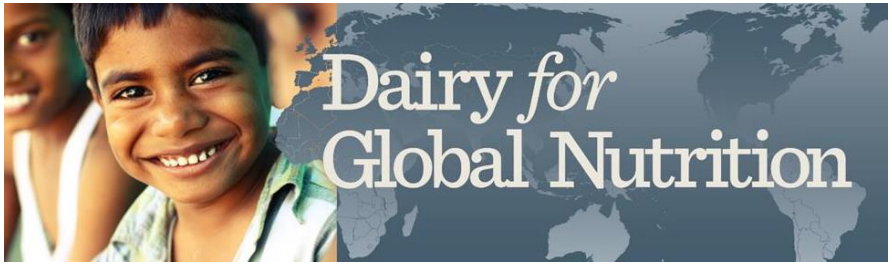


The Growth Components of Milk

Dairy Nutrition:
An engine for
Economic Growth
Boise Idaho May 2017

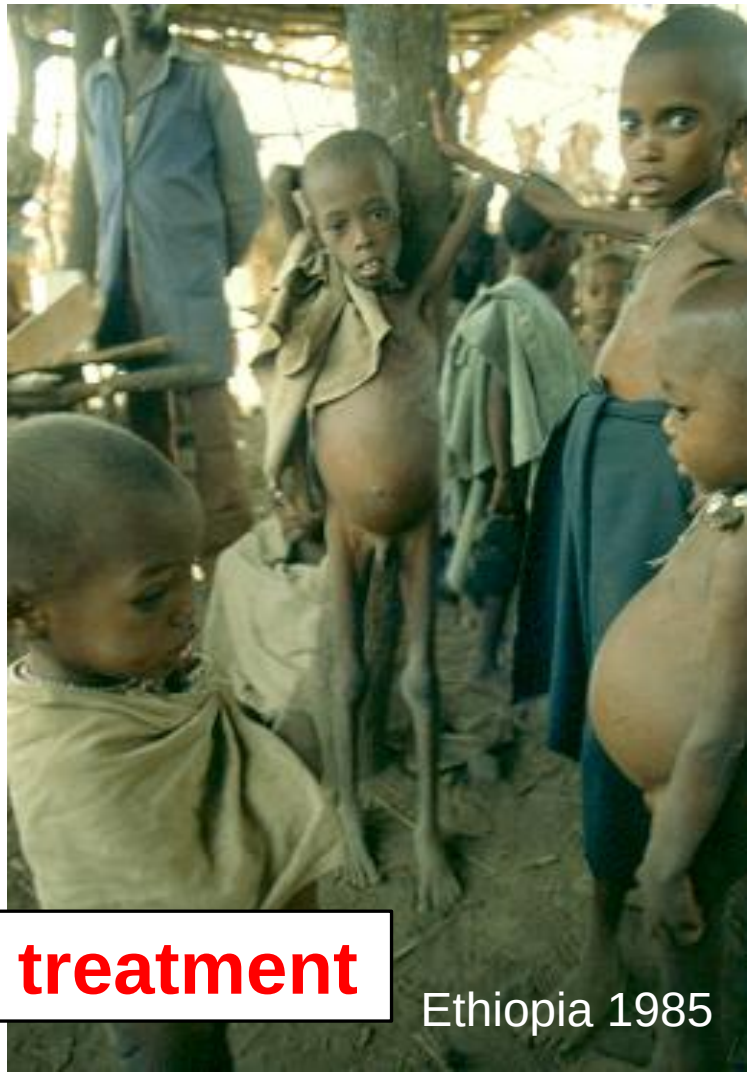
Kim Fleischer Michaelsen
Paediatric and International Nutrition
Department of Nutrition, Exercise and Sports
University of Copenhagen


Ethiopia 1985

Child undernutrition < 5y

Lancet series 6. June 2013

- 165 mill stunted
- 33 mill moderately wasted - MAM
- 19 mill severely wasted - SAM
- 3.1 mill deaths due to undernutrition



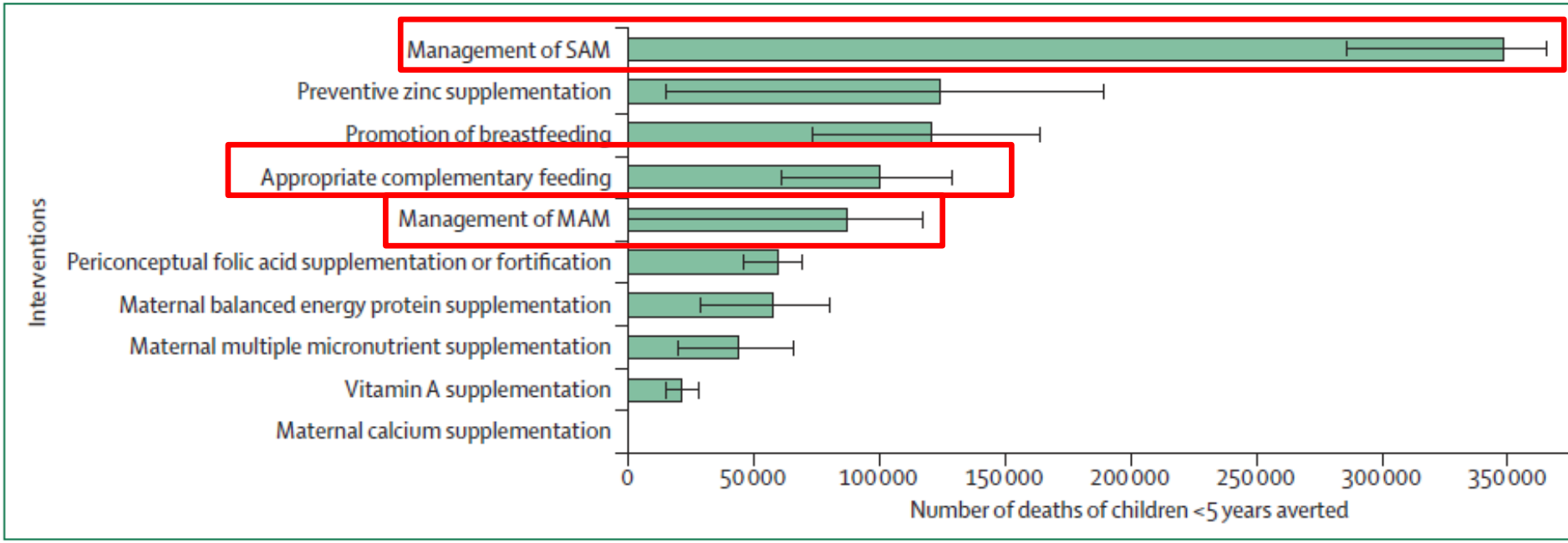
Ethiopia 1985

Milk has an important role in treatment

Effect of scale up on deaths - children < 5 y

Lancet series 2013 - Bhutta et al: Interventions

500.000 deaths can be saved each year if management of SAM and MAM and complementary feeding is optimal



What are the growth components in milk?

- **Protein** – DSM and Whey
- **Lactose**
- **Minerals** – Permeate

- Bioactive peptides
- Less antinutrients

Protein energy percentage from milk in foods for MAM and SAM

- Therapeutic formula (F- 100) 100%
- RUTF or LNS - typically 40-50%
- CSB++ (Super cereal plus) 20%

The Use of Whey or Skimmed Milk Powder in Fortified Blended Foods for Vulnerable Groups[1,2]

Camilla Hoppe, Gregers S. Andersen, Stine Jacobsen, Christian Mølgaard, Henrik Friis, Per T. Sangild, and Kim F. Michaelsen*

- Improves weight gain, linear growth, and recovery from malnutrition
- Improves the protein quality, measured as PDCAAS/DIAAS
- With improved protein quality it is possible to reduce the total amount of protein in the blend, which could have potential metabolic advantages.
- Allows for a reduced content of soy and cereal and thereby a reduction of potential anti-nutritional effects
- Improves flavor; SMP more so than WPC
- Increases the price considerably – limiting factor in food aid
- Adds lactose which potentially have positive effects

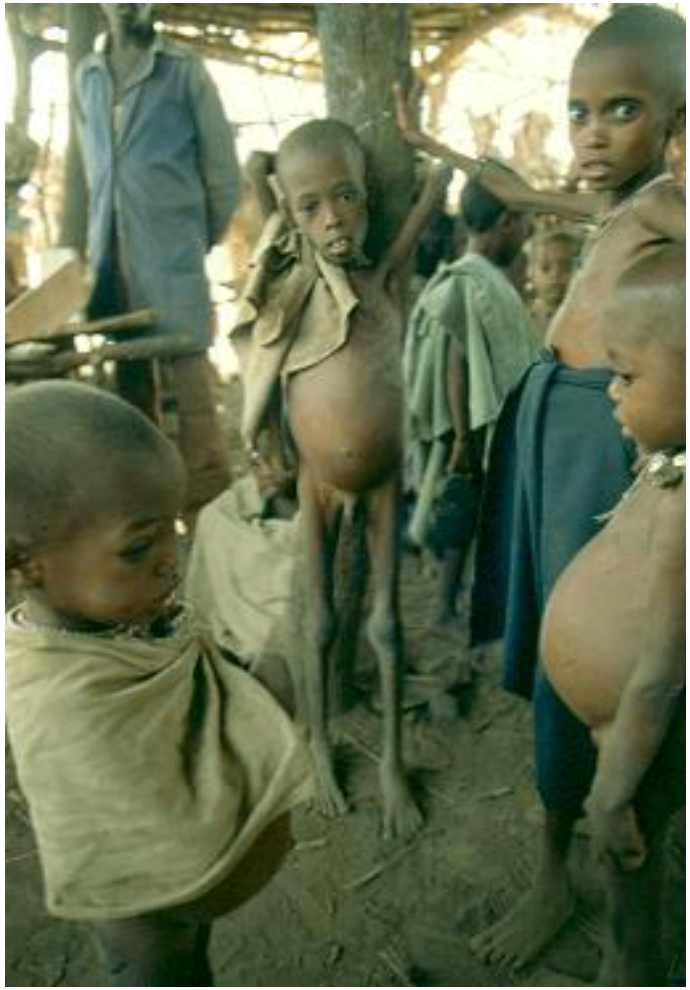
Updated from Hoppe et al. 2008

J. Nutrition 2008, Free access
Unconditional funding from USDEC

Using whey (WPC34%) compared with SMP

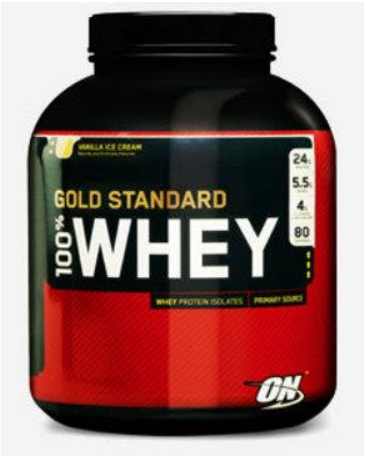
- Slightly better protein quality measured as PDCAAS, but not likely to be important.
- Potential beneficial effects on the immune system and muscle synthesis have been suggested, but convincing evidence still lacking
- Not as widely available as SMP
- Price lower than SMP?

Modified from Hoppe et al.
J Nutr 2008



Whey and muscle mass

?

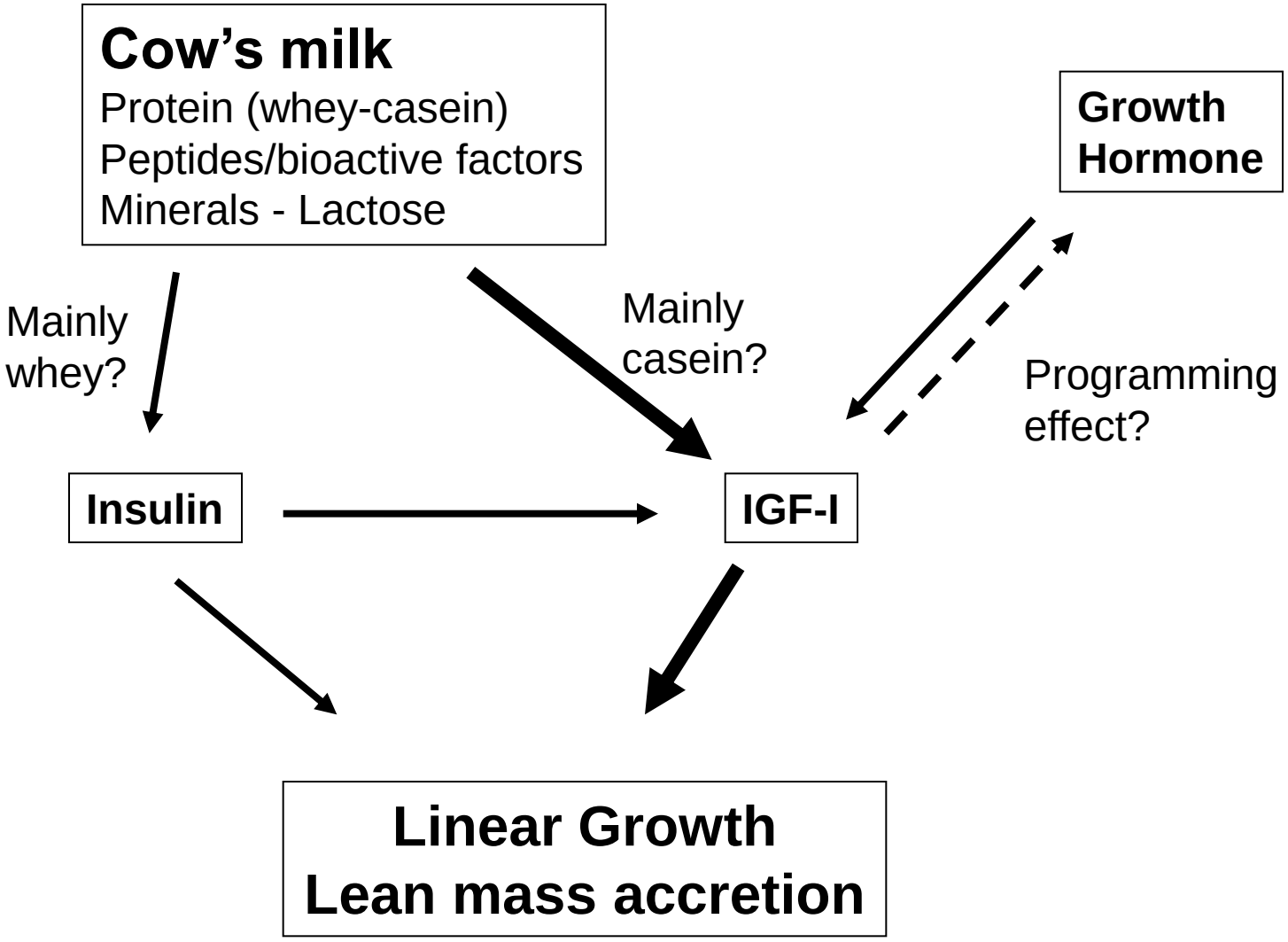


Whey and muscle syntesis

- Increase in muscle mass beneficial in malnutrition
- Aminoacid pattern (espec. BCAAs) of whey protein is similar to skeletal muscle
- Whey seems to stimulate insulin and thus protein synthesis
- Most data from sport nutrition show convincing positive effect of intake of whey
  - but only immidiately after endurance training
- Whey contains arginine and lysine which stimulates growth hormone, an anabolic hormone - speculative
- Effects of encouraging physical activity during whey supplementation?

Skimmed milk powder might have comparable effects on muscle mass?

Cow's milk and growth



Hoppe et al
EJCN 2005

What are the growth components in milk?

- **Protein** – DSM and Whey
- **Lactose**
- **Minerals** – Permeate

- Bioactive peptides
- Less antinutrients

Is lactose a problem in undernourished children?

Focus on MAM and SAM < 3 y

Denmark 2017

Ethiopia 1985

Food Nutr Bull 2016

Undernourished Children and Milk Lactose

Benedikte Grenov, MSc[1], André Briend, MD, PhD[1,2], Per T. Sangild, PhD[3], Thomas Thymann, PhD[3], Maren H. Rytter, MD, PhD[1], Anne-Louise Hother, MSc[1], Christian Mølgaard, MD, PhD[1], and Kim F. Michaelsen, PhD, MD[1]

Supported by unconditional grant from Arla

Effects of lactose

- Potential negative effects
  - Lactose intolerance
- Potential positive effects
  - Prebiotic effects
  - Increased mineral absorption
  - Improved growth? (pig studies)
  - Energy density, palatability and dental effects

Definitions

Lactose intolerance	GI symptoms: abdominal pain, diarrhea, nausea, flatulence after ingestion of lactose. Depends on the amount of lactose ingested and residual lactase activity **Balance**
Lactose malabsorption	Occurs when the capacity of the small intestine to hydrolyze the ingested amount of lactose is exceeded **Preterm infants and breastfeeding**
Primary lactase "deficiency"	Genetically programmed reduction of lactase activity after weaning **No symptoms before 3-4 years**
Secondary lactase deficiency	Temporary lactase deficiency as a consequence of small bowel injury, eg. acute gastroenteritis, persistent diarrhea, enteropathies

Heymann Pediatrics 2006

Primary lactase deficiency

– no symptoms before 3-4 y

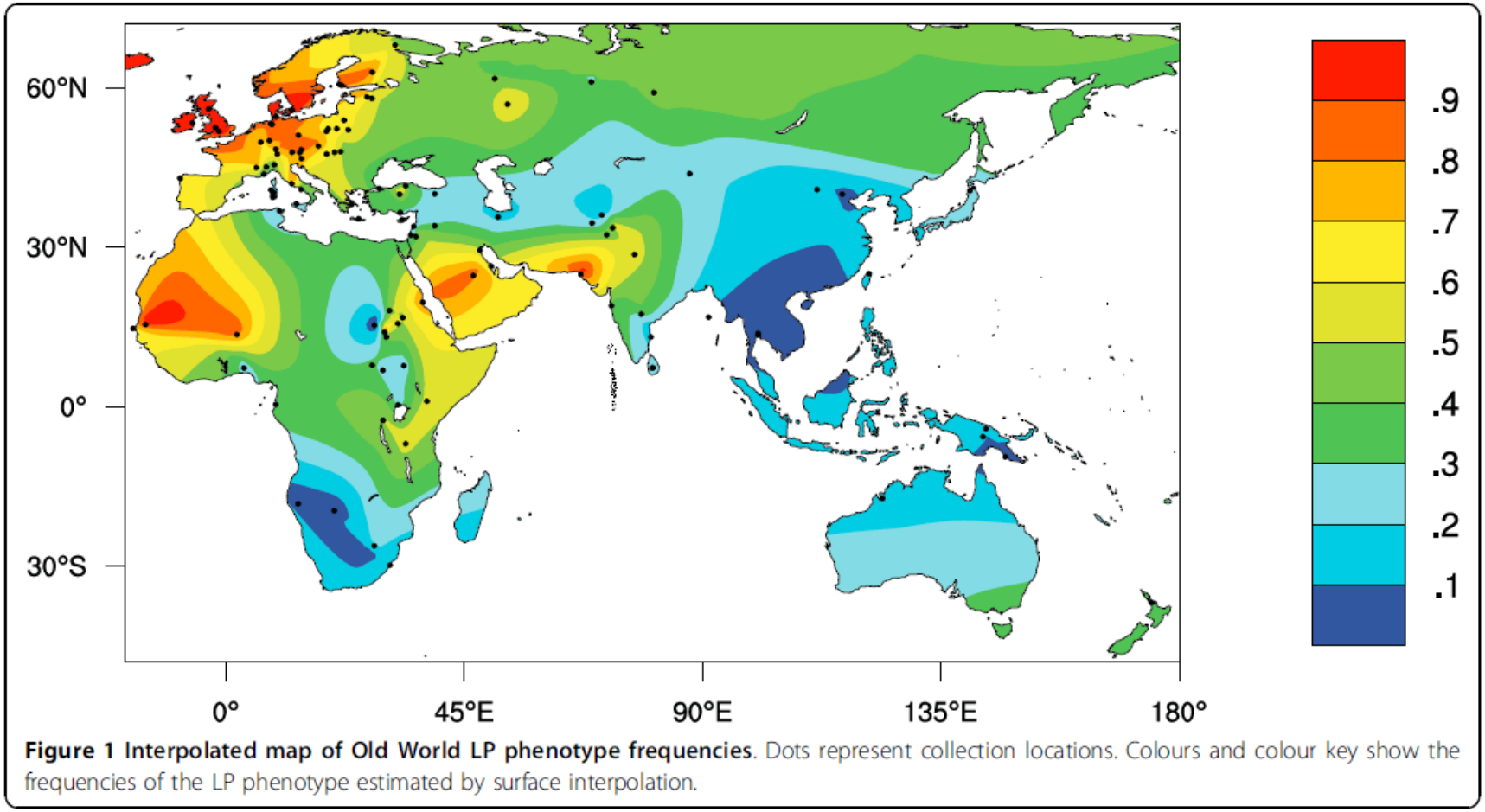


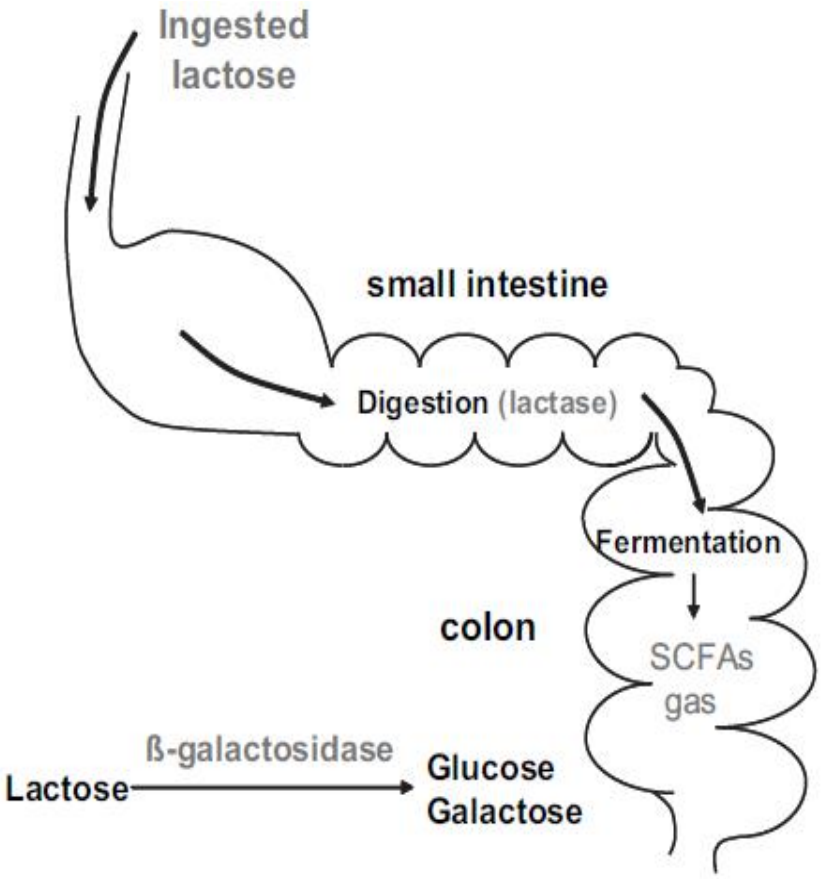
Figure 1 Interpolated map of Old World LP phenotype frequencies. Dots represent collection locations. Colours and colour key show the frequencies of the LP phenotype estimated by surface interpolation.

Frequency of LP phenotype

Itan et al. Evolutionary Biology 2010

Lactose malabsorption causes prebiotic effects

- Non digested lactose continues to the large intestine
- Lactose is hydrolyzed and fermented to SCFAs and gas (CO_2, H_2, CH_4)
- Reduces pH
- Preterm infants - 50-70% lactose passes into the large intestine
- Term infants – some lactose passes to the large intestine?



Klein J Nutr 2002

After He et al 2008

Prebiotic effects of lactose

- Buturate (SCFA) is an important fuel for colonocytes
- Lactose passing to the colon seems to stimulate a beneficial flora with more bifidobacteria and lactobacilla and less E.coli and bacteroides
- In maldigestion lactose content should be balanced between beneficial probiotic effects and osmotic diarrea

Lactose stimulate weight gain in studies of weanling piglets

- Whey used to feed piglets for decades - very effective in stimulating weight gain
- Discussed if the effect is due to whey protein or lactose
- Several studies suggest that the lactose fraction has an important effect and some suggest that the lactose effect is stronger than the protein effect
- Growth effect stronger in younger piglets

Lactose to piglets during weaning

Cromwell et al. J Anim Sci 2008

- 1320 crossbred pigs were studied at 3 sites
- Pigs were weaned at 15 – 20 days
  - Phase 1: 20% lactose (week 1 after weaning)
  - Phase 2: 15% lactose (week 2 after weaning)
  - Phase 3: Randomized to 0, 2.5%, 5%, 7.5%, 10% lactose (w 3 + 4 after weaning)
  - Corn substituted by equal amounts of permeate

Lactose to piglets during weaning

Cromwell et al. J Anim Sci 2008

Average daily weight gain and average daily feed intake increased linearly ($p<0.05$) with increasing levels of lactose in phase 3.

Highest lactose content

- 350 g of additional body weight
- 420 g additional feed intake

Does lactose have a positive effect on growth in undernourished children?

Percent of Energy from Lactose

- Human milk ≈40 E%
- Cows milk ≈25 E%
- F-100 16 E%
- RUTF up to 11 E%
- F-75 6 E%
- CSB++ 4 E%

Sources of lactose for food aid

Lactose in SMP and Whey

w/w%	SMP	WPC34	WPC80	WPI
Lactose	50	50	10	≈1

Permeate

Crystalline lactose

Conclusions on lactose

- Lactose intolerance can be a problem during initial treatment of children with SAM with GI problems
- Lactose content in breastmilk is high (≈40 E%); Infants and young children with MAM and SAM tolerate breastmilk well
- Lactose in foods to infants and young children is likely to have beneficial effects:
  - Modify microbiota – prebiotic effect
  - Increase mineral absorption
  - Improve energy density and taste
  - Improve dental health
  - Might increase growth? (piglets)

Conclusions on lactose

- Lactose content in foods for MAM and SAM can be increased by choosing protein sources with high content (WPC34 and SMP) or permeate
- Optimal amount of lactose need to be determined
- Guestimate:
  - 5 E%?
  - 15 E% as in F-100?
  - Higher and closer to breastmilk (40 E%)?

What are the growth components in milk?

- **Protein** – DSM and Whey
- **Lactose**
- **Minerals** – Permeate

- Bioactive peptides
- Less antinutrients

Golden MH Acta Paediatr Scand 1991; 374:94

Characteristics of nutritional deficiency

Type I nutrients

- Late or no growth response
- Tissue level variable
- Characteristic physical signs
- Stored in body
  - Selenium
  - Iron
  - Copper
  - Calcium
  - Retinol
  - Tocopherol
  - +others

Type II nutrients

- Immediate growth response
- Tissue level fixed
- No characteristic signs
- No body store
  - Nitrogen
  - Sulphur
  - Essential amino acids
  - Potassium
  - Sodium
  - Magnesium
  - Zinc
  - Phosphorus

Minerals for growth (type II)

High content of bioavailable minerals in cow's milk

- Potasium
- Phosphorus
- Zinc

SMP contains twice the amount of minerals compared to WPC34%

Low S-phosphate predicts death in malnourished children

Rytter et al. Risk factors for death in children during inpatient treatment of SAM: a prospective cohort study. AJCN 2017

Permeate

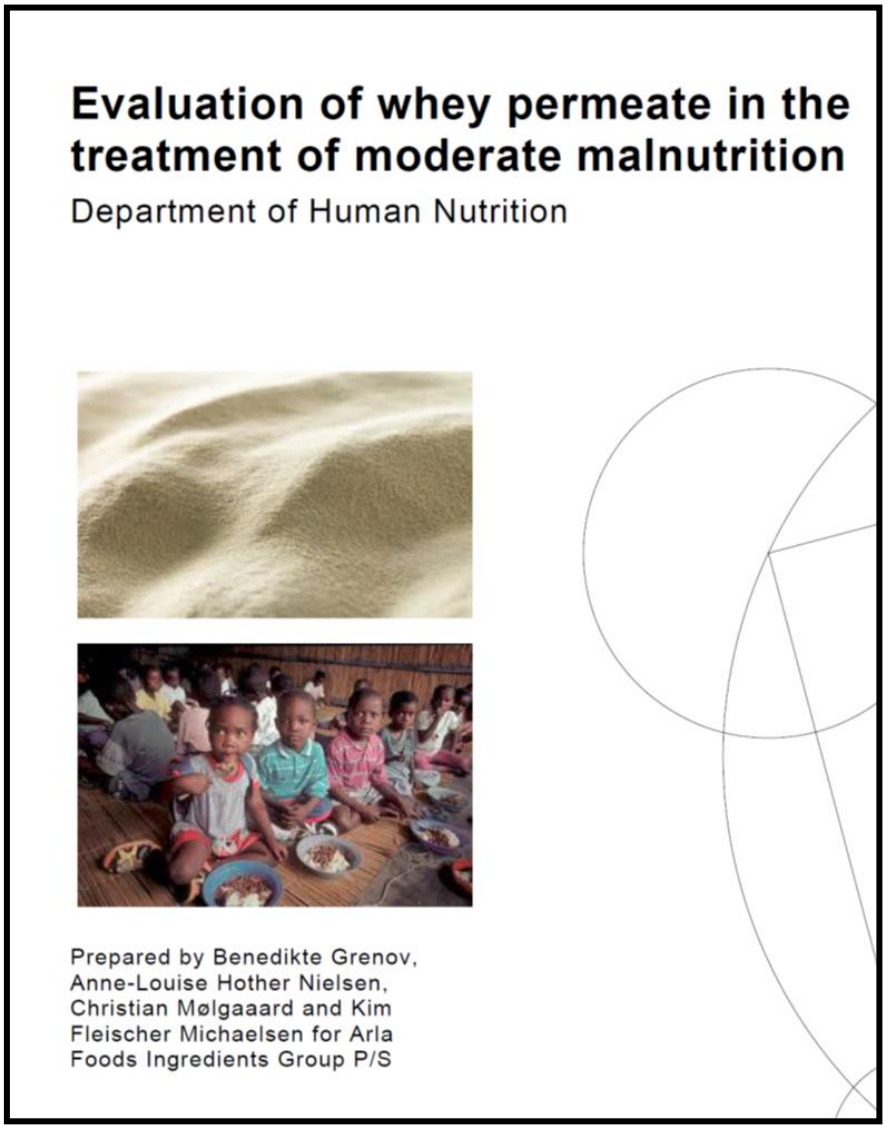
Milk

→ Cheese

Whey

→ Whey protein

Permeate



http://www.arlafoodsingredients.com

Permeate contains 85% lactose and minerals important for growth (type II)

Mg per 100 g powder	Permeate	Permeat content relative to SMP (%)
Potassium	1715	107
Magnesium	121	110
Phosphorus	636	67
Zinc	0.1	2
Calcium	554	45
Sodium	575	132

Variolac 850

Minerals in whey permeate and SMP

- Milk products contain important growth minerals including phosphate, magnesium and potassium
- High bioavailability
- Bioavailability might be increased through interaction with lactose
- Content should be adjusted to recommended levels in foods for MAM and SAM
- Relative high sodium content is a limitation in whey permeate – up to 20% w/w whey permeate in FBF seems to be OK

Cow's milk and..
Linear growth and stunting
Adult stature

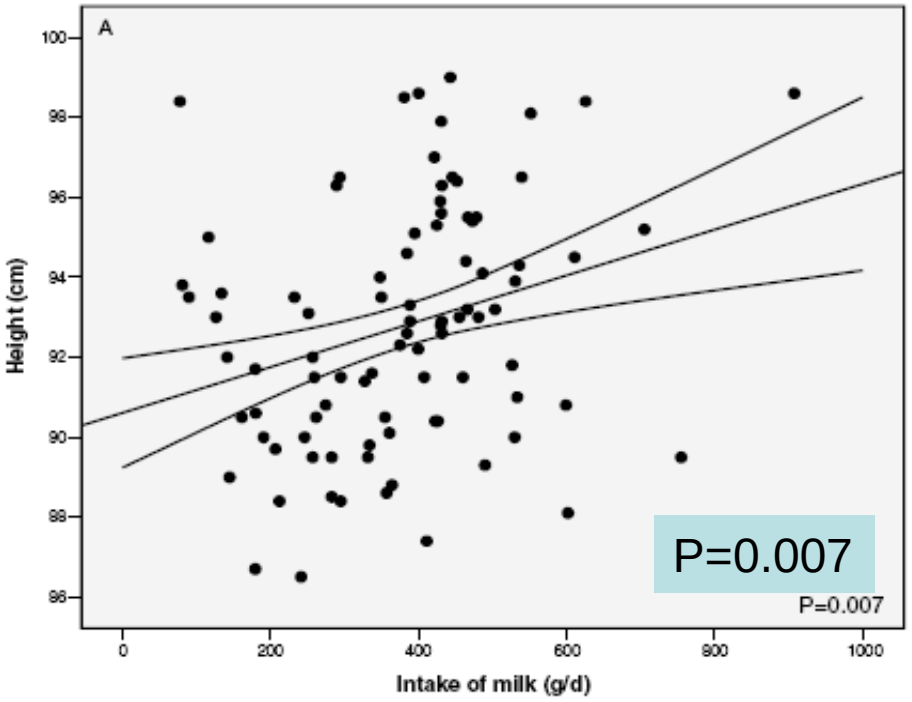
Cow's Milk and Linear Growth in Industrialized and Developing Countries

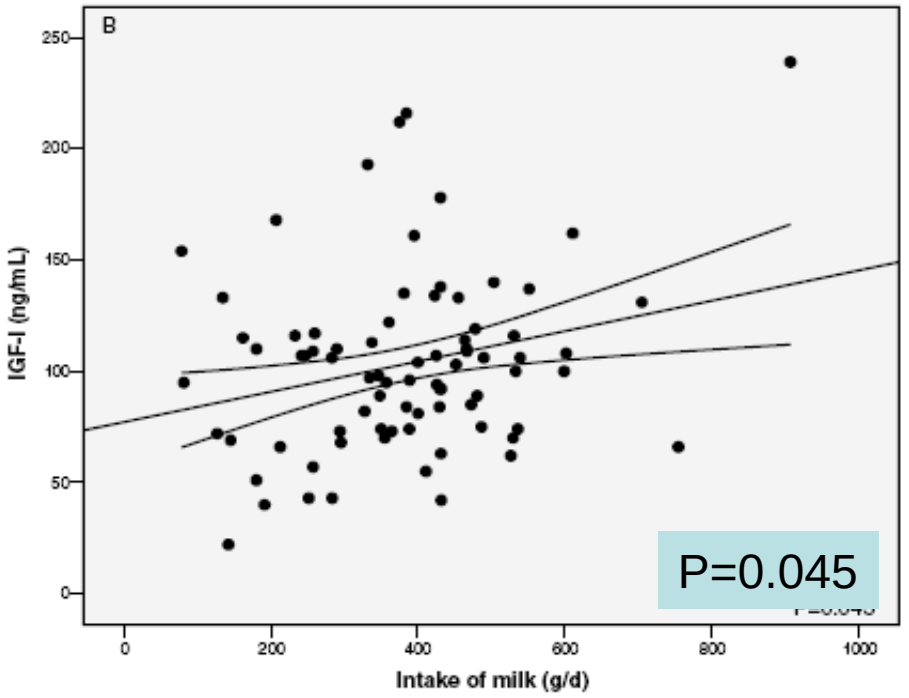
Hoppe. Mølgaard and Michaelsen. Annu Rev Nutr. 2006.

- The strongest evidence that cow's milk stimulates linear growth comes from observational and intervention studies in low-income countries
- Many observational studies from well-nourished populations also show an association between milk intake and linear growth
- These results suggest that milk has a growth-stimulating effect even in situations where the nutrient intake is adequate.

Strong evidence that cows milk stimulate linear growth

Height and serum IGF-I levels according to milk intake in 2.5 y old healthy children





95 % confidence intervals, controlled for sex and body weight

Hoppe et al, AJCN 2004

Continuing positive Secular Growth Change in The Netherlands 1955-1997

Fredriks et al, Ped Res 2000;47:316-23

Suggests that the explanation for the Dutch population being the tallest in the world could be a high consumption of dairy products, one of the highest in the world

Economics and Human Biology 10 (2012) 299–309

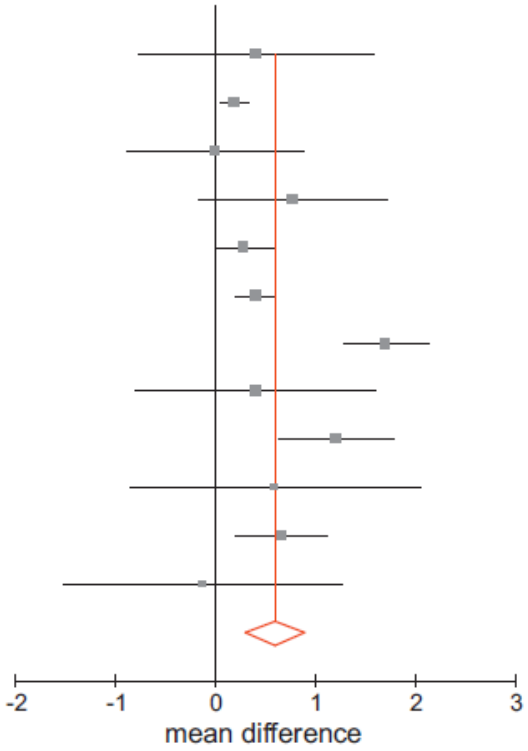
Review

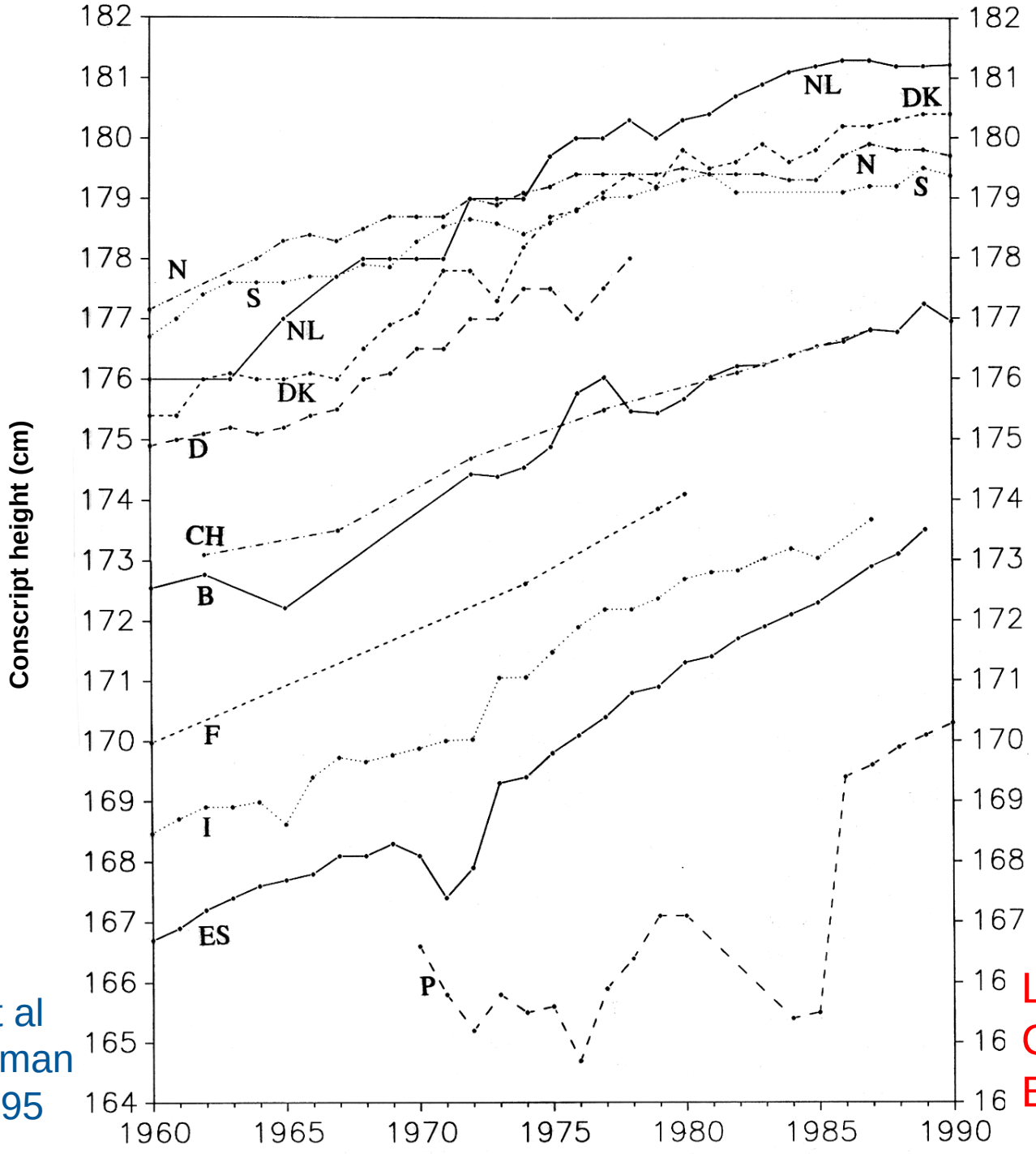
Dairy products and physical stature: A systematic review and meta-analysis of controlled trials

Hans de Beer *

245 ml milk daily results in an increase of 0.4 cm/y

Study ID	Year	Age (years)	Weight (%)	Association measure with 95% CI
Chan	1995	11.1	4,41%	0,4 (-0,7721 to 1,5721)
He	2005	3.3	14,26%	0,19 (0,0481 to 0,3319)
Grillenberger	2003	7.1	6,30%	0 (-0,8865 to 0,8865)
Morgan	1926	10	5,83%	0,78 (-0,1667 to 1,7267)
Baker	1980	8	12,91%	0,28 (-0,0088 to 0,5688)
Cheng	2005	11	13,87%	0,4 (0,2069 to 0,5931)
Lampl	1978	8-13	11,21%	1,7 (1,2696 to 2,1304)
Lien	2009	7-8	4,29%	0,4 (-0,7952 to 1,5952)
Du	2004	10	9,40%	1,2 (0,623 to 1,777)
Cadogan	1997	12	3,19%	0,6 (-0,8585 to 2,0585)
Aykroyd	1937	12	10,88%	0,66 (0,2039 to 1,1161)
Bailey	1962	7-13	3,45%	-0,13 (-1,5152 to 1,2552)
META-ANALYSIS:			100%	0,5888 (0,2949 to 0,8828)





NL: 320L
DK: 295L
N: 261L
S: 355L

F: 260L
I: 256L
ES: 177L

P: 222L

L/capita/year
ChartsBin.com
Bernhard Watzl

Schmidt et al
Annals Human
Biology 1995

eLIFE 2016

A century of trends in adult human height

NCD Risk Factor Collaboration (NCD-RisC)*

1472 population-based studies, with more than 18.6 million participants born between 1896 and 1996 in 200 countries

Tallest men

1. Netherlands – 182.5 cm
2. Belgium
3. Estonia
4. Latvia
5. Denmark

Tallest women

1. Latvia – 170.0 cm
2. Netherlands
3. Estonia
4. Czech Republic
5. Serbia

Shortest

East Timor – 160 cm

Guatemala – 149 cm

Authors: 800+ – 9 pages

(Instituto Mexicano del Seguro Social, Mexico)*; Robert Adams (The University of Adelaide, Australia)*; Wichai Aekplakorn (Mahidol University, Thailand)*; Carlos A Aguilar-Salinas (Instituto Nacional de Ciencias Médicas y Nutricion, Mexico)*; Charles Agyemang (University of Amsterdam, The Netherlands)*; Alireza Ahmadvand (Non-Communicable Diseases Research Center, Iran)*; Wolfgang Ahrens (Leibniz Institute for Prevention Research and Epidemiology - BIPS, Germany)*; Hazzaa M Al-Hazzaa (King Saud University, Saudi Arabia)*; Amani Rashed Al-Othman (Kuwait Institute for Scientific Research, Kuwait)*; Rajaa Al Raddadi (Ministry of Health, Saudi Arabia)*; Mohamed M Ali (World Health Organization Regional Office for the Eastern Mediterranean, Egypt)*; Ala'a Alkerwi (Luxembourg Institute of Health, Luxembourg)*; Mar Alvarez-Pedrerol (ISGlobal Centre for Research in Environmental Epidemiology, Spain)*; Eman Aly (World Health Organization Regional Office for the Eastern Mediterranean, Egypt)*; Philippe Amouyel (Lille University and Hospital, France)*; Antoinette Amuzu (London School of Hygiene & Tropical Medicine, UK)*; Lars Bo Andersen (Sogn and Fjordane University College, Norway)*; Sigmund A Anderssen (Norwegian School of Sport Sciences, Norway)*; Ranjit Mohan Anjana (Madras Diabetes Research Foundation, India)*; Hajer Aounallah-Skhiri (National Institute of Public Health, Tunisia)*; Inger Ariansen (Norwegian Institute of Public Health, Norway)*; Tahir Aris (Ministry of Health Malaysia, Malaysia)*; Nimmathota Arlappa (Indian Council of Medical Research, India)*; Dominique Arveiler (University of Strasbourg and Strasbourg University Hospital, France)*; Felix K Assah (University of Yaoundé 1, Cameroon)*; Mária Avdicová (Regional Authority of Public Health, Banska Bystrica, Slovakia)*; Fereidoun Azizi (Shahid Beheshti University of Medical Sciences, Iran)*; Bontha V Babu (Indian Council of Medical Research, India)*; Suhad Bahijri (King Abdulaziz University, Saudi Arabia)*; Nagalla Balakrishna (Indian Council of Medical Research, India)*; Piotr Bandosz (Medical University of Gdansk, Poland)*; José R Banegas (Universidad Autónoma de Madrid, Spain)*; Carlo M Barbagallo (University of Palermo, Italy)*; Alberto Barceló (Pan American Health Organization, USA)*; Amina Barkat (Mohammed V University de Rabat, Morocco)*; Mauro V Barros (University of Pernambuco, Brazil)*; Iqbal Bata (Dalhousie University, Canada)*; Anwar M Batieha (Jordan University of Science and Technology, Jordan)*; Rosangela L Batista (Federal University of Maranhao, Brazil)*; Louise A Baur (University of Sydney, Australia)*; Robert Beaglehole (University of Auckland, New Zealand)*; Habiba Ben Romdhane (University Tunis El Manar, Tunisia)*; Mikhail Benet (University Medical Science, Cuba)*; James E Bennett (Imperial College London, UK)*; Antonio Bernabe-Ortiz (Universidad Peruana Cayetano Heredia, Peru)*; Gailute Bernotiene (Lithuanian University of Health Sciences, Lithuania)*; Heloisa Bettiol (University of São Paulo, Brazil)*; Aroor Bhagyalaxmi (B. 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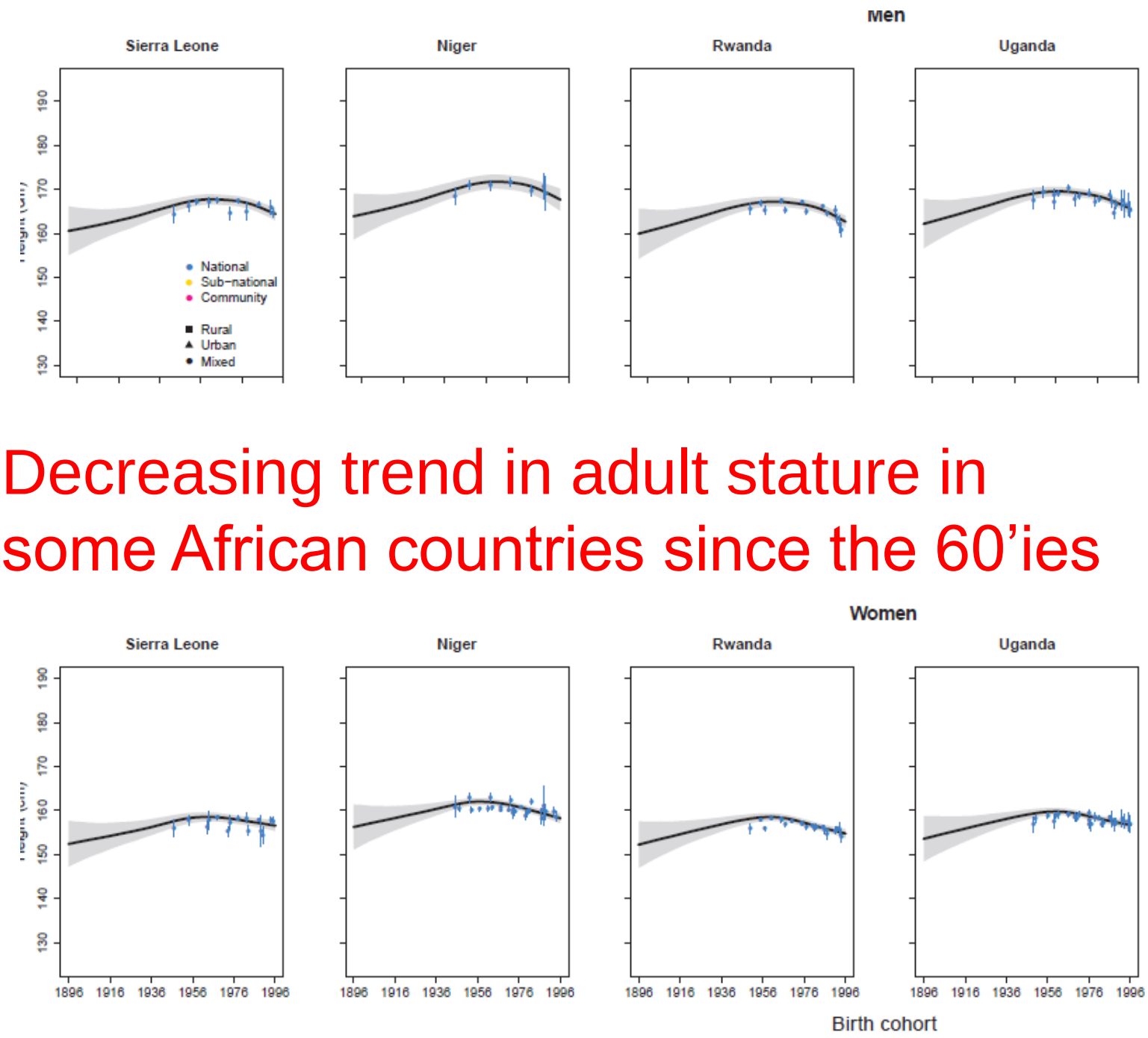


Decreasing trend in adult stature in some African countries since the 60'ies

Major correlates of male height: A study of 105 countries

P. Grasgruber *, M. Sebera, E. Hrazdíra, J. Cacek, T. Kalina

Faculty of Sports Studies, Masaryk University, Kamenice 5, 625 00 Brno, Czech Republic

Economics and Human Biology 2016

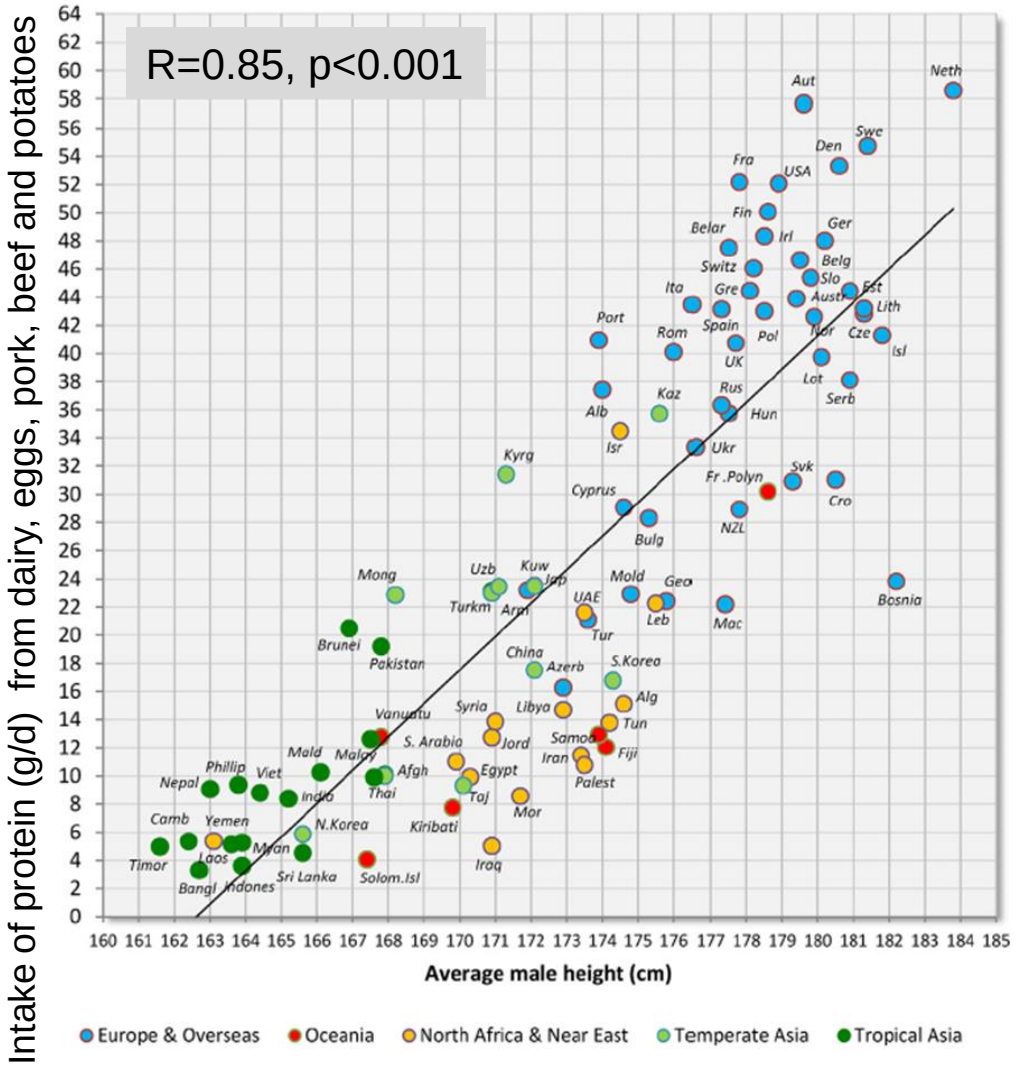
Three "fundamental" types of diet

Dairy and animal protein
Europe and the US

Wheat
North Africa and Near East

Rice
Tropical Asia

Causality?



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