

# Nutrition and Maternal & Child Health: An Overview

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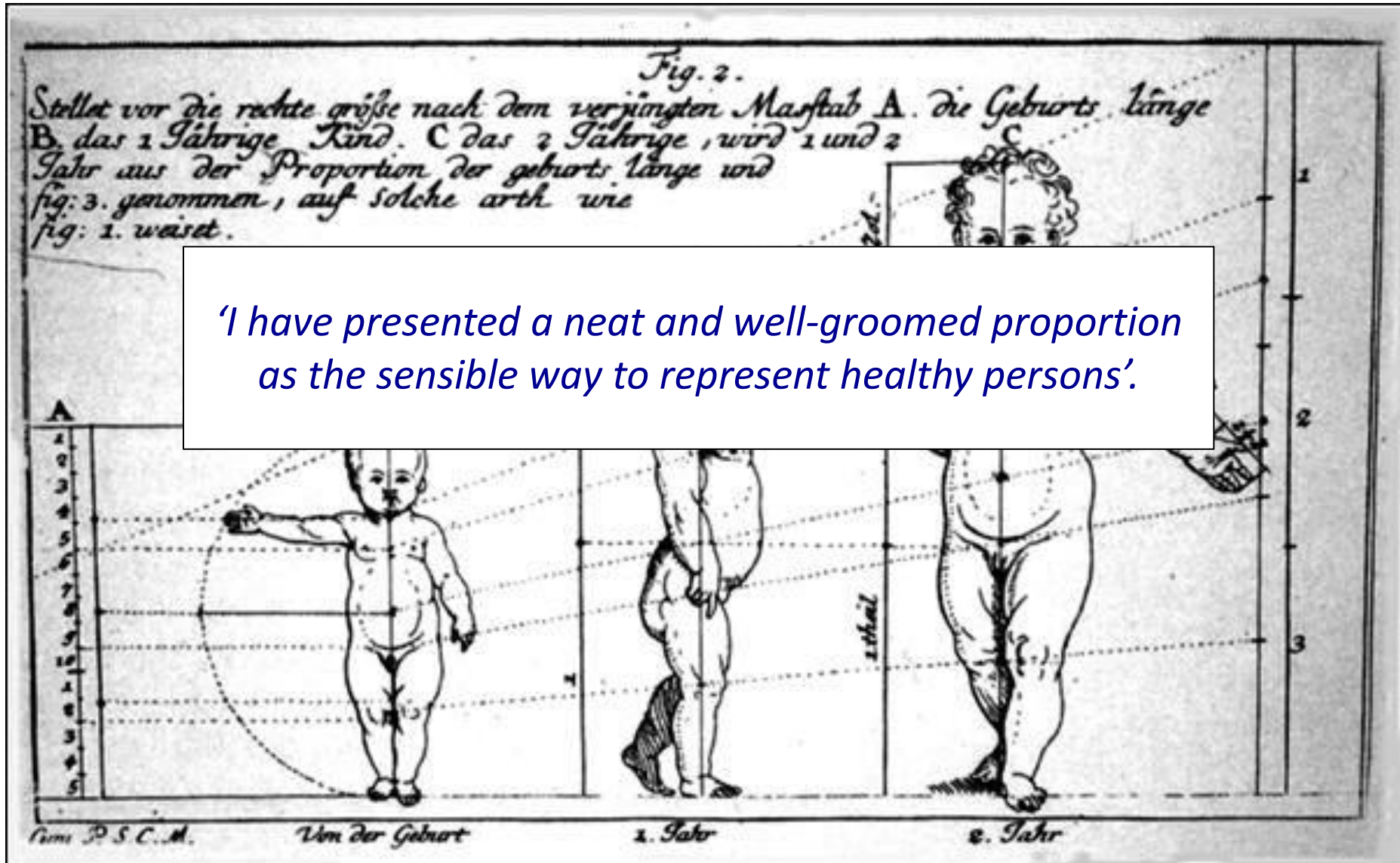


Oxford Maternal & Perinatal  
Health Institute  
Green Templeton College





# Geometric laws governing growth of the child





A Medical Historical Investigation of Human Growth in Length, being what Doctors as well as all Growing and Grown-up People should know about its Natural Properties and Conditions.

Johann Augustin Stöller (1729)

Dedicated to Frederick-William I

*‘Growth in length stems principally from linear extension of the skeleton, and comes under the heading of nutrition’.*

Georges-Louis Leclerc  
Comte de Buffon  
(1707-88)



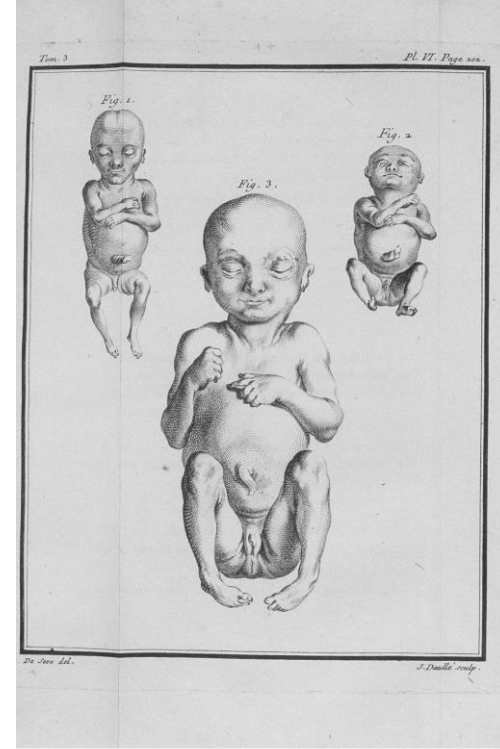
HISTOIRE  
NATURELLE,  
GENERALE ET PARTICULIERE,  
AVEC LA DESCRIPTION  
DU CABINET DU ROY.

*Tom. Premier.*

TROISIEME EDITION.



A PARIS,  
DE L'IMPRIMERIE ROYALE.  
M. DCCL



Source gallica.bnf.fr / Bibliothèque nationale de France

*'All diseases which proceed from vitiated humours may be communicated from the mother to the fetus.'*

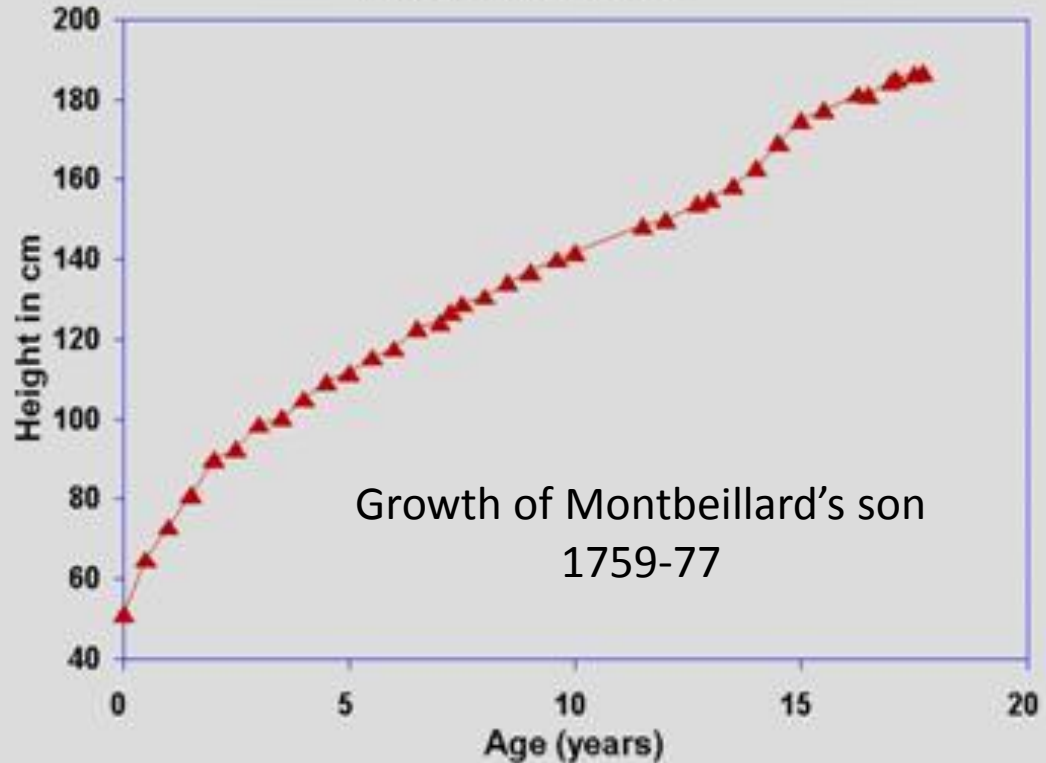
Georges-Louis Leclerc  
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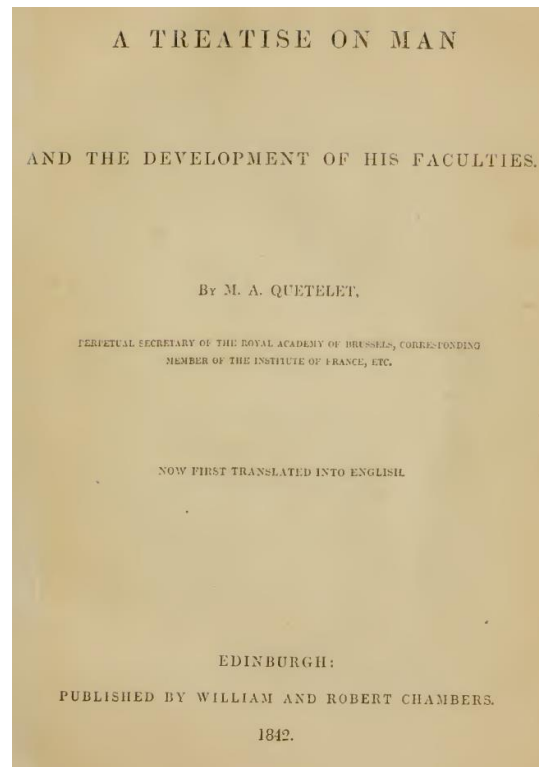


Human Longitudinal Growth  
Montbeillard-Buffon

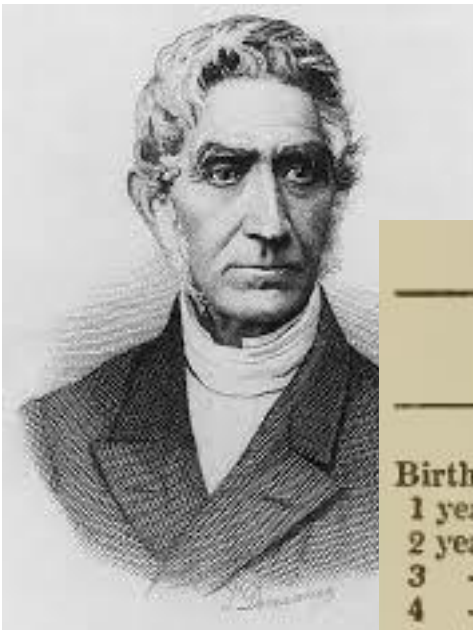




**Adolphe Quetelet**  
**1796 - 1874**



*'Affluence, abundance of food, and moderate exercise, favourably assist the development of the physical powers .... The man who finds himself in affluent circumstances possesses the advantages of longer life and less liability to disease; he has also better opportunities for the proper development of his physical qualities'.*



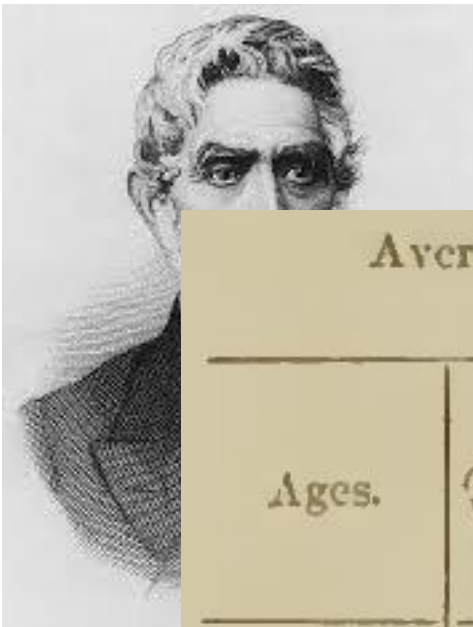
Adolphe Quetelet  
1796 - 1874

A TREATISE ON MAN

AND THE DEVELOPMENT OF HIS FACULTIES.

Table showing the rate of Growth in the two Sexes.

Ages.				Boys.	Girls.	Difference.
				metres.	metres.	metres.
Birth,	-	-	-	0.500	0.490	0.010
1 year,	-	-	-	0.698	..	..
2 years,	-	-	-	0.796	0.780	0.016
3 ..	-	-	-	0.867	0.853	0.014
4 ..	-	-	-	0.930	0.913	0.017
5 ..	-	-	-	0.986	0.978	0.008
6 ..	-	-	-	1.045	1.035	0.010
7 ..	-	-	-	..	1.091	..
8 ..	-	-	-	1.160	1.154	0.006
9 ..	-	-	-	1.221	1.205	0.016
10 ..	-	-	-	1.280	1.256	0.024
11 ..	-	-	-	1.334	1.286	0.048
12 ..	-	-	-	1.384	1.340	0.044
13 ..	-	-	-	1.431	1.417	0.014
14 ..	-	-	-	1.489	1.475	0.014
15 ..	-	-	-	1.549	1.496	0.053
16 ..	-	-	-	1.600	1.518	0.082
17 ..	-	-	-	1.640	1.553	0.087
18 ..	-	-	-	..	1.564	..
19 ..	-	-	-	1.665	1.570	0.095
20 ..	-	-	-	..	1.574	..
Growth terminated,	-	-	-	1.684	1.579	0.105



A TREATISE ON MAN

AND THE DEVELOPMENT OF HIS FACULTIES.

Average Stature of Children of the Lower Orders,  
at Manchester and Stockport.†

Ages.	Boys		Girls	
	Working in Factories.	not Working in Factories.	Working in Factories.	not Working in Factories.
	metres.	metres.	metres.	metres.
9 years,	1·222	1·233	1·218	1·230
10 ..	1·270	1·286	1·260	1·254
11 ..	1·302	1·296	1·290	1·323
12 ..	1·355	1·345	1·364	1·363
13 ..	1·383	1·396	1·413	1·399
14 ..	1·437	1·440	1·467	1·479
15 ..	1·515	1·474	1·486	1·502
16 ..	1·565	1·605	1·521	1·475
17 ..	1·592	1·627	1·535	1·542
18 ..	1·608	1·775	1·593	1·645

Adolphe  
179

## Fat-free, skeletal markers best indicators of nutritional status

Head circumference

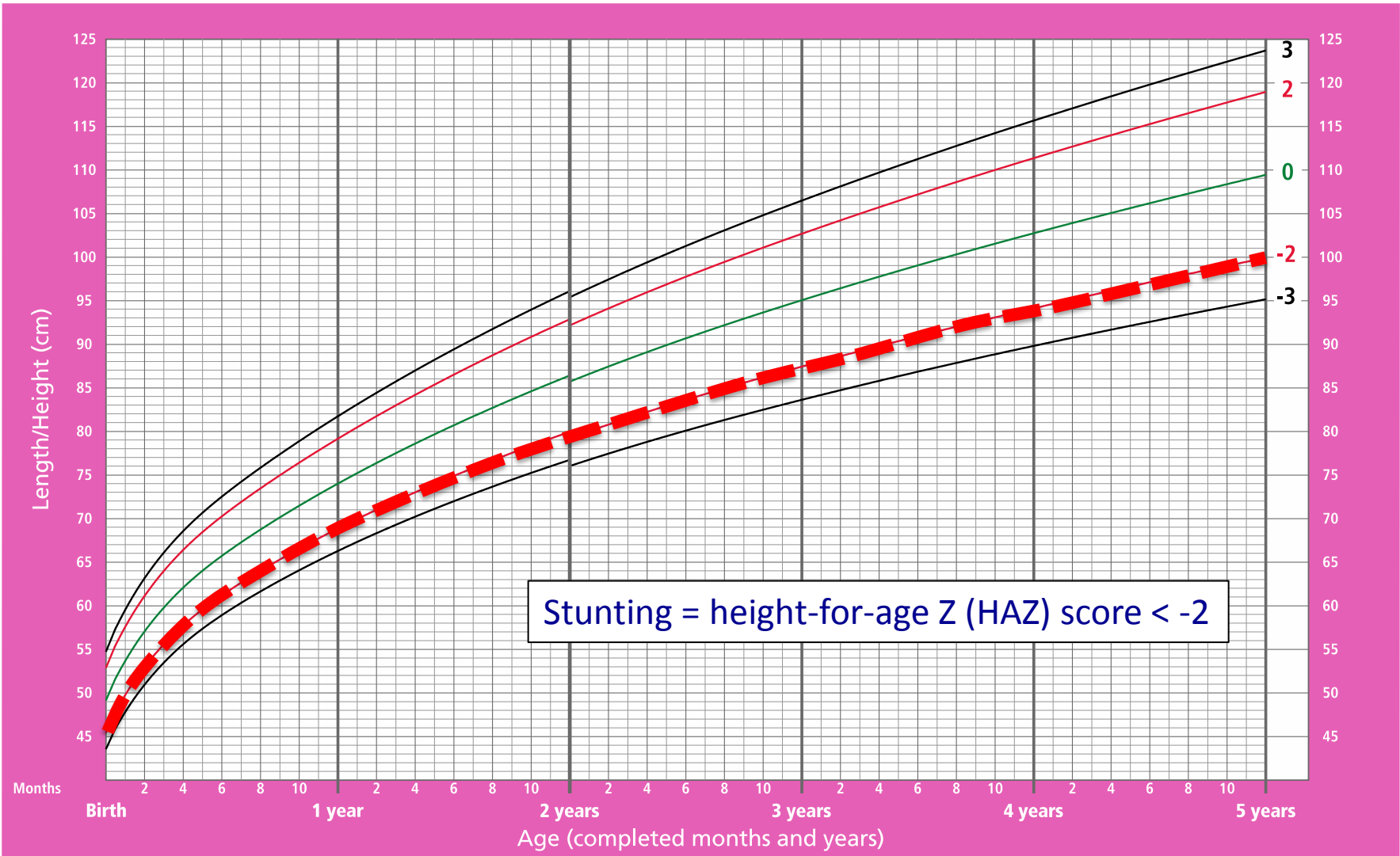


Length/height



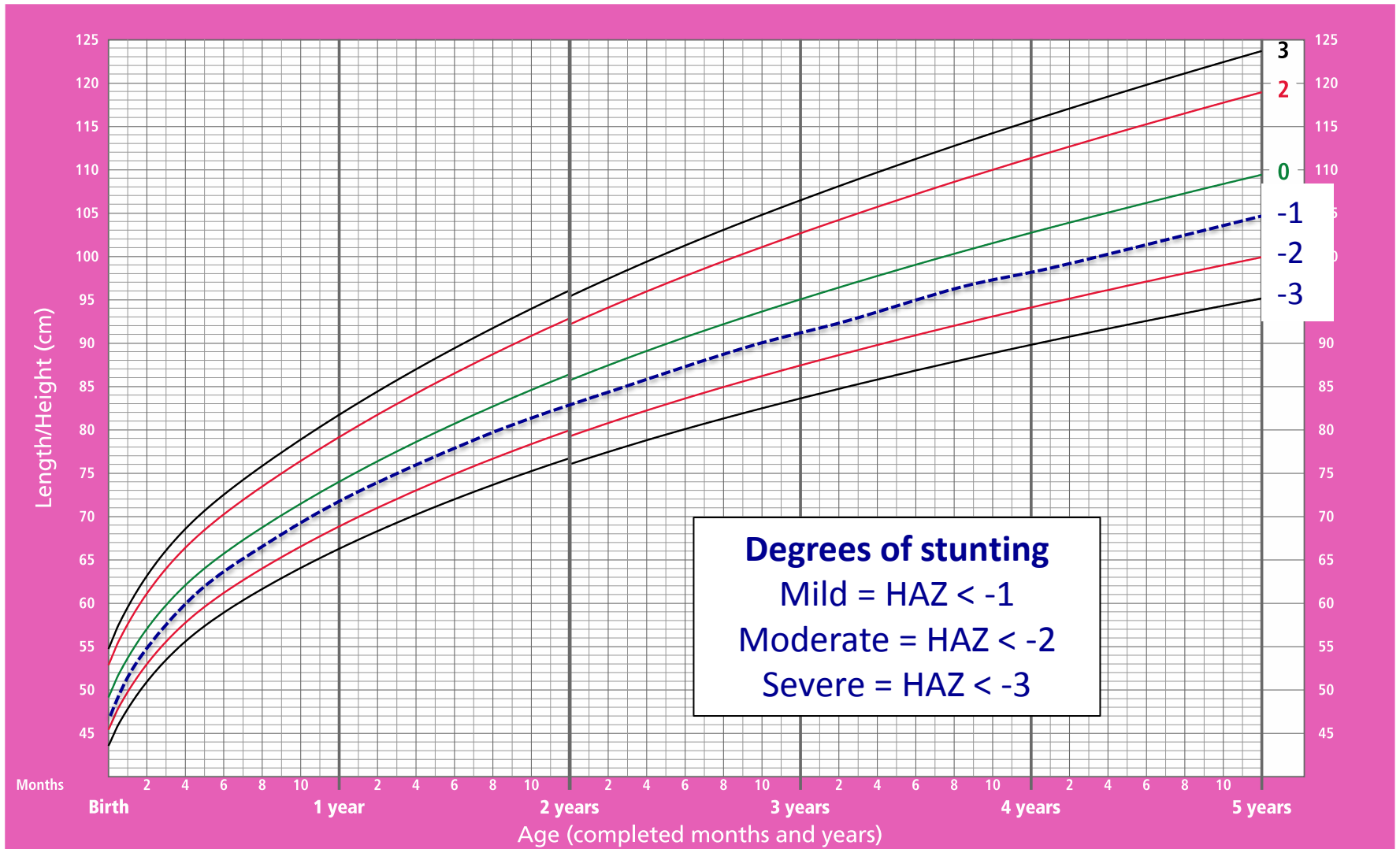
# Length/height-for-age GIRLS

Birth to 5 years (z-scores)



# Length/height-for-age GIRLS

Birth to 5 years (z-scores)



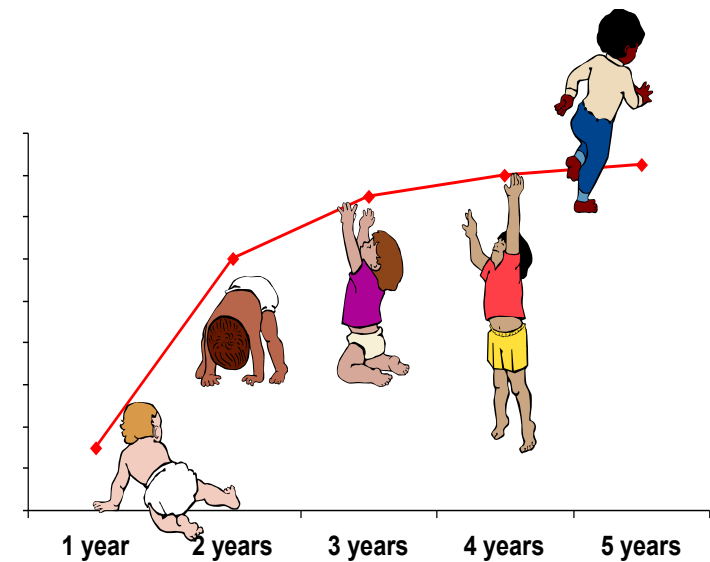
# WHO Multicentre Growth Reference Study (MGRS)

To build a set of growth curves for children < 5 as an international, 'prescriptive' standard to assess growth and development of populations and individual children



# WHO Child Growth Standards

de Onis et al. *Acta Paediatr* 2006;450:1-101



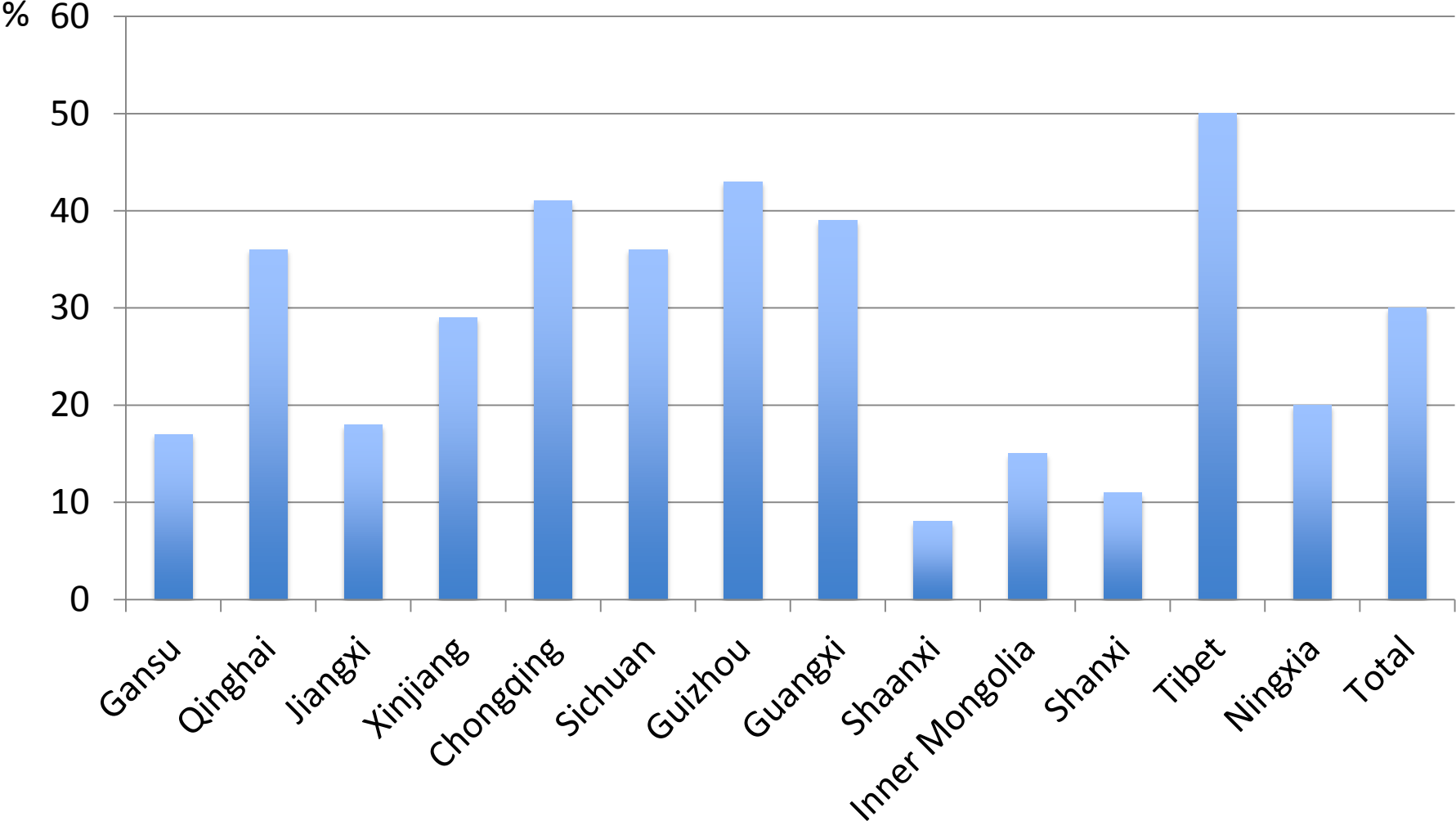
*‘The new growth standards are referable to all children everywhere, clearly show that all children in the world can and should grow equally well, and also demonstrate that in today’s world adequate nutrition, environment, and health are stronger determinants of growth than are gender or ethnicity’.*



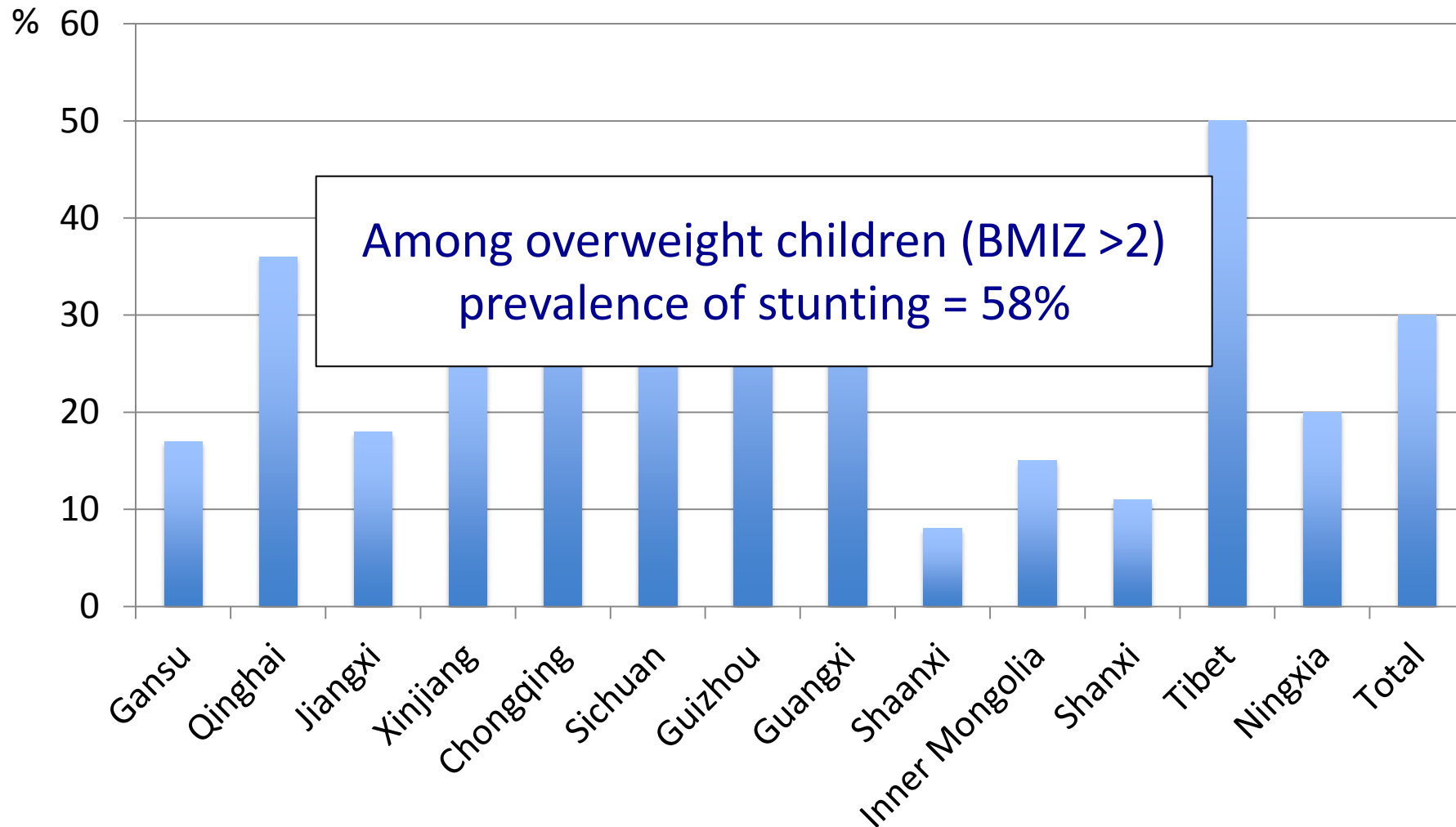
international pediatric association  
association internationale de pédiatrie  
asociación internacional de pediatria

20<sup>th</sup> April 2006

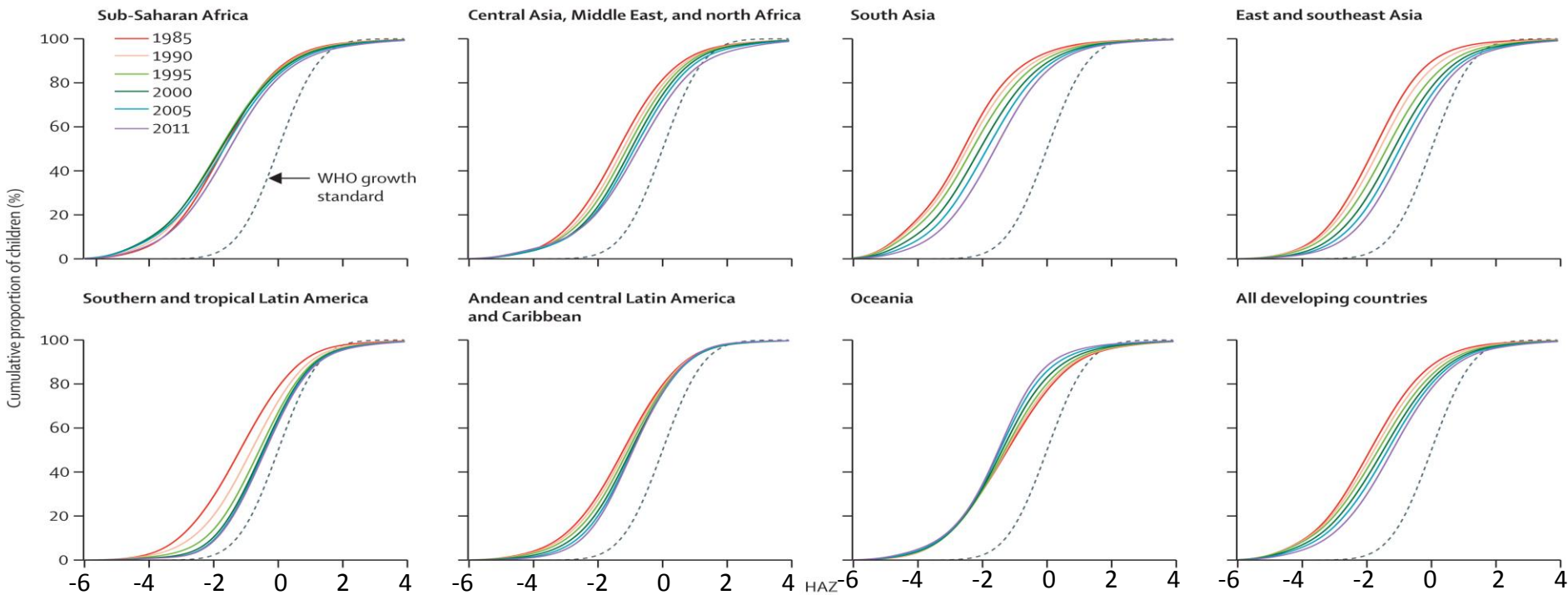
# Prevalence of stunting (HAZ < -2) in children <5 in rural mid-western China assessed using WHO Child Growth Standards



## Prevalence of stunting (HAZ < -2) in children <5 in rural mid-western China assessed using WHO Child Growth Standards



# Trends in the cumulative distribution functions for height-for-age Z (HAZ) scores by region - Progress towards MDG 1 in 141 developing countries: a systematic analysis of population representative data

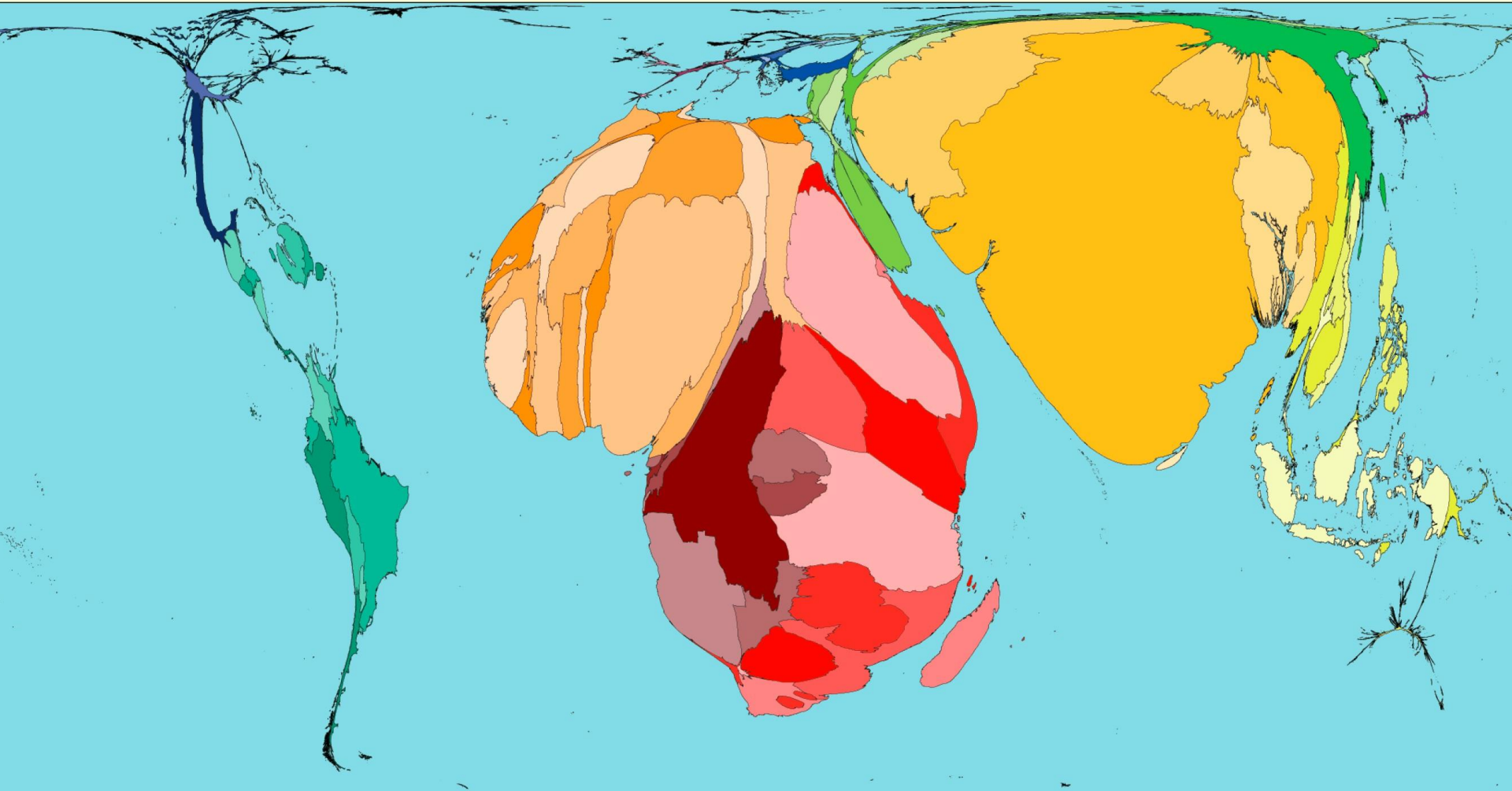


In developing countries, mean HAZ improved from -1.86 in 1985 to -1.16 in 2011

In 2011, 314 million children <5 years old were mildly, moderately or severely stunted



## Early neonatal deaths



# Child mortality due to nutritional disorders

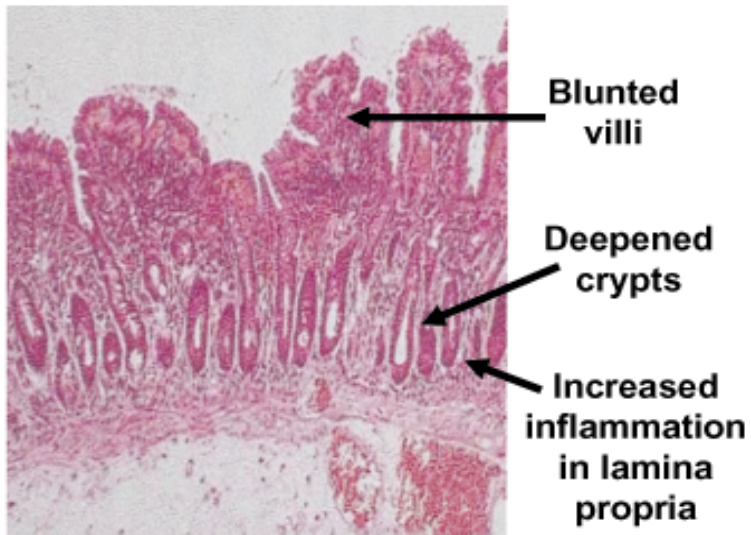
Nutritional disorders	Attributable deaths with UN prevalences	Proportion of total deaths of children < 5 years
Fetal growth restriction (<1 month)	817,000	11.8%
Stunting (1-5 years)	1,017,000	14.7%
Underweight (1-5 years)	999,000	14.4%
Wasting (1-5 years)	875,000	12.6%
Severe Wasting (1-5 years)	516,000	7.4%
Zinc deficiency (1-5 years)	116,000	1.7%
Vitamin A deficiency (6 months - 5 years)	157,000	2.3%
Suboptimal breastfeeding (0 - 2 years)	804,000	11.6%
<b>Joint effect all nutritional disorders above</b>	<b>3,097,000</b>	<b>44.7%</b>

## In association with infectious diseases, stunting increases the hazard of death

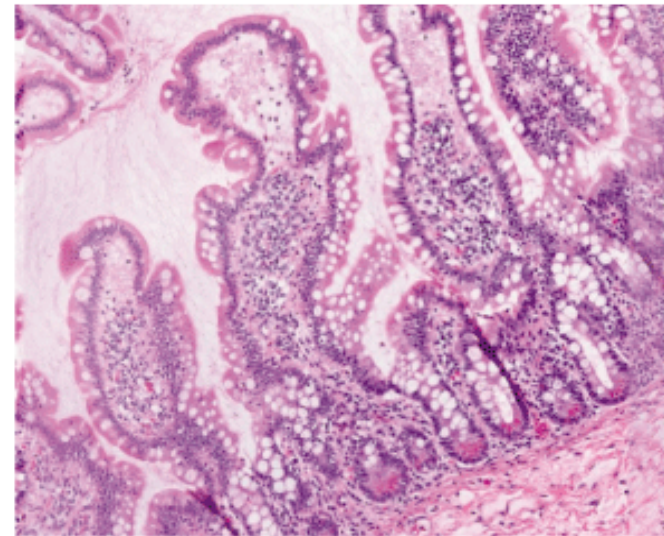
Height/Length-for-Age Z-Score	All Deaths HR (95% CI)	Pneumonia HR (95% CI)	Diarrhoea HR (95% CI)	Measles HR (95% CI)	All others HR (95% CI)
> -1	1.0	1.0	1.0	1.0	1.0
-1 to -2	1.5 (1.2, 1.7)	1.6 (1.0, 2.4)	1.7 (1.2, 2.3)	1.3 (0.6, 2.6)	0.9 (0.5, 1.9)
-2 to -3	2.3 (1.9, 2.7)	2.2 (1.4, 3.4)	2.4 (1.7, 3.3)	2.8 (1.4, 5.6)	1.9 (1.0, 3.6)
< -3	5.5 (4.6, 6.5)	6.4 (4.2, 9.8)	6.3 (4.6, 8.7)	6.0 (3.0, 12.0)	3.0 (1.6, 5.8)

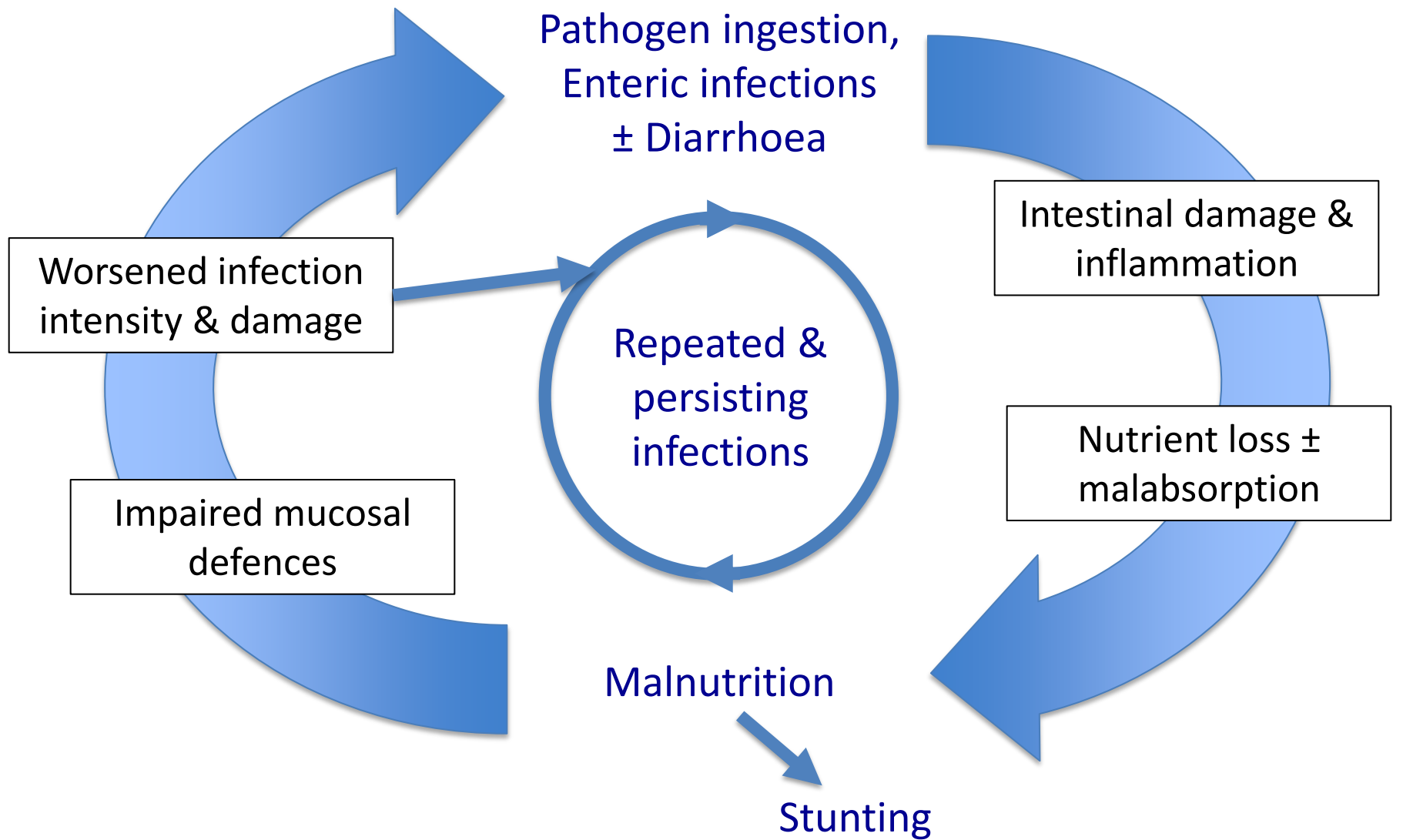
# The impoverished gut - a triple burden of diarrhoea, stunting & chronic disease

**A** Environmental enteropathy

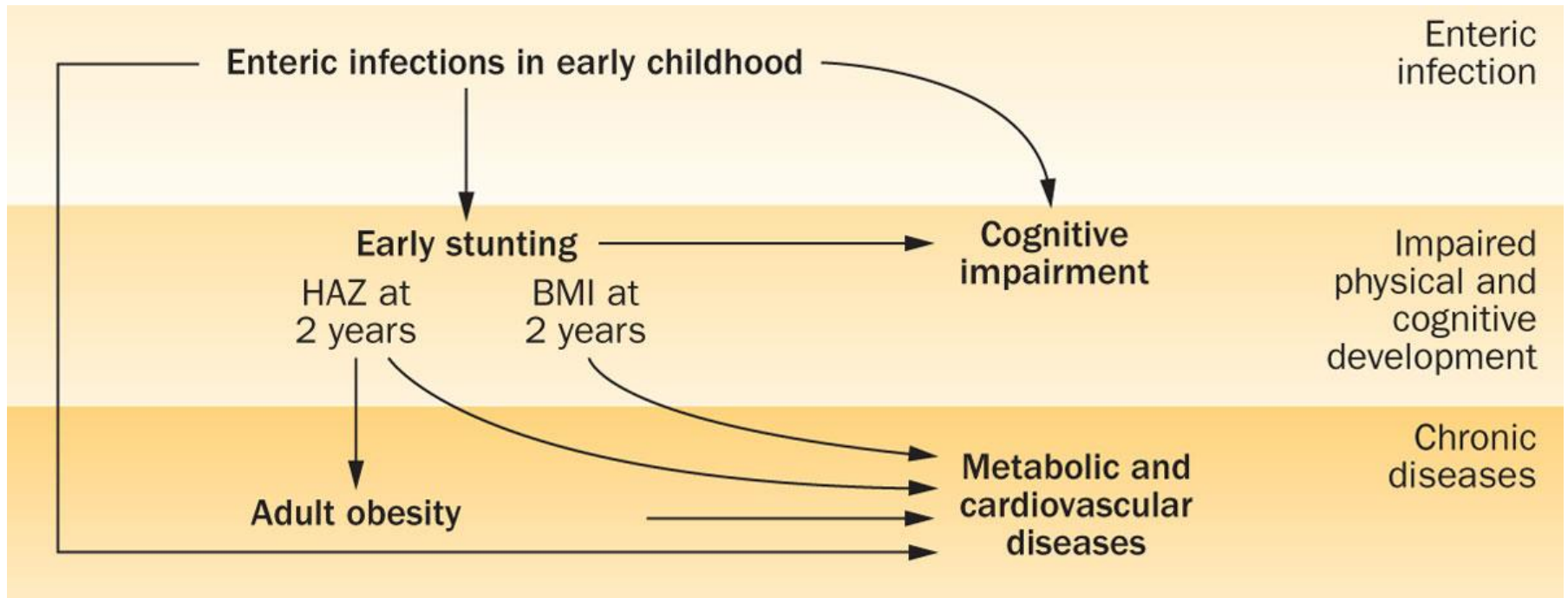


**B** Normal intestinal mucosa





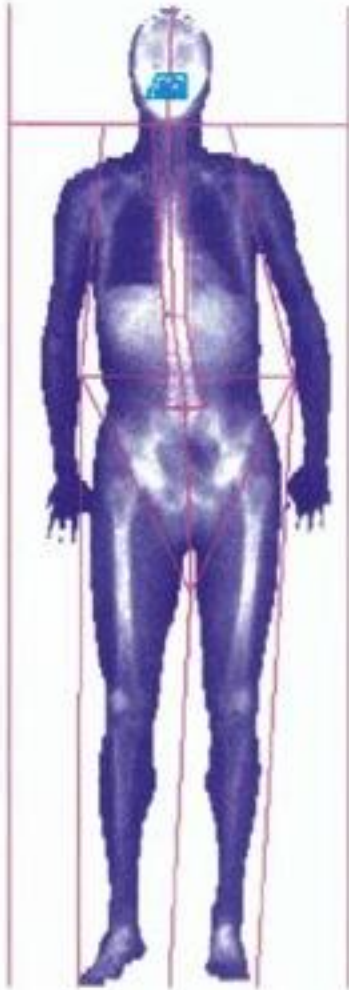
## Chronic sequelae of early childhood enteric infections and stunting



**BMI**

22.3

22.3



**Body fat**

9.1%

21.2%

*Lancet 2004*

**Suboptimal maternal-fetal nutritional environment**  
Maternal nutrient restriction, gestational diabetes, maternal obesity

Programming

**Mediated by epigenetic mechanisms**

**Cellular energy metabolism**  
Glucose handling, lipid metabolism, mitochondrial biogenesis

↑ Storage ↓ Oxidation

Critical windows: organogenesis



**Adipose tissue**

Excess lipid storage  
Lipolysis  
ER stress



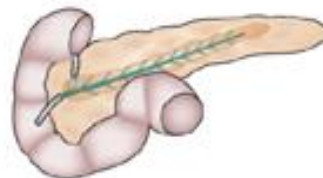
**Muscle**

Lipid accumulation



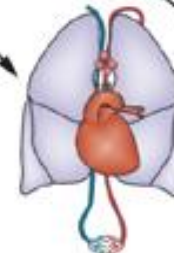
**Liver**

Gluconeogenesis  
Lipogenesis  
Lipid accumulation



**Pancreas**

Impaired glucose sensing  
Hyperinsulinism



**Cardiovascular system**

Fetal metabolism  
Lipid accumulation



**Brain**

Leptin resistance  
Lipid accumulation

Insulin resistance and/or  
type 2 mellitus diabetes

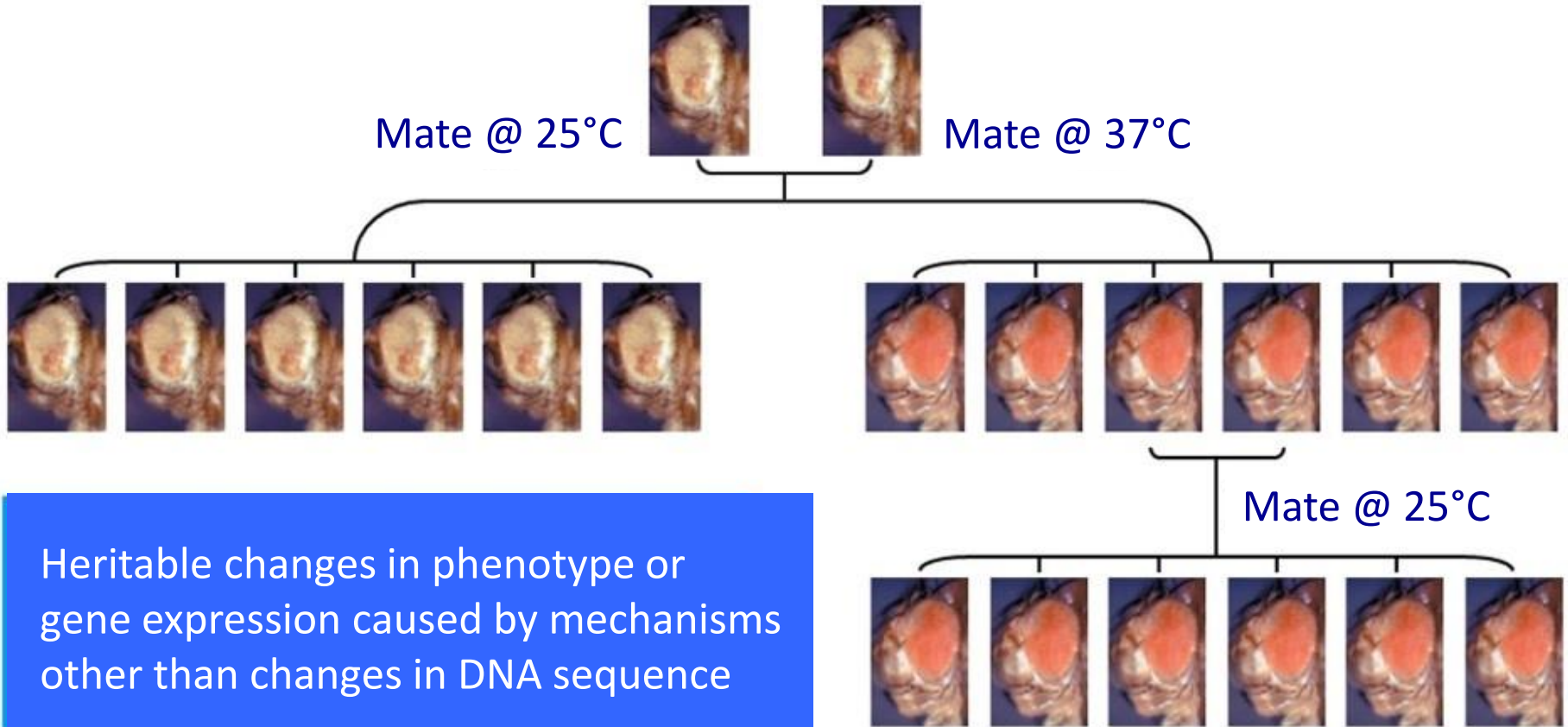
Hyperglycemia

Hyperinsulinemia

CVD

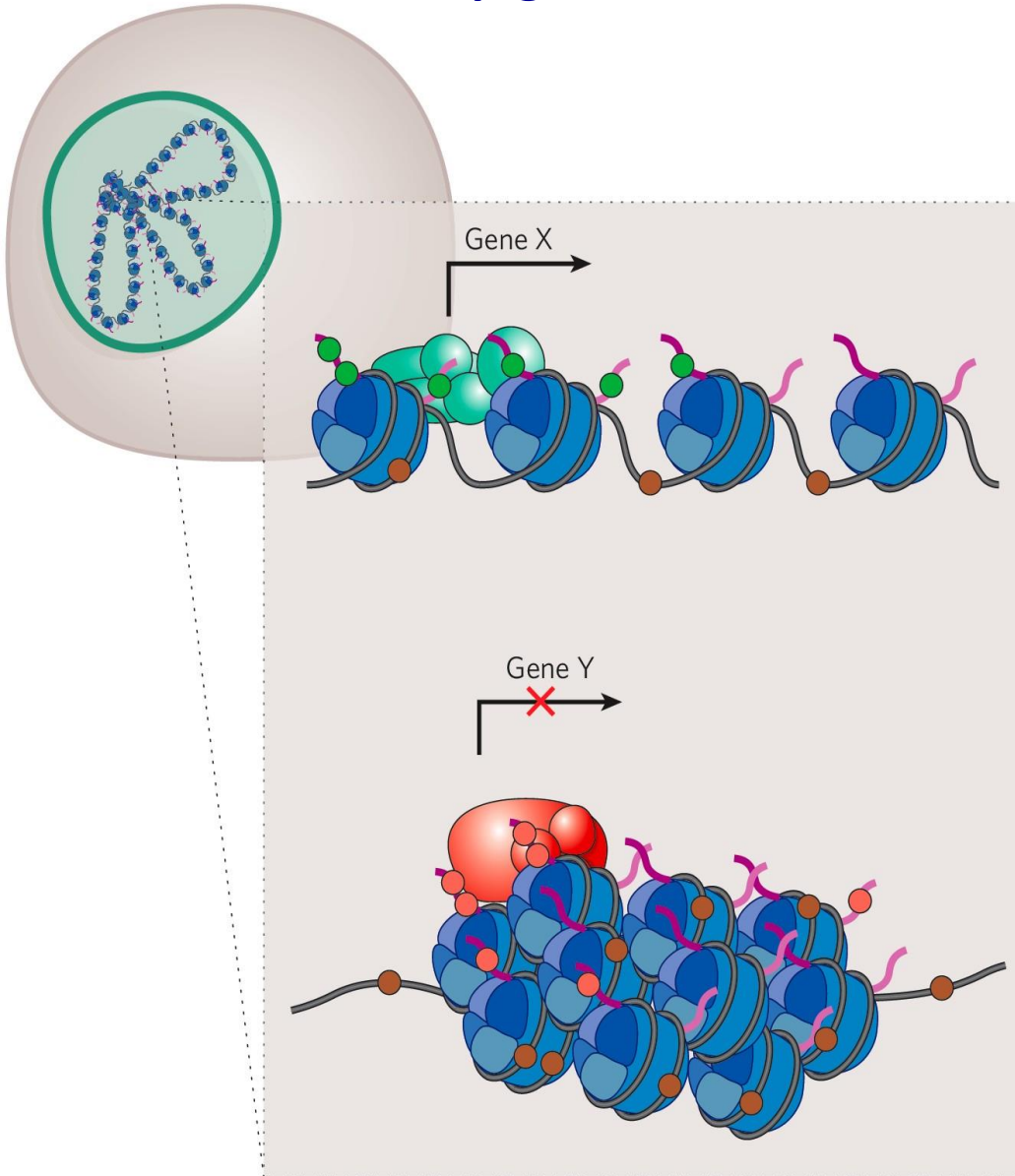
Obesity

Genetically identical fruit flies, white eyes



Heritable changes in phenotype or gene expression caused by mechanisms other than changes in DNA sequence

# Epigenetic function in normal cell



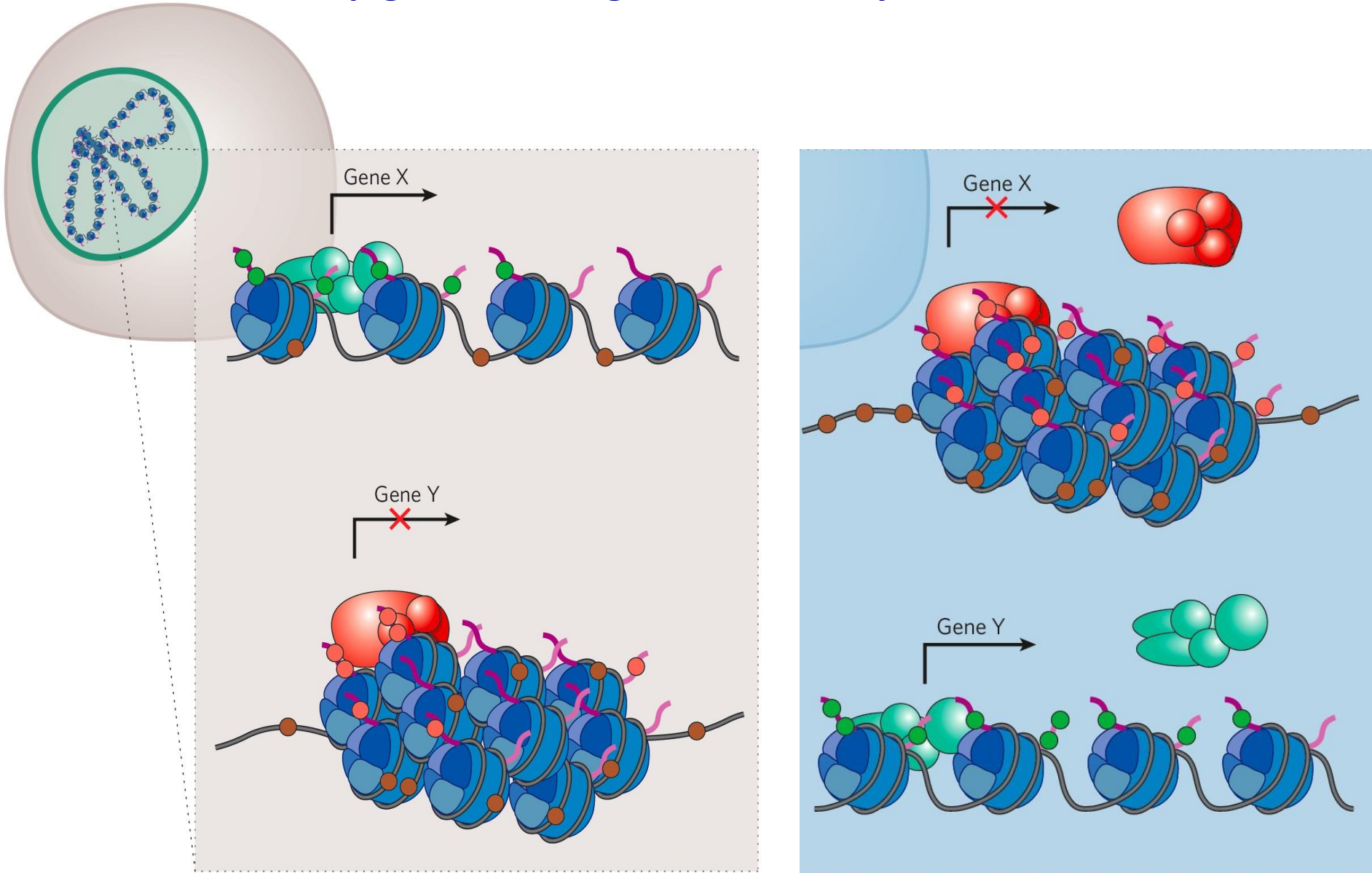
## Gene X active:

- open chromatin structure
- sparse methylation (brown circles)
- interaction with euchromatin proteins (green complex)
- positive histone modifications (green circles)

## Gene Y inactive:

- closed chromatin structure
- dense methylation (brown circles)
- interaction with heterochromatin proteins (red complex)
- negative histone modifications (pink circles)

# Epigenetic changes mediated by environmental factors





Agouti mRNA briefly made during development  
Agouti gene **silenced** remainder of mouse life

Healthy mouse with brown fur

Agouti gene **continually active**, producing mRNA throughout mouse life

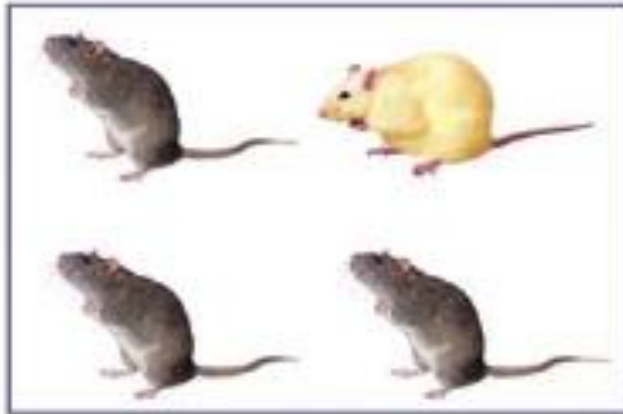
Mouse with yellow fur  
Develops diabetes and obesity in adulthood

Female yellow mouse (Agouti gene unmethylated and active)



Diet supplemented during pregnancy with methyl donors (e.g. folic acid, choline, vitamin B12 and betaine)

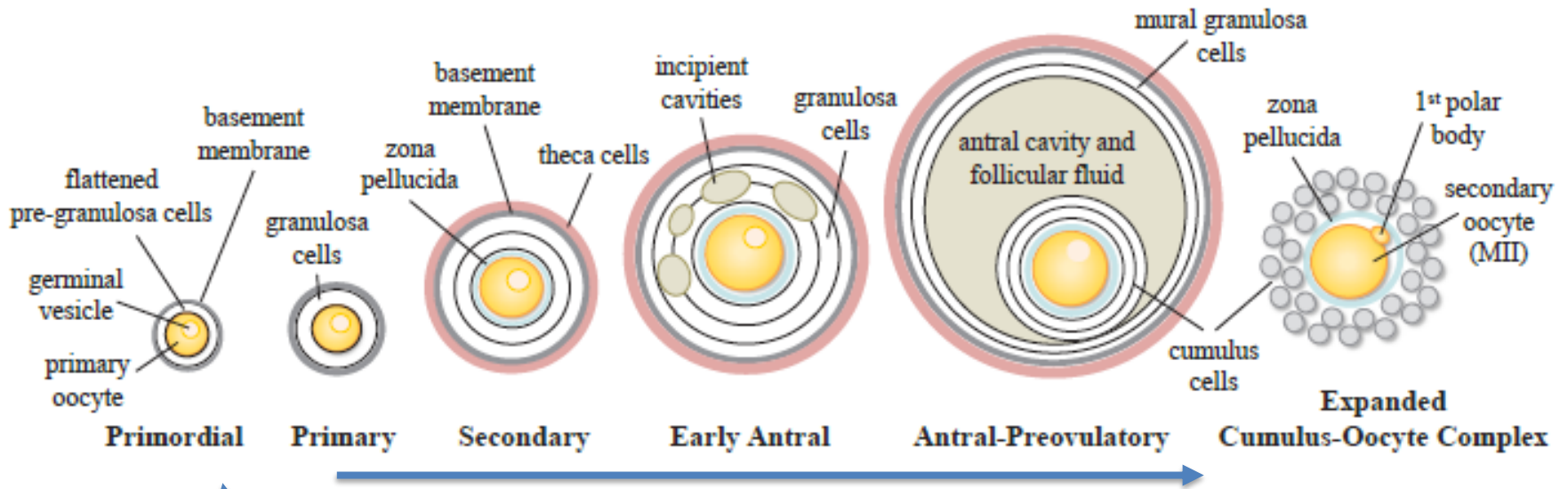
No dietary supplementation



Offspring mostly brown and healthy; Agouti gene methylated and silenced

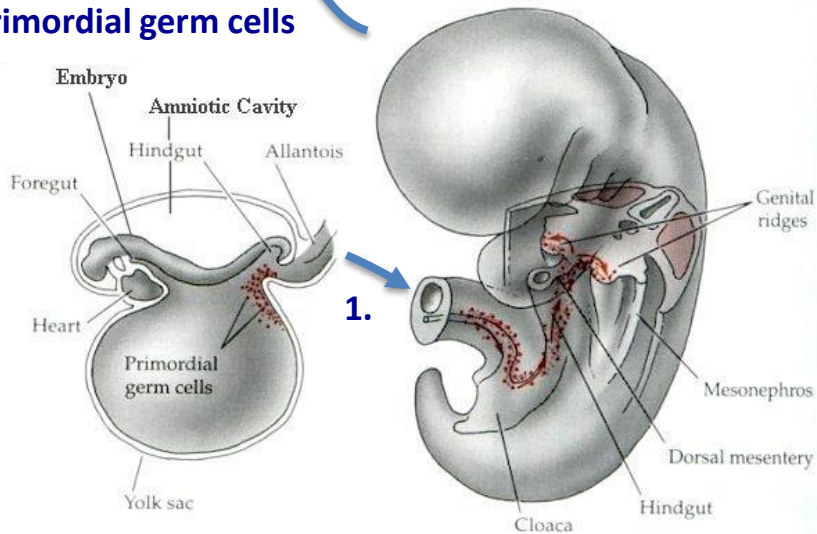


Offspring mostly yellow and unhealthy; Agouti gene unmethylated and active



**3. Folliculogenesis and oocyte growth**

**2. Proliferation of primordial germ cells**



**1. Migration of primordial germ cells**

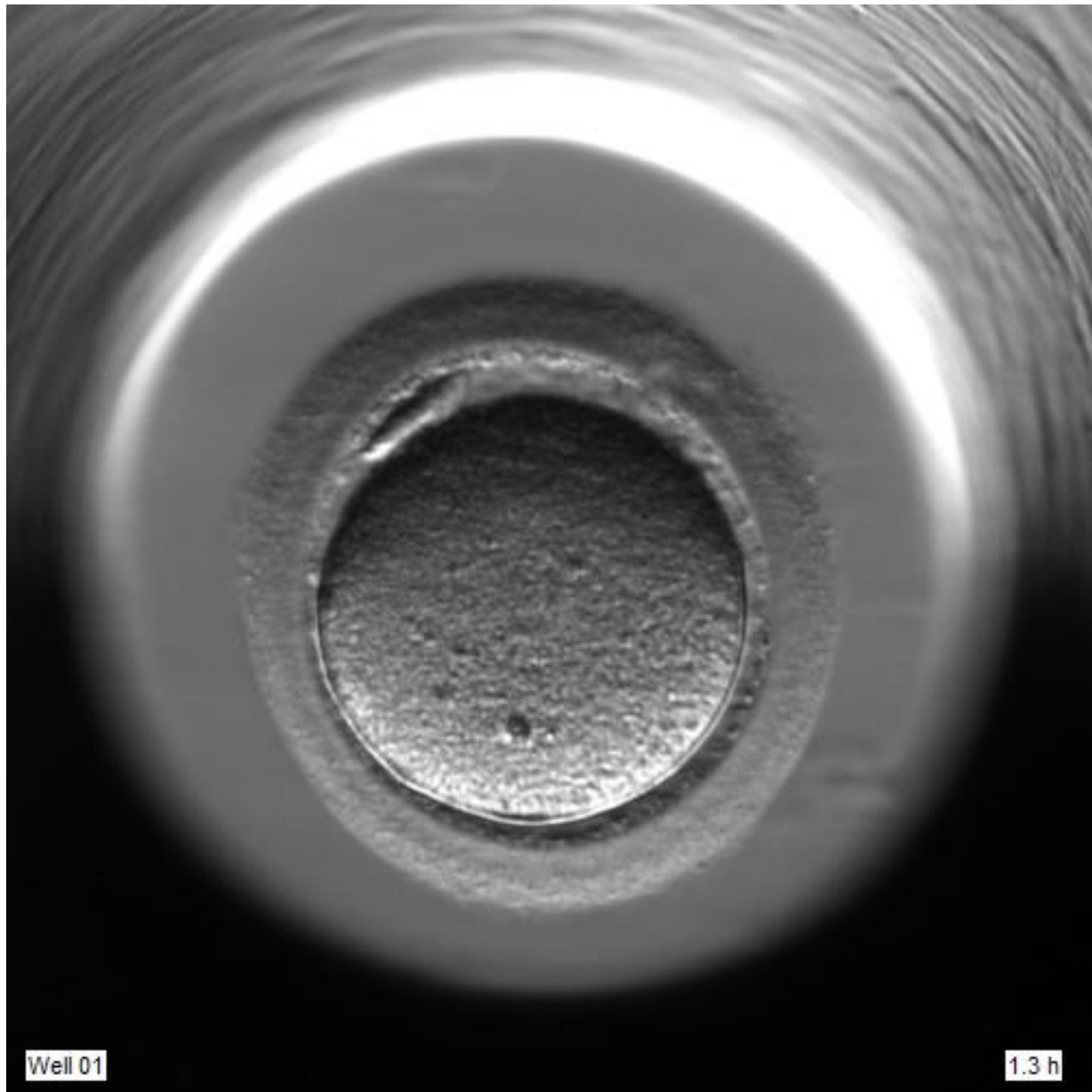
**5-6 weeks' gestation**

Oocyte quality = developmental competence

Embryo quality

Fetal growth potential





Well 01

1.3 h

# Mouse embryo culture induces changes in postnatal phenotype including raised systolic blood pressure

Adam J. Watkins<sup>\*†‡</sup>, Duncan Platt<sup>\*</sup>, Tom Papenbrock<sup>\*</sup>, Adrian Wilkins<sup>\*</sup>, Judith J. Eckert<sup>\*†</sup>, Wing Yee Kwong<sup>\*</sup>, Clive Osmond<sup>§</sup>, Mark Hanson<sup>†</sup>, and Tom P. Fleming<sup>\*</sup>

<sup>\*</sup>School of Biological Sciences, University of Southampton, Bassett Crescent East, Southampton SO16 7PX, United Kingdom; <sup>§</sup>Medical Research Council Epidemiology Resource Centre, Southampton General Hospital, Southampton SO16 6YD, United Kingdom; and <sup>†</sup>Centre for the Developmental Origins of Health and Disease, School of Medicine, Princess Anne Hospital, Coxford Road, Southampton SO16 5YA, United Kingdom

Watkins et al (2007) *PNAS* 104, 5449

# Maternal undernutrition during the preimplantation period of rat development causes blastocyst abnormalities and programming of postnatal hypertension

Wing Yee Kwong<sup>1</sup>, Arthur E. Wild<sup>1</sup>, Paul Roberts<sup>1</sup>, Antony C. Willis<sup>2</sup> and Tom P. Fleming<sup>1,\*</sup>

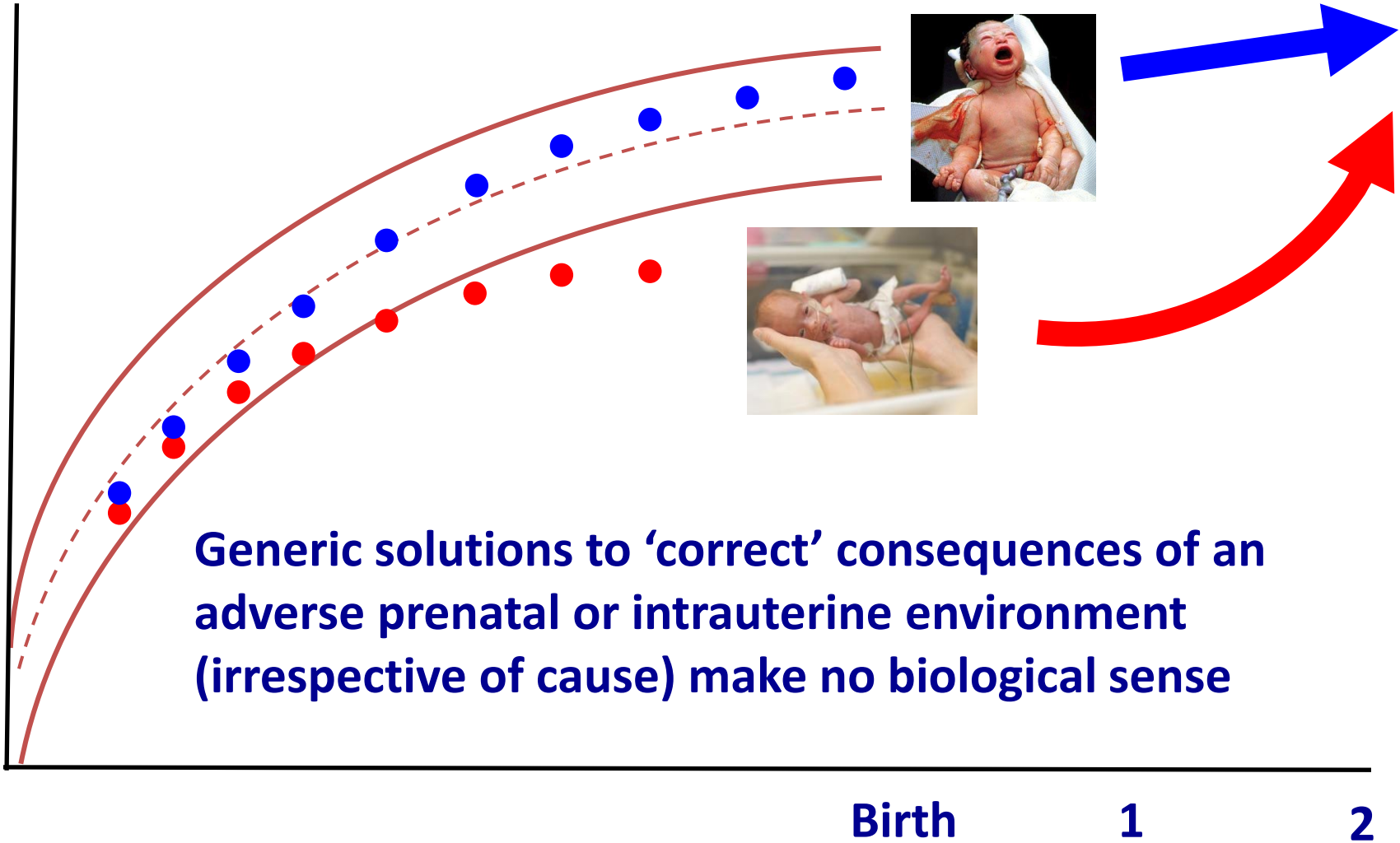
<sup>1</sup>Division of Cell Sciences, School of Biological Sciences, University of Southampton, Bassett Crescent East, Southampton SO16 7PX, UK

<sup>2</sup>MRC Immunochemistry Unit, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, UK

\*Author for correspondence (e-mail: tpf@soton.ac.uk)

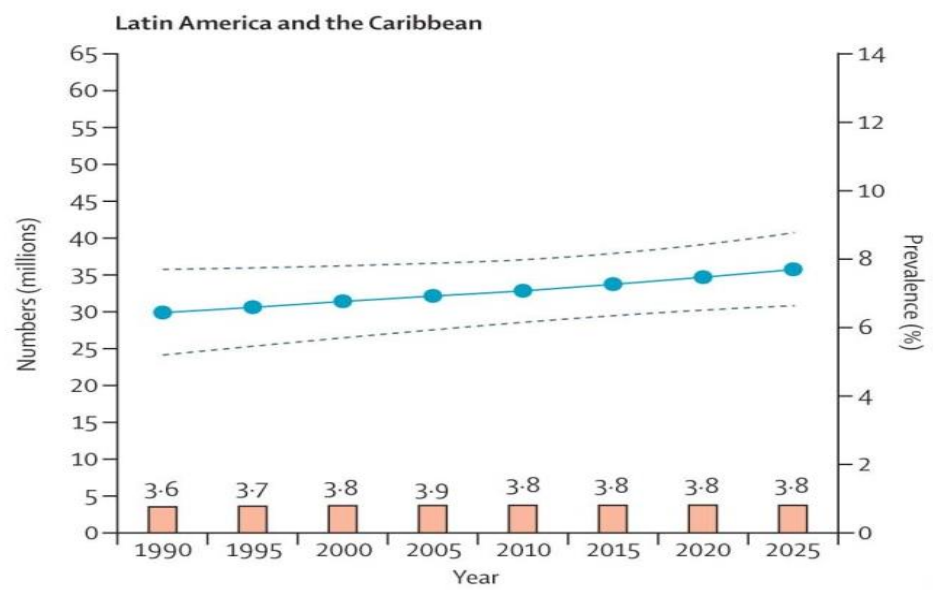
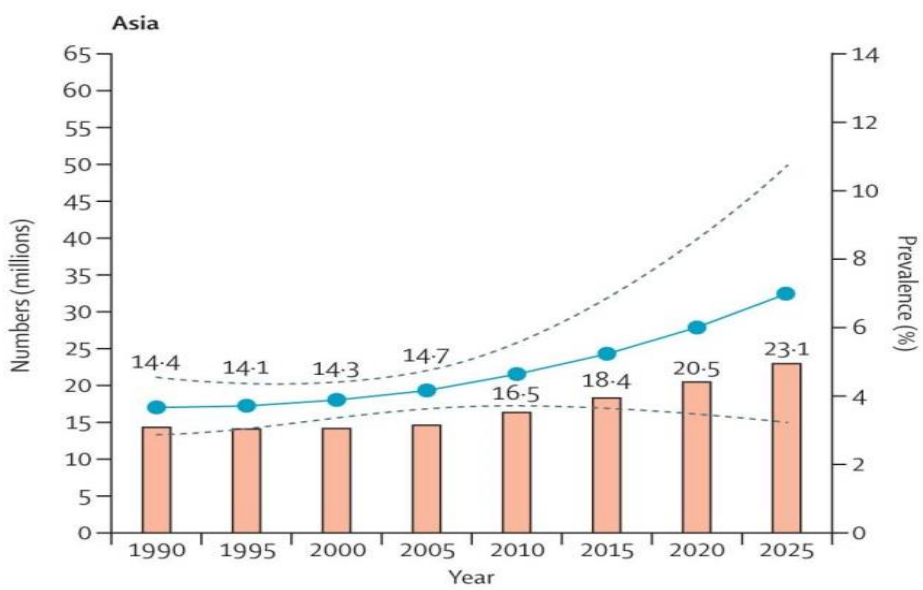
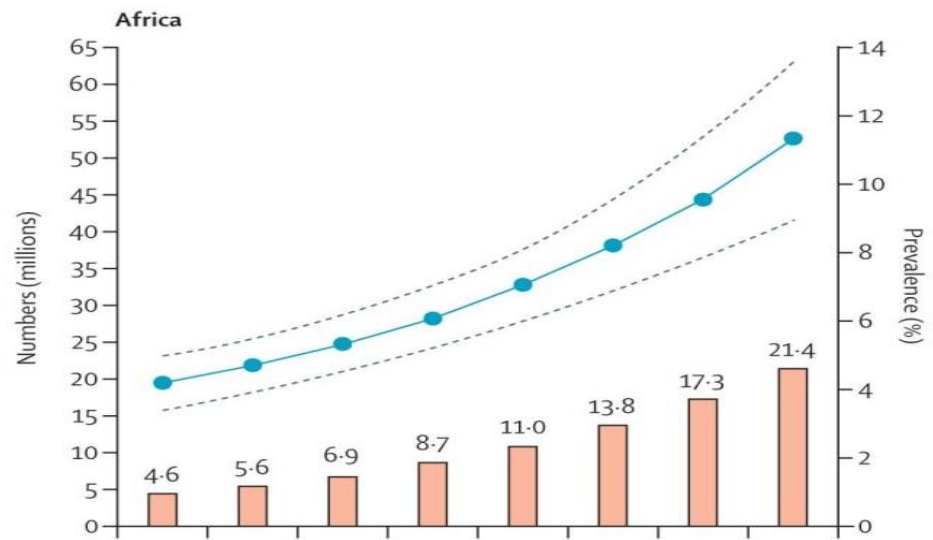
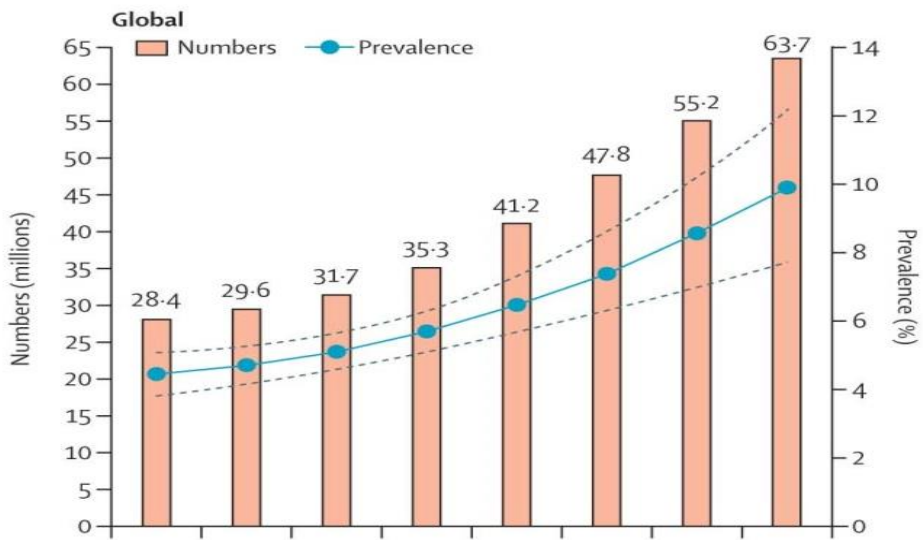
Kwong et al (2000) *Development* 127, 4195

# First 1,000 days



**Generic solutions to 'correct' consequences of an adverse prenatal or intrauterine environment (irrespective of cause) make no biological sense**

# Global rise in Child Obesity (1990-2025)



# Global rise in Child Obesity (1990-2025)



## Maternal malnutrition

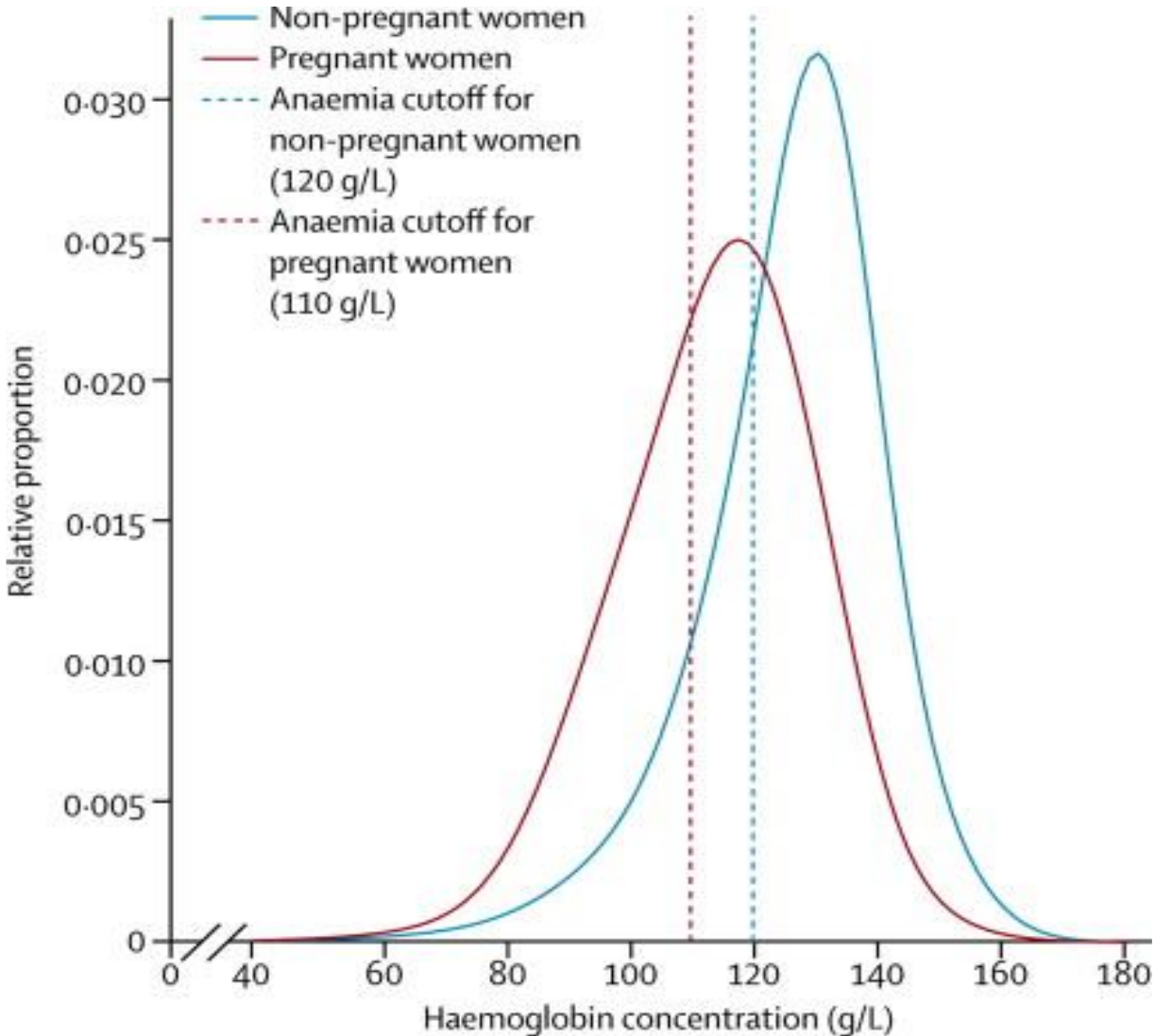


## **Anaemia: health consequences**

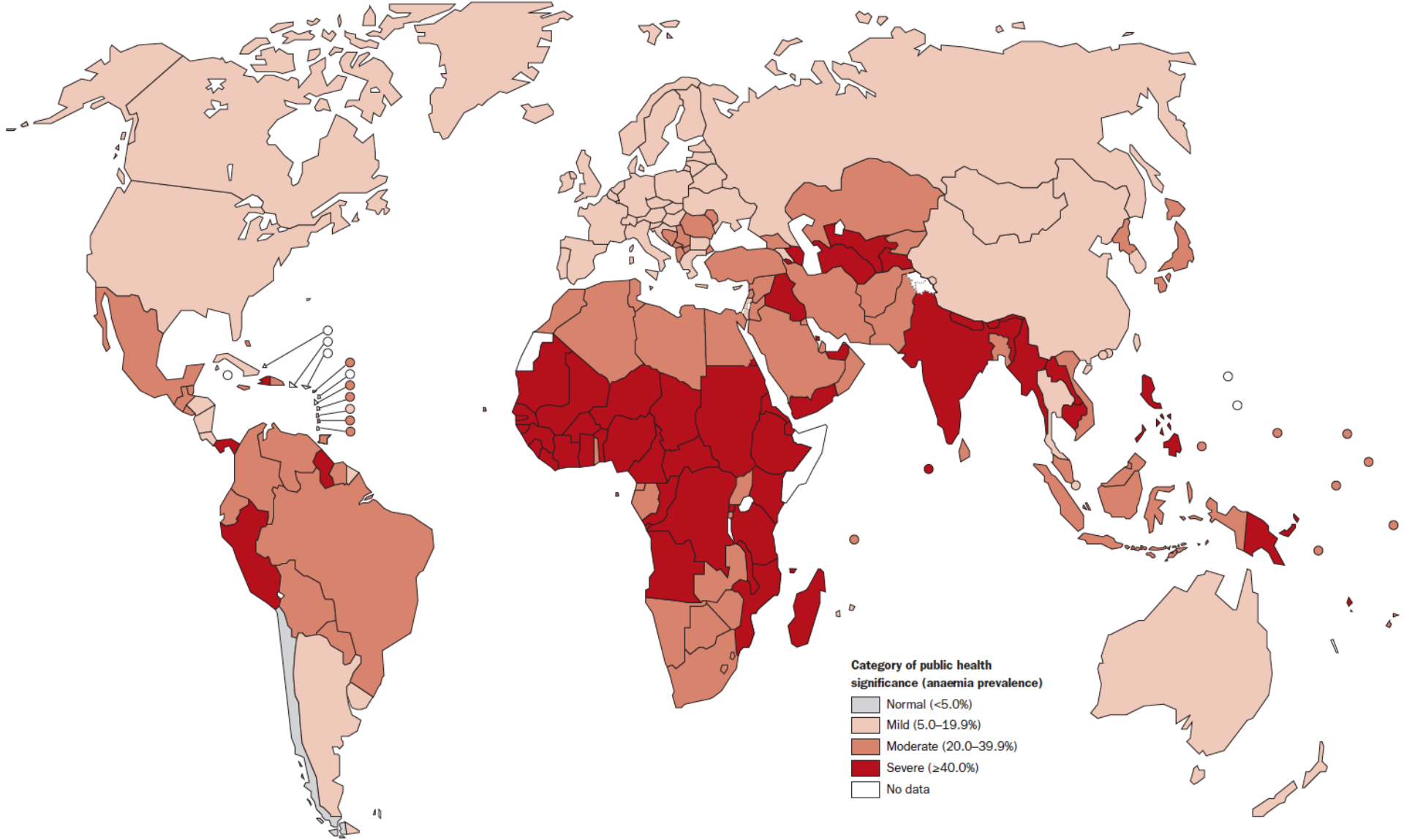
*Prime indicator malnutrition & poor health*

1. Increased risks of maternal & child mortality
2. Negative effects on infant cognitive & physical development
3. Decreased work productivity in adults

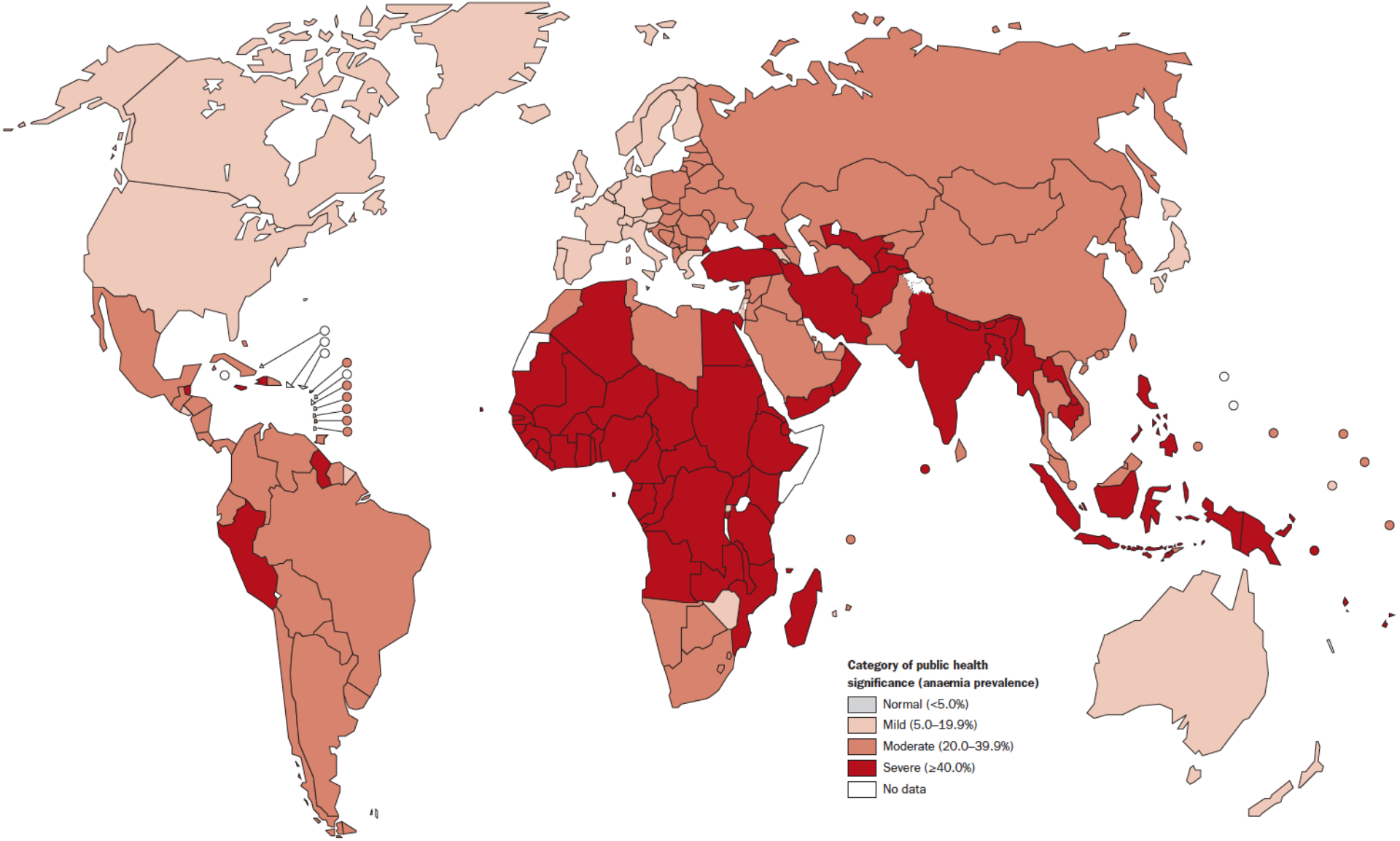
# Global distribution haemoglobin concentrations (2011)



# Anaemia: Non-pregnant women of reproductive age



# Anaemia: Pregnant women



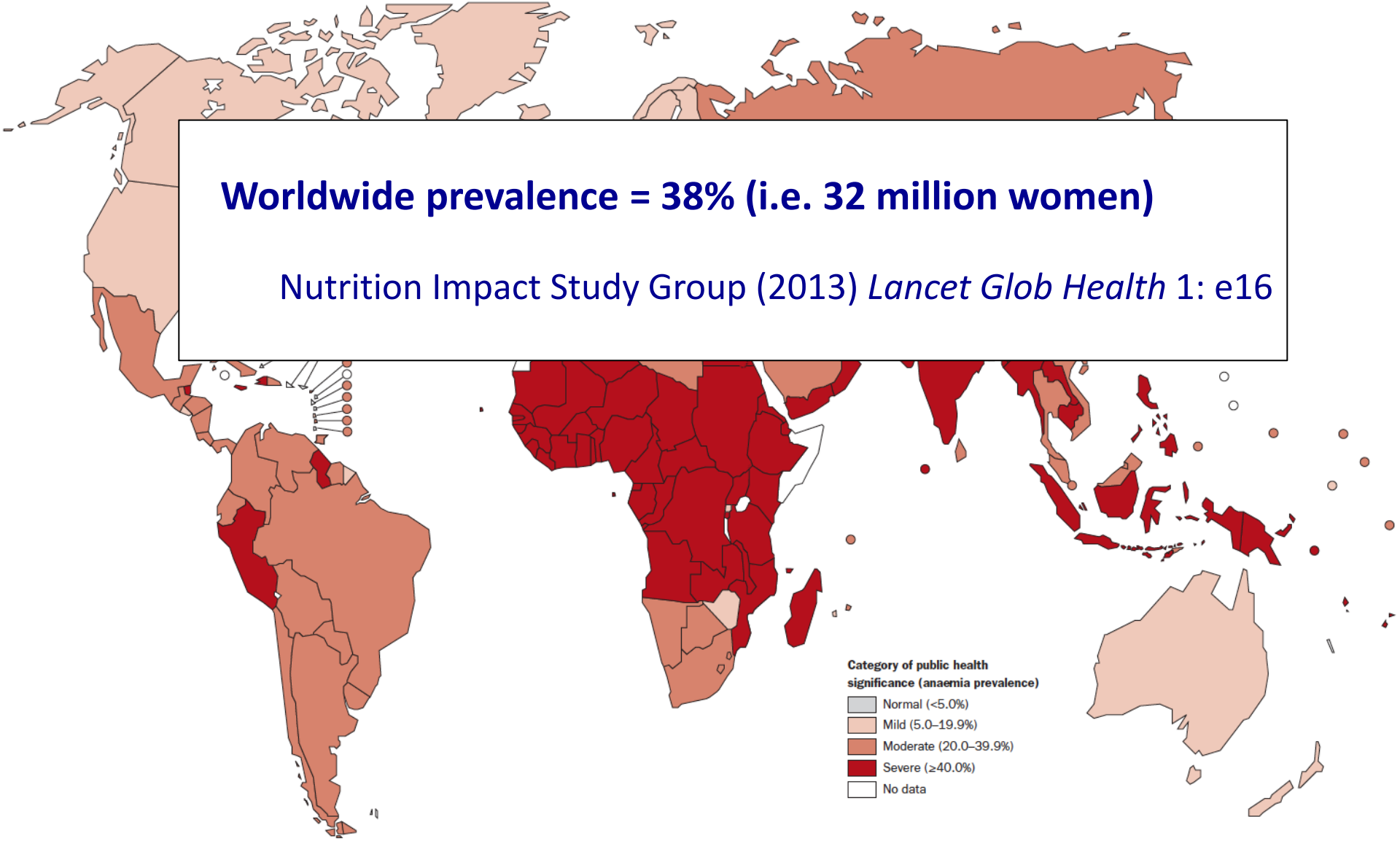
# Anaemia: Pregnant women

**Worldwide prevalence = 38% (i.e. 32 million women)**

Nutrition Impact Study Group (2013) *Lancet Glob Health* 1: e16

Category of public health significance (anaemia prevalence)

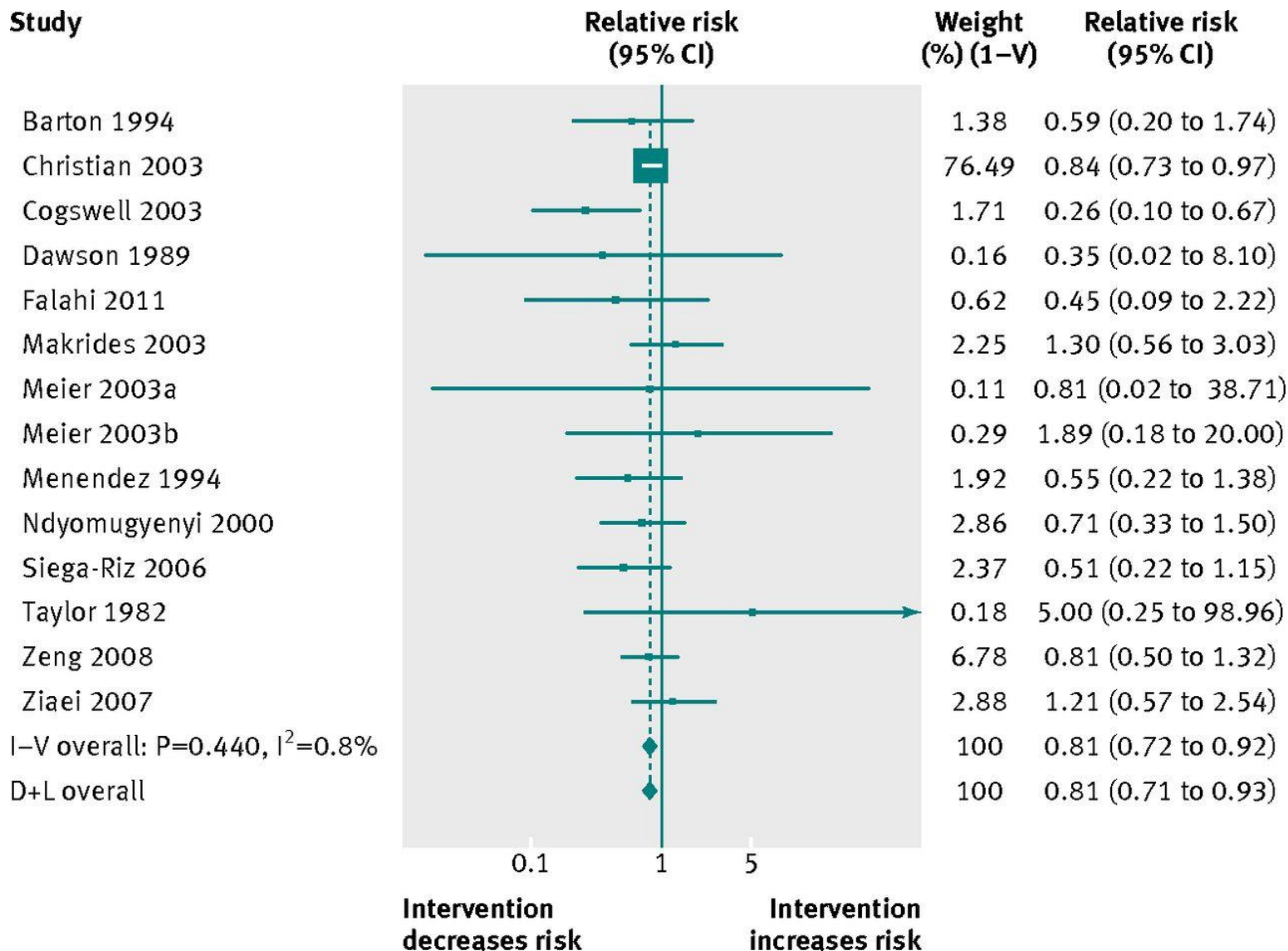
- Normal (<5.0%)
- Mild (5.0–19.9%)
- Moderate (20.0–39.9%)
- Severe (≥40.0%)
- No data



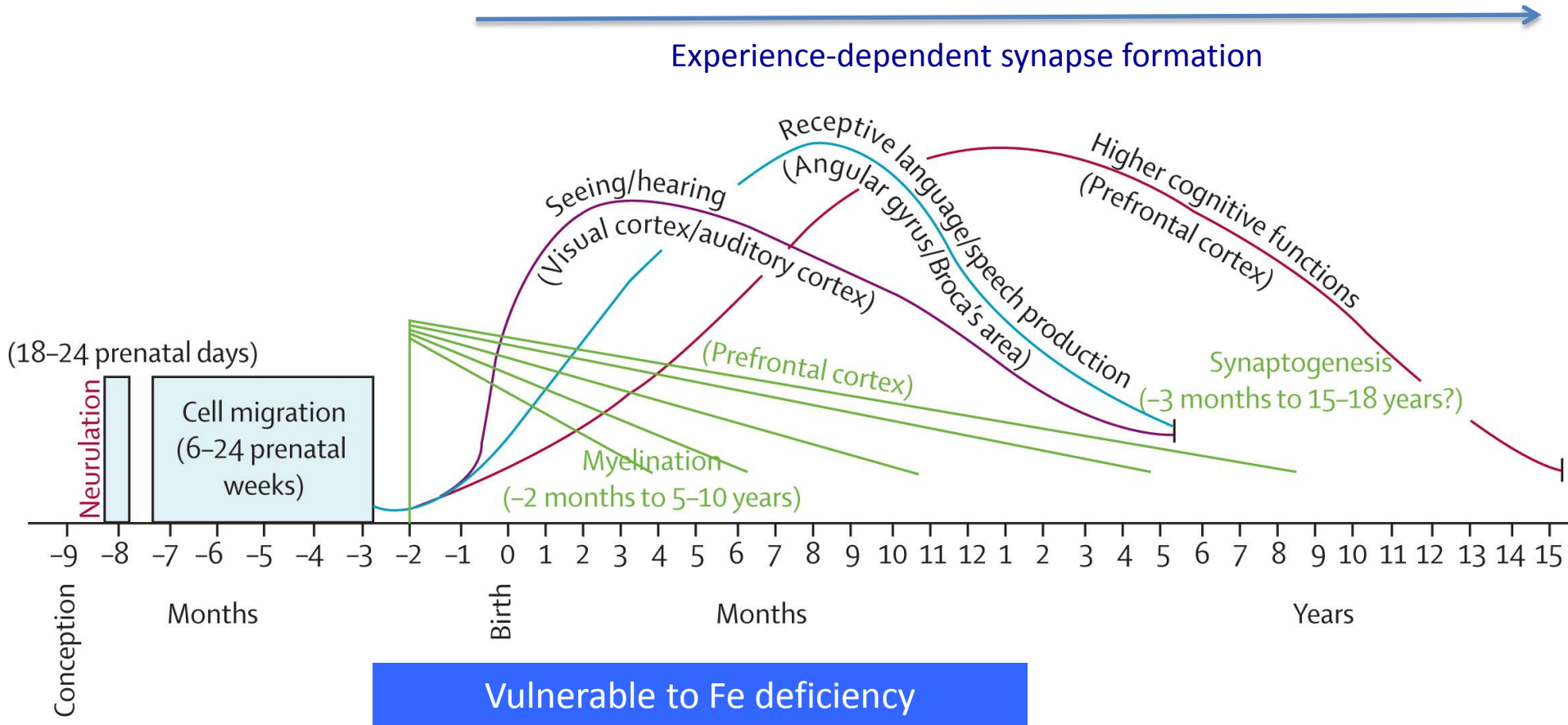
## Anaemia: causes

1. Iron deficiency (50%)
  - Low iron intake
  - Poor absorption
  - High requirements (e.g. pregnancy, child growth)
2. Heavy menstrual blood loss
3. Parasitic infections (e.g. hookworms, schistosomiasis)
4. Systemic infection (e.g. malaria, TB, HIV)
5. Other micronutrient deficiencies (e.g. vitamins A & B12, folate)
6. Haemoglobinopathies

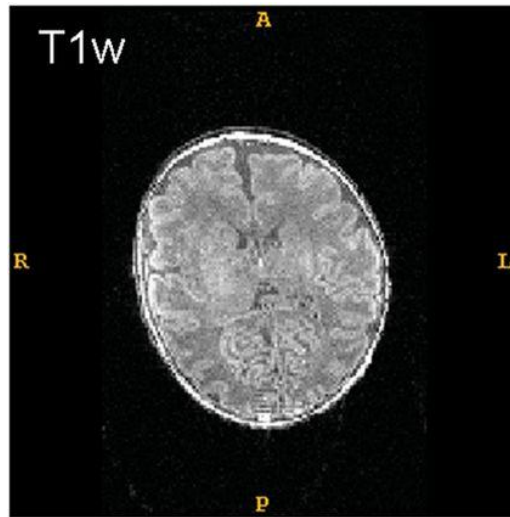
# Forest plot for effect of iron use on low birth weight



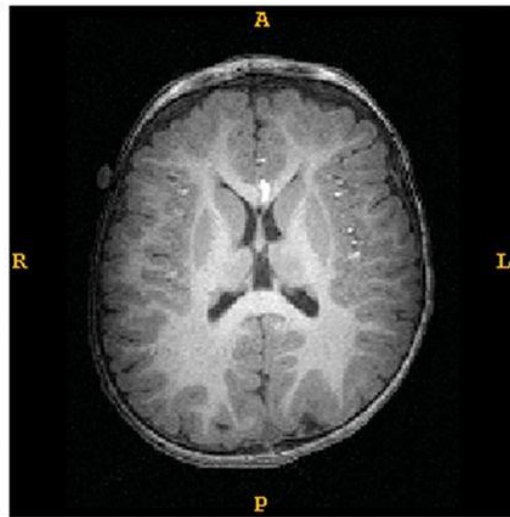
# Human brain development



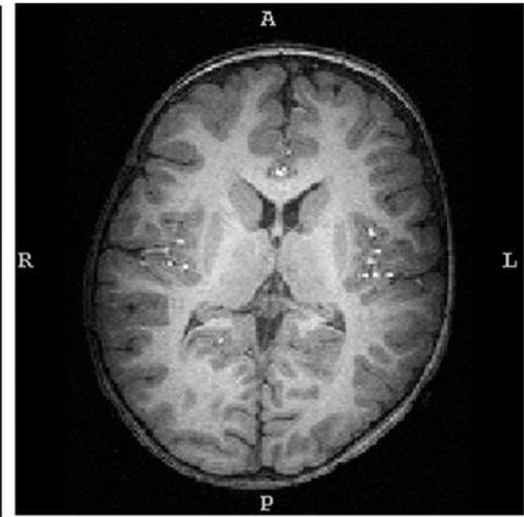
## Serial MRI scans in a neonate, 1 and 2 year old



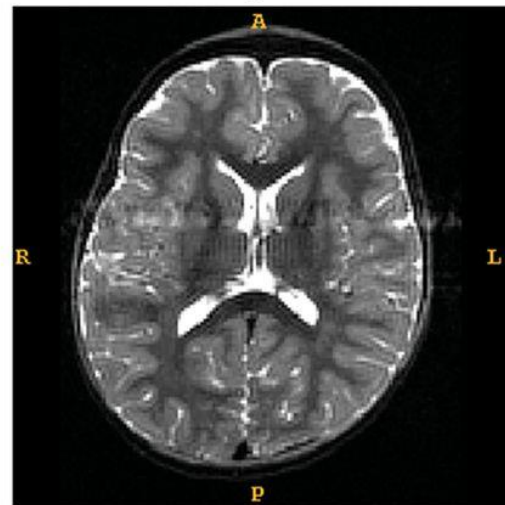
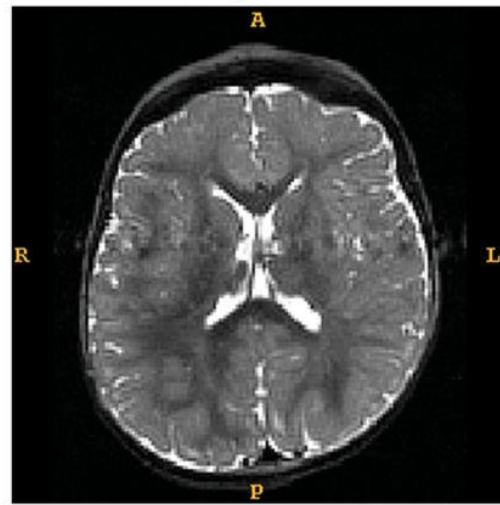
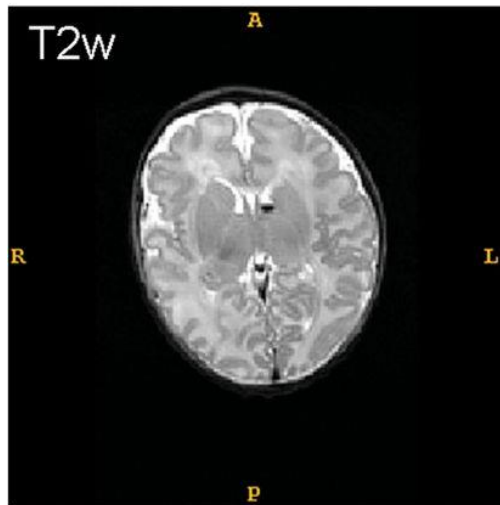
2 weeks



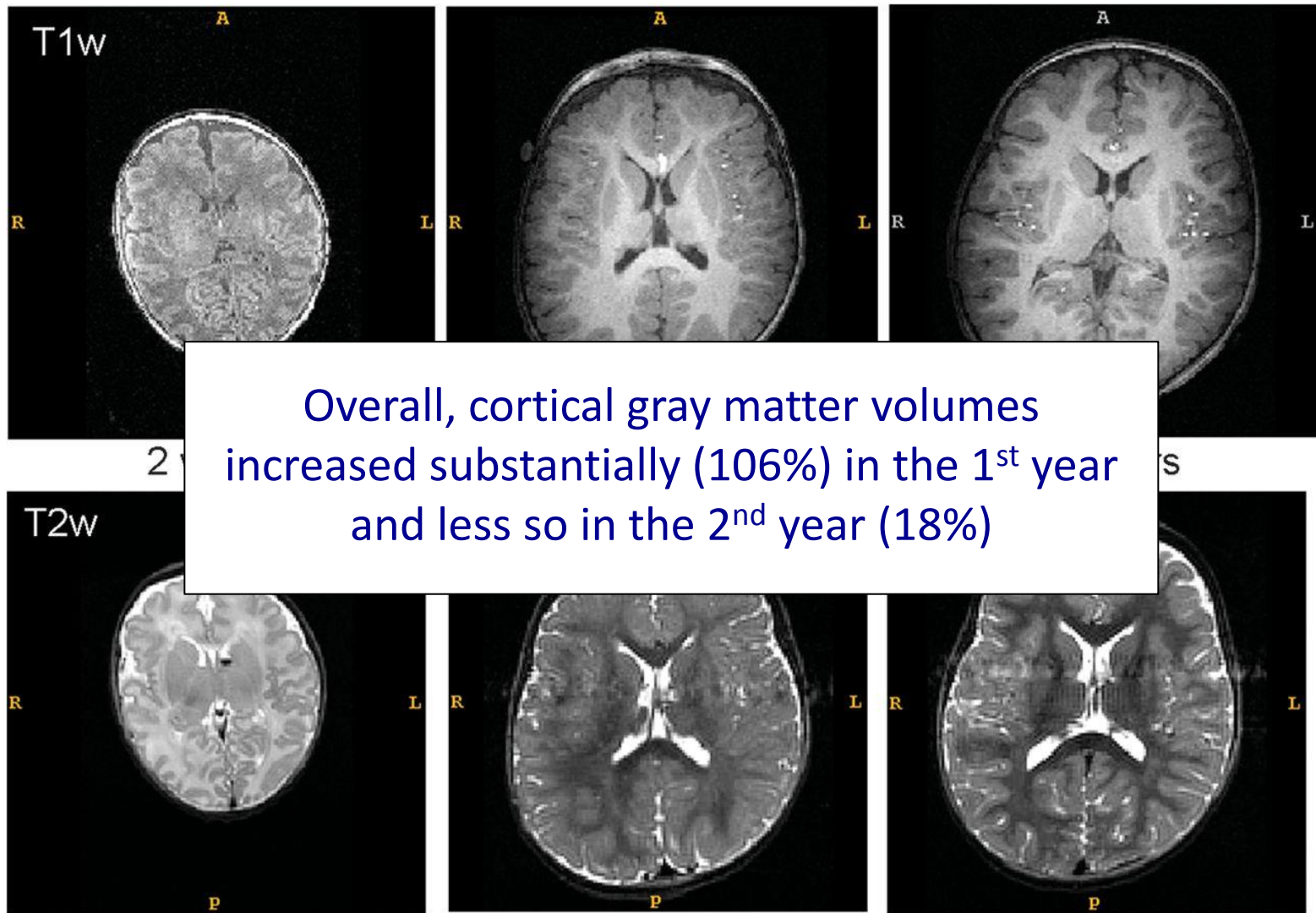
1 year



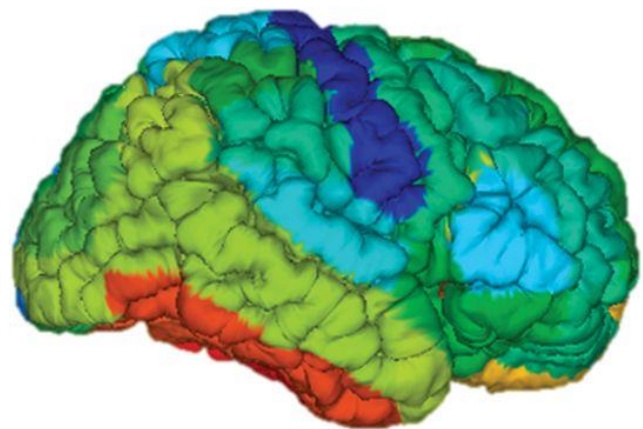
2 years



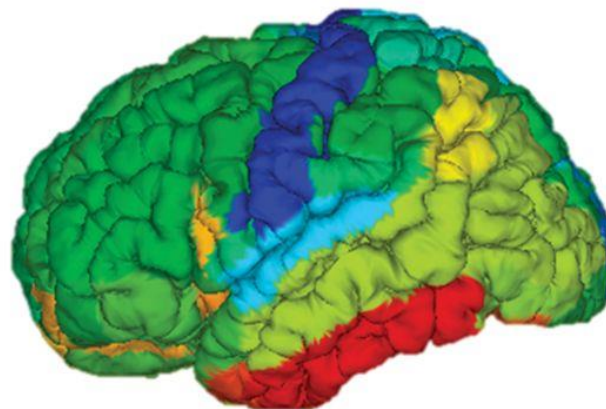
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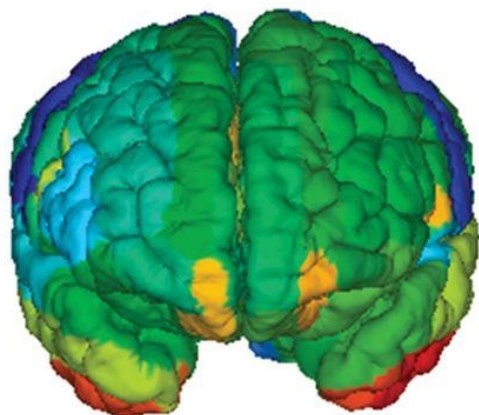
# Regional growth rates of cortical gray matter volume from birth to 1 year of age



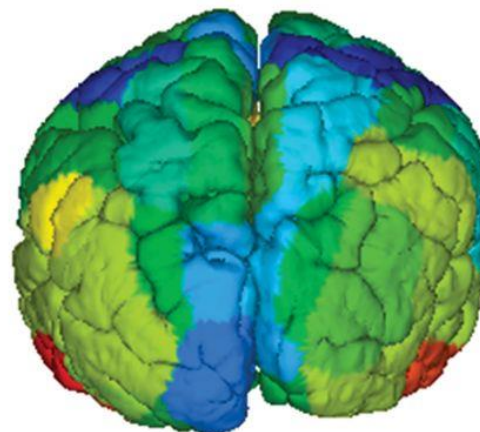
**Left**



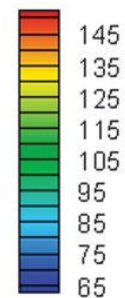
**Right**



**Frontal**

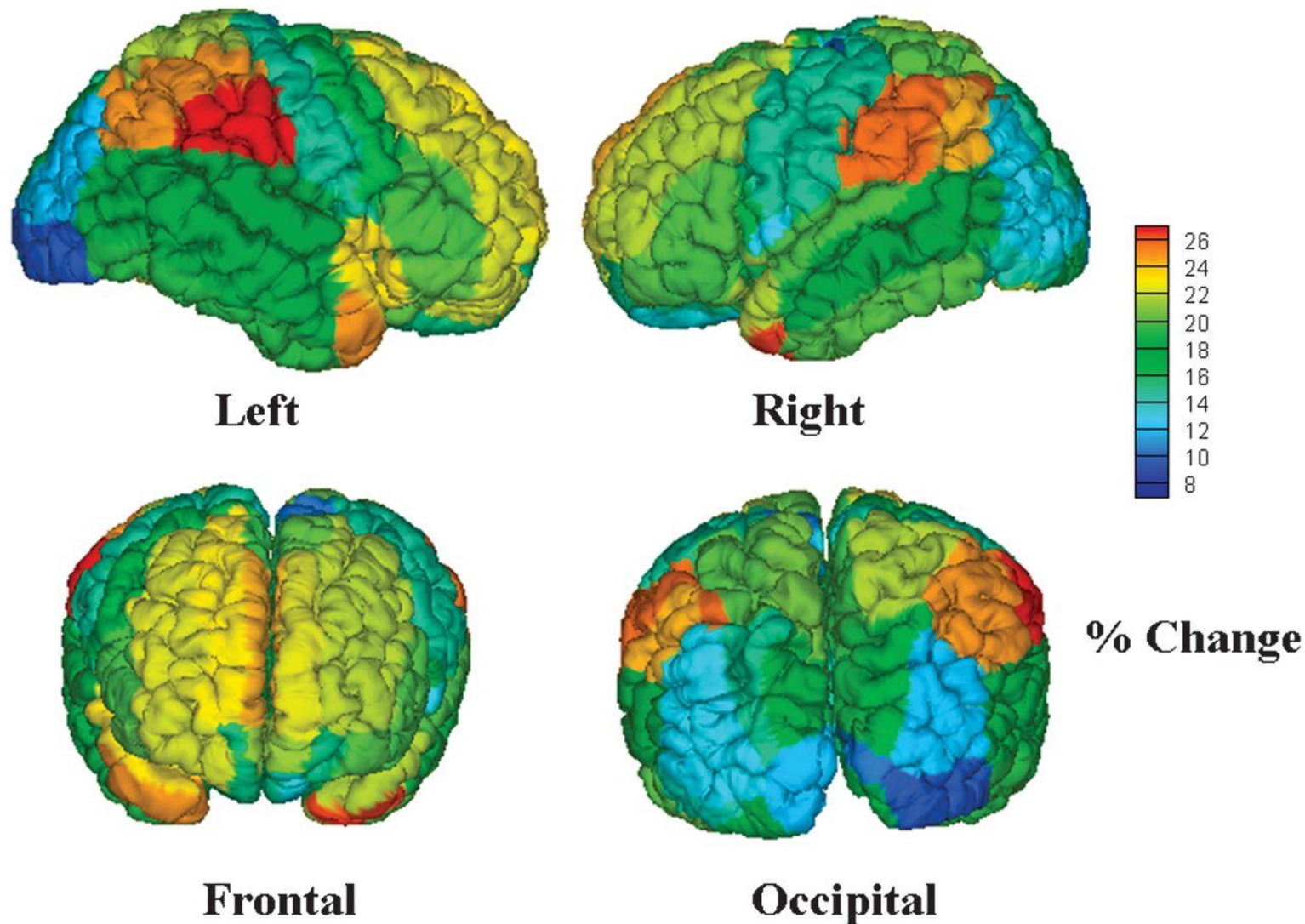


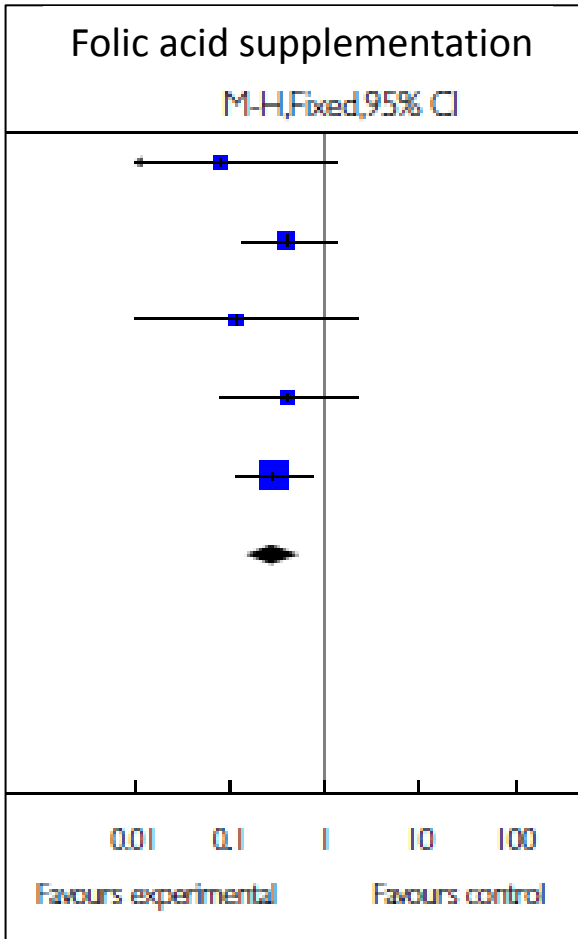
**Occipital**



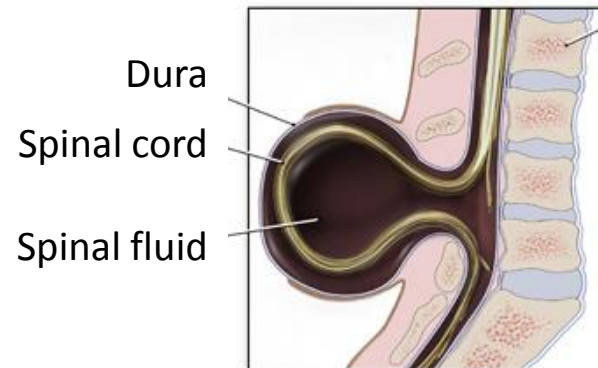
**% Change**

## Regional growth rates of cortical gray matter volume from 1 to 2 years of age

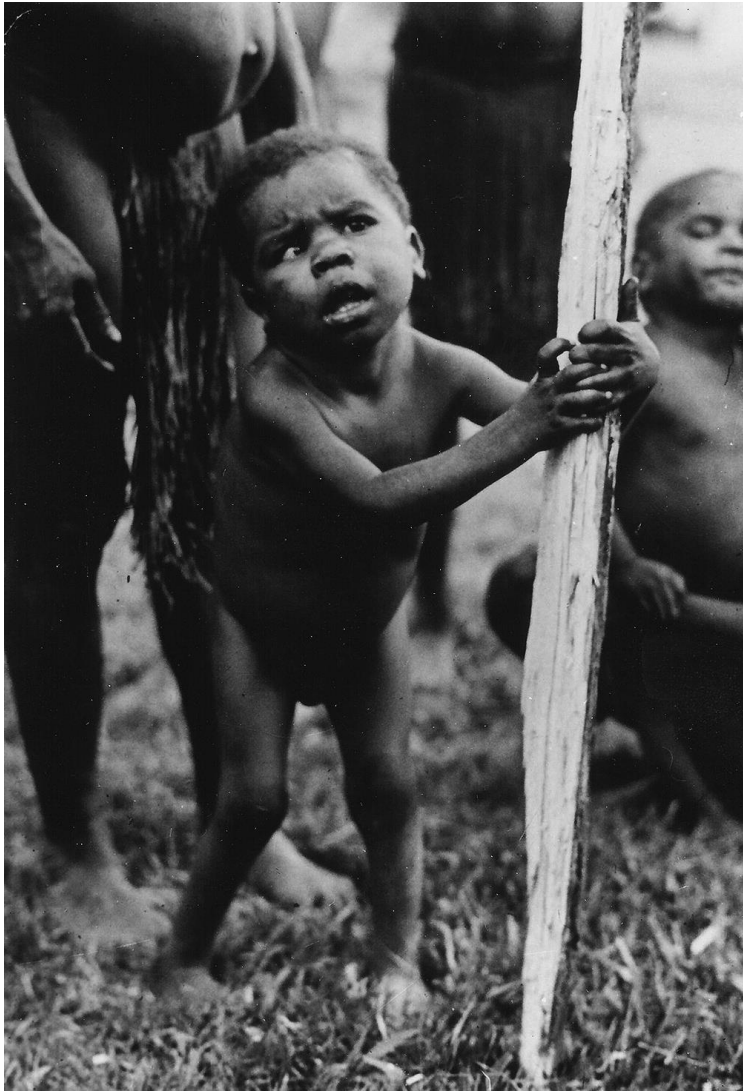




Open spina bifida



Prevention of neural tube defects  
Risk ratio = 0.28 (95% CI 0.15 to 0.52)



*Papua New Guinea*



*Xinjiang, China*

# Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults

*John Hoddinott, John A Maluccio, Jere R Behrman, Rafael Flores, Reynaldo Martorell*

(1969-77) Four villages randomised to a drink:

- Atole – 6.4 g protein + 380 kJ per 100 ml
- Fresco – No protein + 138 kJ per 100 ml from sugar

(From 1971) Both drinks fortified with micronutrients

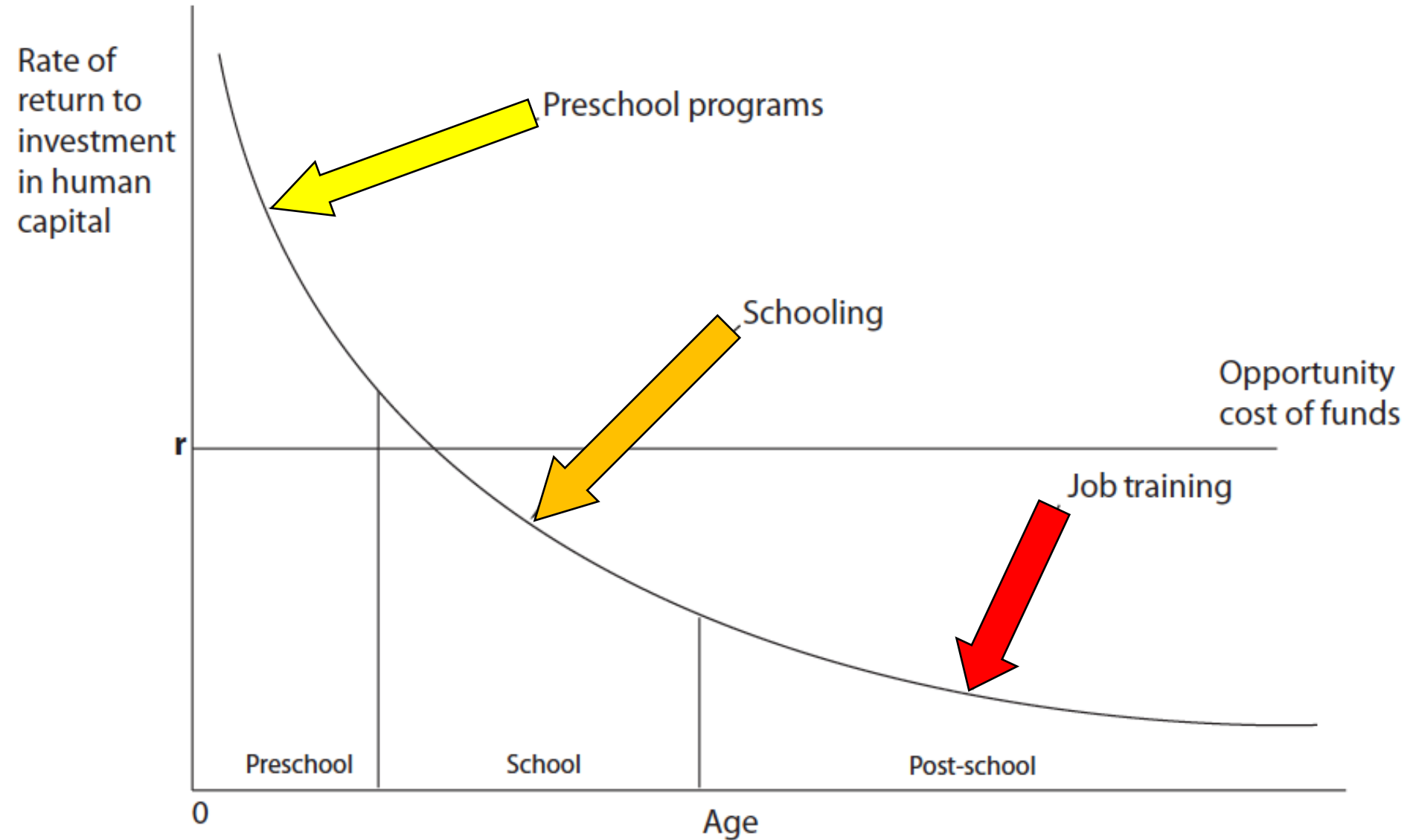
(2002-04) Economic data from 60% individuals (average age = 30) showed Atole exposure:

- 0-36 mths → higher hourly wages in men
- 0-24 mths → 46% increase in wages

*‘Besides improving health, investing in health is also an investment in prosperity, social and financial protection, and national security’.*

Horton & Lo (2013) *Lancet* 382, 1859  
Investing in health: why, what, and three reflections

# Investing in the early years



Rates of return to human capital investment initially setting investment to be equal across all ages

# Packages of Nutrition Interventions

## Optimal maternal nutrition during pregnancy

- Maternal multiple micronutrient supplements to all
- Calcium supplementation to mothers at-risk of low intake
- Maternal balanced energy protein supplements as needed
- Universal salt iodization

## Infant and young child feeding

- Promotion of early, exclusive breastfeeding for 6 months; continued breastfeeding until 2 years
- Appropriate complementary feeding education in food secure populations and complementary food supplements in food insecure populations

## Micronutrient supplementation in children at risk

- Vitamin A supplementation between 6 months - 5 years
- Preventive zinc supplements between 1 - 5 years

## Management of acute malnutrition

- Supplementary feeding for moderate acute malnutrition
- Management of severe acute malnutrition

# Packages of Nutrition Interventions

## Optimal maternal nutrition during pregnancy

- Maternal multiple micronutrient supplements to all
- Calcium supplementation to mothers at-risk of low intake
- Maternal balanced energy protein supplements as needed

## Potential impact of scaling up 10 proven interventions from current population coverage to 90%:

- **900,000 lives saved in 34 high burden countries (where 90% of world's stunted children live)**
- **33 million fewer children with stunted growth**

- Preventive zinc supplements between 1 - 5 years

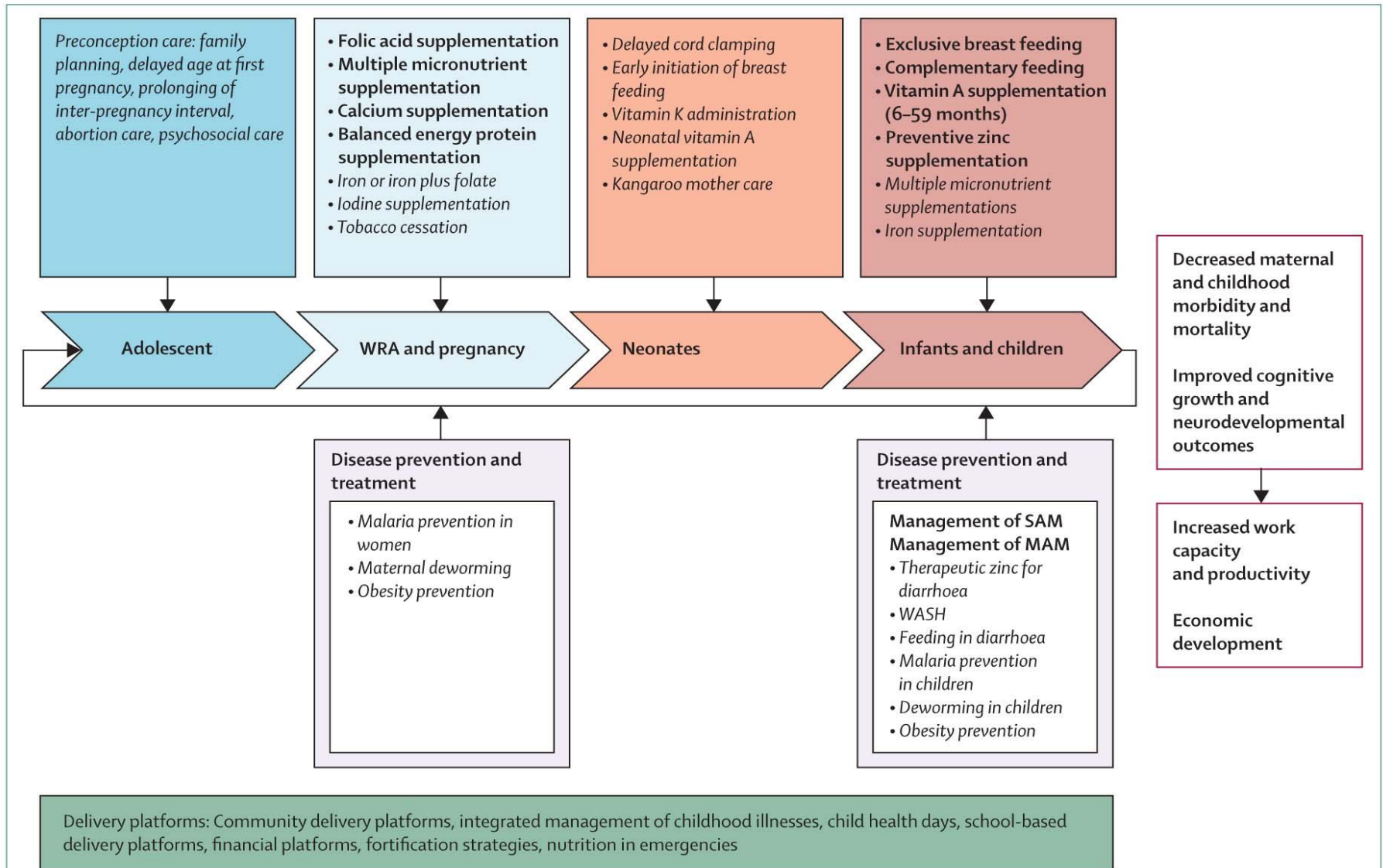
## Management of acute malnutrition

- Supplementary feeding for moderate acute malnutrition
- Management of severe acute malnutrition

## Total additional annual cost of achieving 90% coverage with Nutrition Interventions

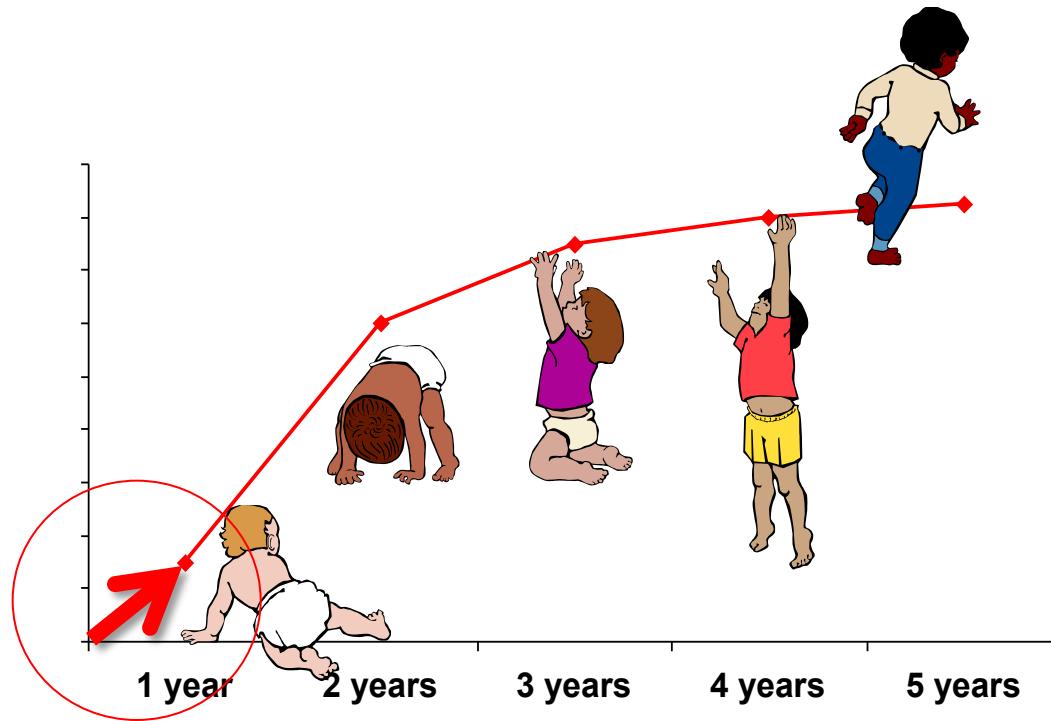
<b>Nutrition interventions</b>	<b>Cost (millions)</b>
<b>Salt iodization</b>	<b>\$68</b>
<b>Multiple micronutrient supplementation in pregnancy (includes iron-folate)</b>	<b>\$472</b>
<b>Calcium supplementation in pregnancy</b>	<b>\$1,914</b>
<b>Energy-protein supplementation in pregnancy</b>	<b>\$972</b>
<b>Vitamin A supplementation in childhood</b>	<b>\$106</b>
<b>Zinc supplementation in childhood</b>	<b>\$1,182</b>
<b>Breastfeeding promotion</b>	<b>\$653</b>
<b>Complementary feeding education</b>	<b>\$269</b>
<b>Complementary feeding supplementation</b>	<b>\$1,359</b>
<b>Severe acute malnutrition management</b>	<b>\$2,563</b>
<b>Total</b>	<b>\$9,559</b>

# Interventions across the lifecycle



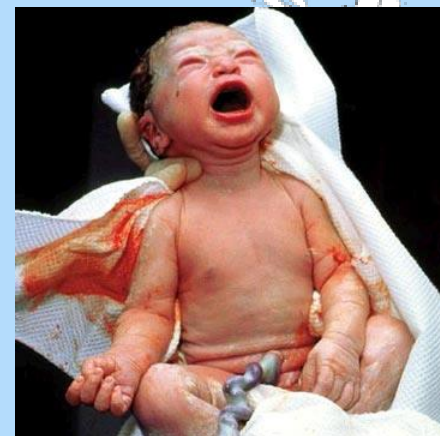
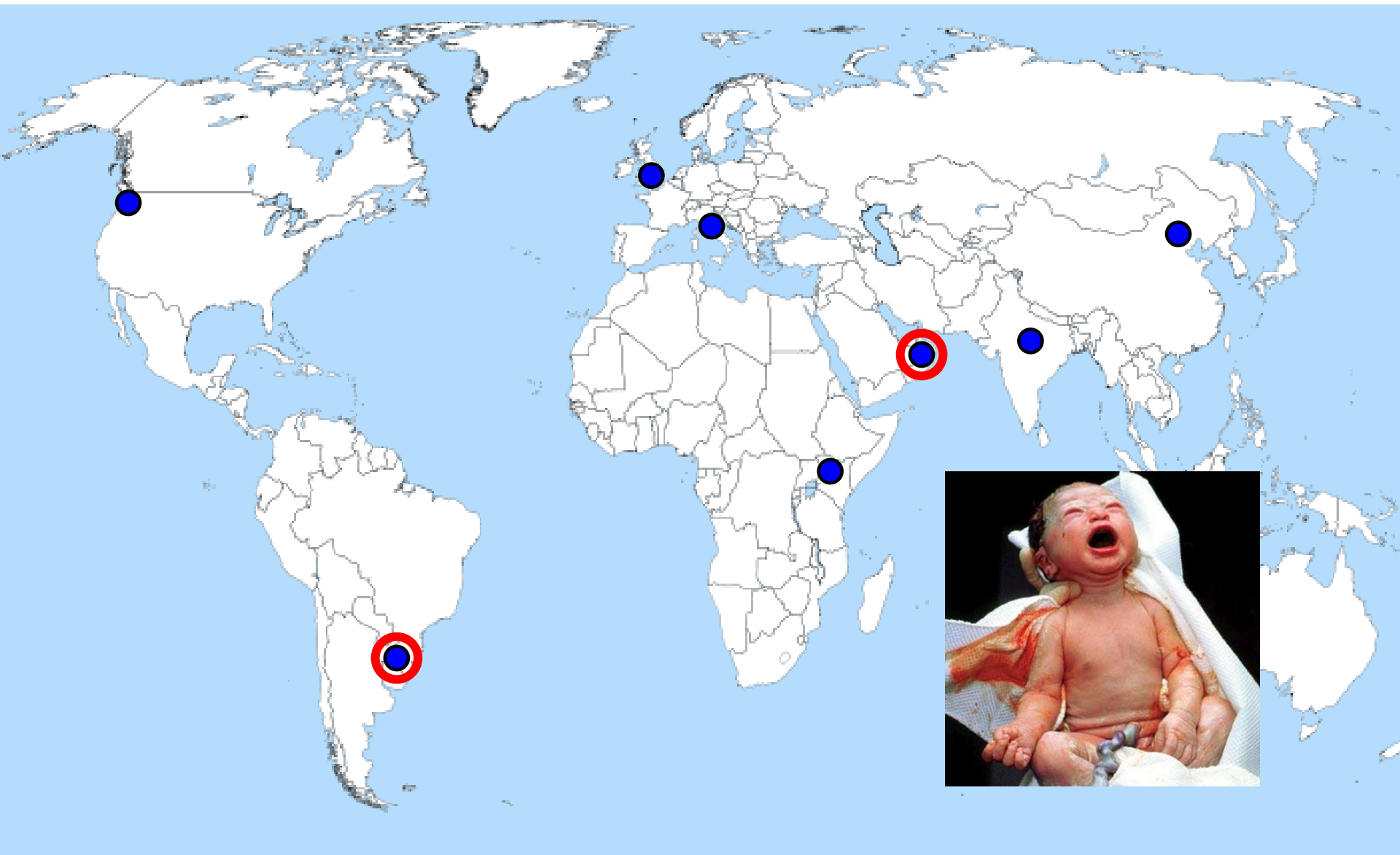
**Bold**=Interventions modelled  
*Italics*=Other interventions reviewed

# New international “prescriptive” fetal and newborn growth standards



**INTERGROWTH-21<sup>st</sup> Project**  
**Fetal Growth Longitudinal Study**





**INTERGROWTH-21<sup>st</sup> sites**

**BILL & MELINDA  
GATES *foundation***

# “Healthy” mother criteria for Fetal Growth Longitudinal Study

- a) aged  $\geq 18$  and  $\leq 35$  years;
- b) BMI  $\geq 18.5$  and  $< 30$  kg/m<sup>2</sup>;
- c) height  $\geq 153$  cm;
- d) singleton pregnancy;
- e) a known LMP with regular cycles (defined as a 26-30 day cycle in the previous 3 months), without hormonal contraceptive use, pregnancy or breastfeeding in the 3 months before pregnancy;
- f) natural conception

**Criteria defining a low-risk study population as healthy and well-nourished (both before and during pregnancy) to ensure that fetal growth is optimal**

condition;

- o) no clinically significant atypical red cell alloantibodies;
- p) negative urinalysis;
- q) systolic blood pressure  $< 140$  mmHg and diastolic blood pressure  $< 90$  mmHg;
- r) haemoglobin  $\geq 11$  g/dl;
- s) negative syphilis test and no clinical evidence of any other sexually transmitted diseases, including clinical Trichomoniasis;
- t) not in an occupation with risk of exposure to chemicals or toxic substances, or very physically demanding activity to be evaluated by local standards. Also women should not be conducting vigorous or contact sports, as well as scuba diving or similar activities

# Fetal Growth Longitudinal Study



**Anthropometric measurements:**  
Length/height  
Weight  
Head circumference

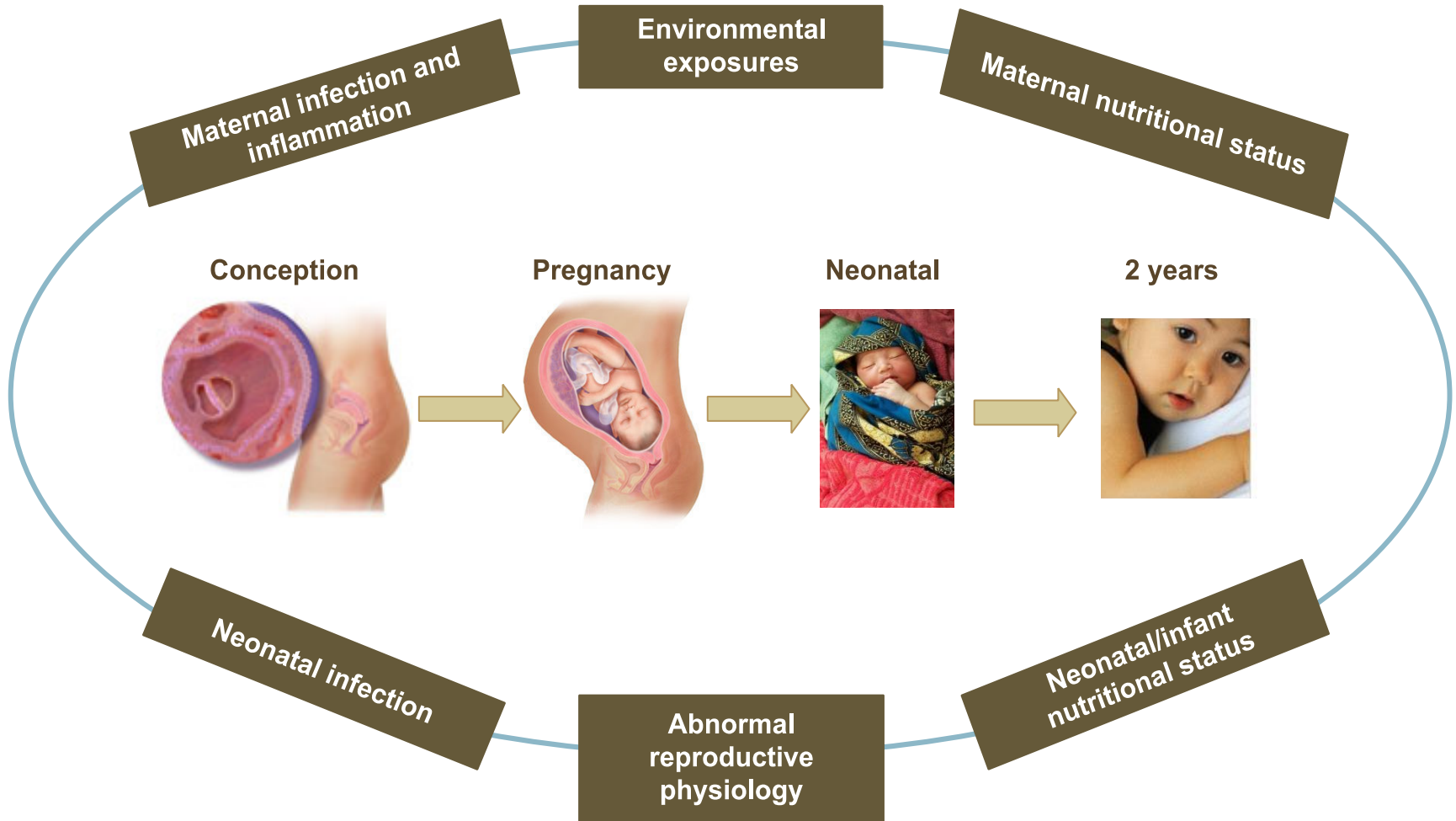
**Ultrasound measures:**  
9-14 weeks  
Then every  $5 \pm 1$  weeks

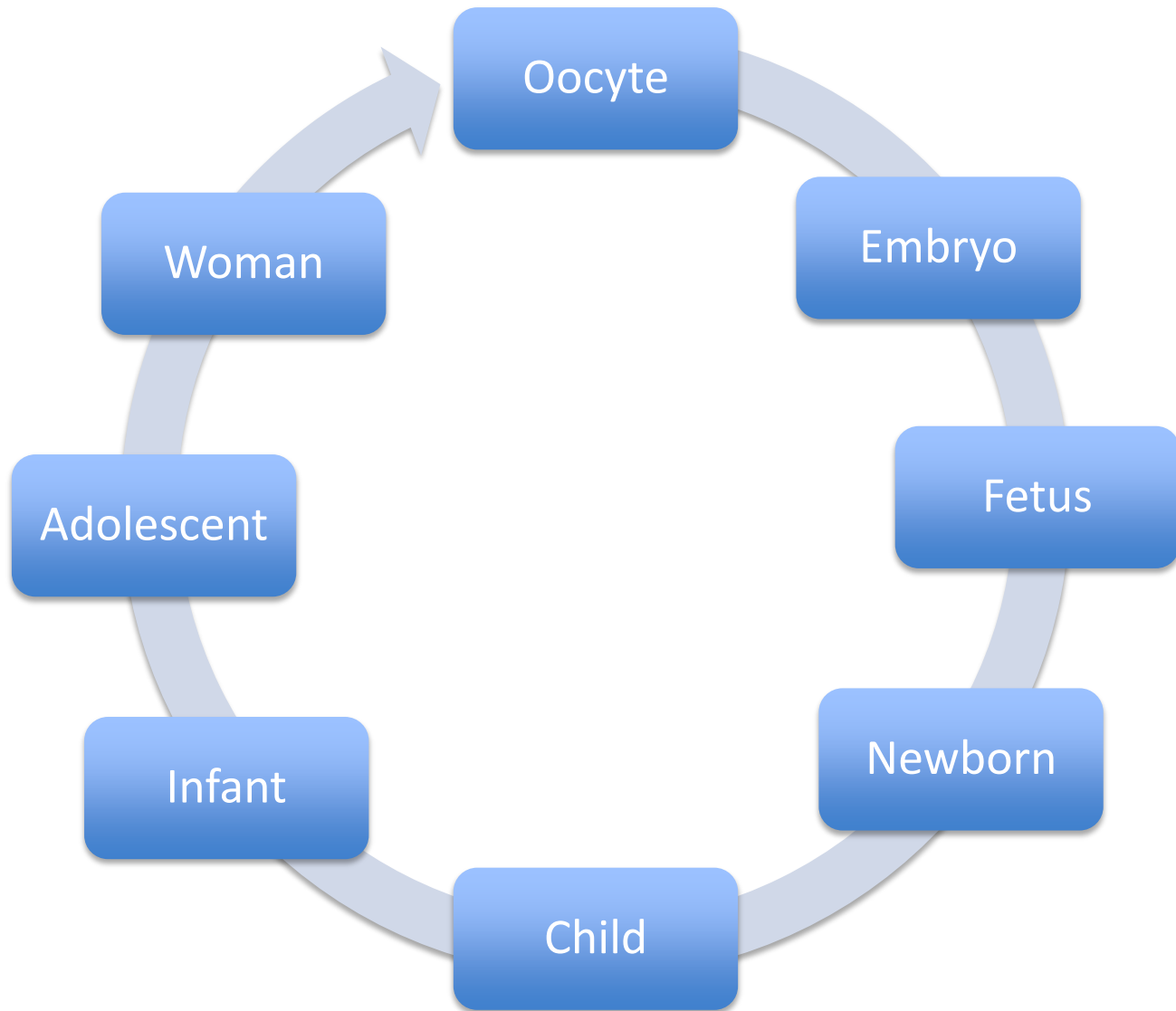
**Neurodevelopment assessment:**  
Psychometric tests  
Wireless EEG  
Actigraphy

# Main INTERGROWTH-21<sup>st</sup> conclusions

- Fetal and newborn size are similar across populations, when constraints on growth are minimal
- Once new international fetal and newborn growth standards are integrated with WHO Child Growth Standards, optimal growth can now be monitored from 9 weeks' gestation to 5 years of age

# Potential factors influencing fetal and child growth in first 1,000 days







On your marks...

MALNUTRITION

MALARIA

HIV