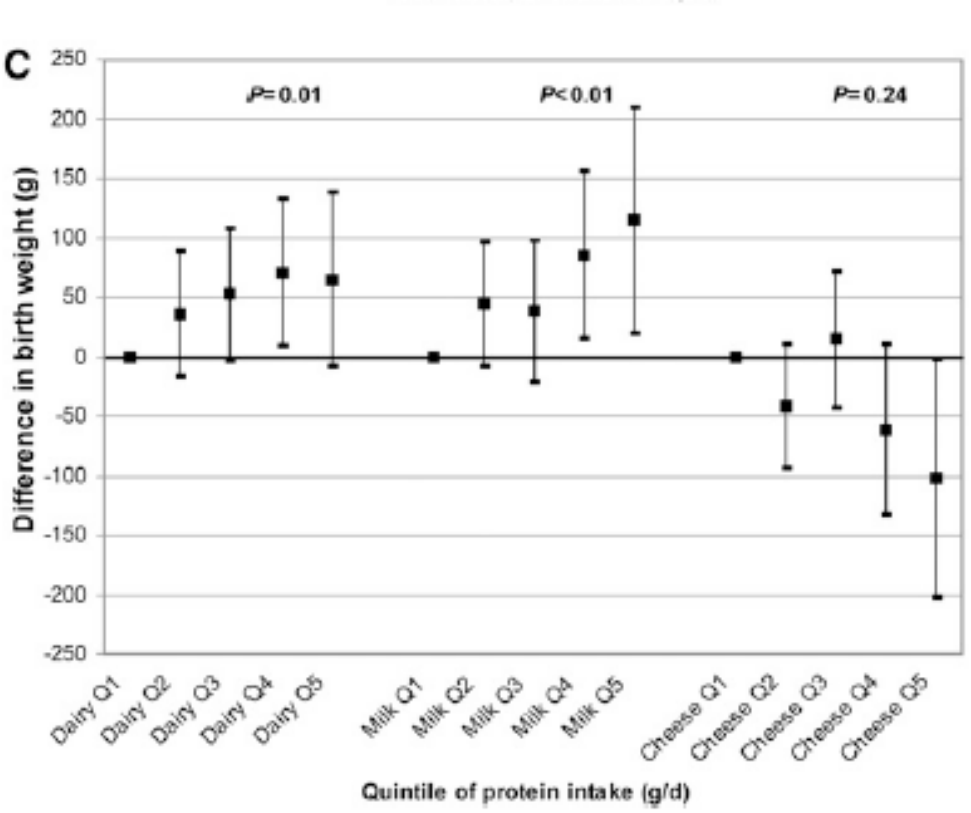
Is there a specific component of milk associated with increased birth weight?

- Dietary pattern studies break down intake into broad classes of food
- Two studies divided dairy into subcategories
- Dairy & Milk - positive association with BW, Cheese – negative
- Does this suggest whey or a component of whey is 'contributing' factor



Source: Heppe et al., 2011; Olsen et al., 2007

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Mechanisms underlying dairy proteins during pregnancy prevent stunting?

Contents lists available at ScienceDirect

EBioMedicine

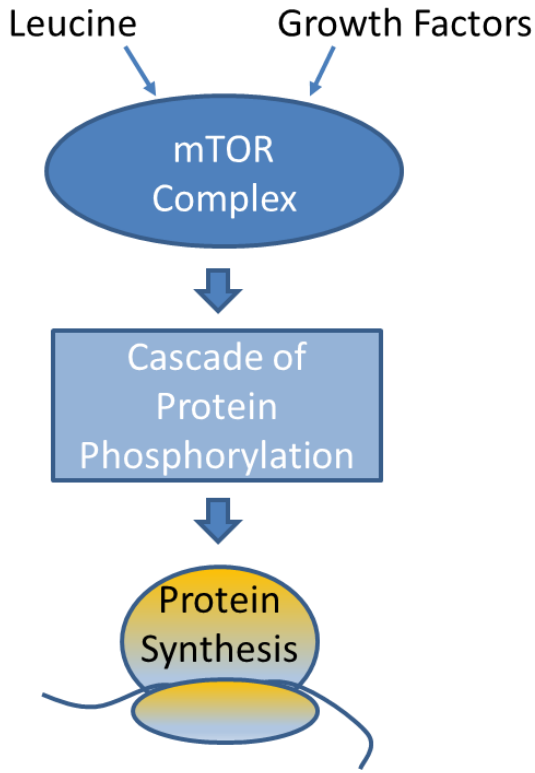
journal homepage: www.ebiomedicine.com

ELSEVIER

Research Paper

Child Stunting is Associated with Low Circulating Essential Amino Acids

Richard D. Semba [a,*], Michelle Shardell [b], Fayrouz A. Sakr Ashour [c], Ruin Moaddel [b], Indi Trehan [d,e], Kenneth M. Maleta [e], M. Isabel Ordiz [d], Klaus Kraemer [f,g], Mohammed A. Khadeer [b], Luigi Ferrucci [b], Mark J. Manary [d,e]



- Human growth controlled by mTOR pathway
- Chondral plate growth – determinant of linear growth - is regulated by mTOR, which represses protein & lipid synthesis when certain amino acids are deficient
- Stunted children have lower serum levels of indispensable and conditionally essential amino acids
- Dairy, particularly whey is a rich source of these amino acids

Sources: Laplante and Sabatini, 2012; Baron et al., 2015; Semba et al., 2016

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Concluding Remarks

- Low Birth Weight and Small for Gestational Age are risk factors for stunting
- Dietary pattern studies show an association between moderate dairy protein intake and increased birth weight/ reduced risk of LBW
- Protein:C/H ratio important in relation to GWG and fetal programing; association between leanness and animal/dairy protein intake
- More research needed to establish whether an association between maternal whey protein intake and birth weight exists

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Thank you for your attention!

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