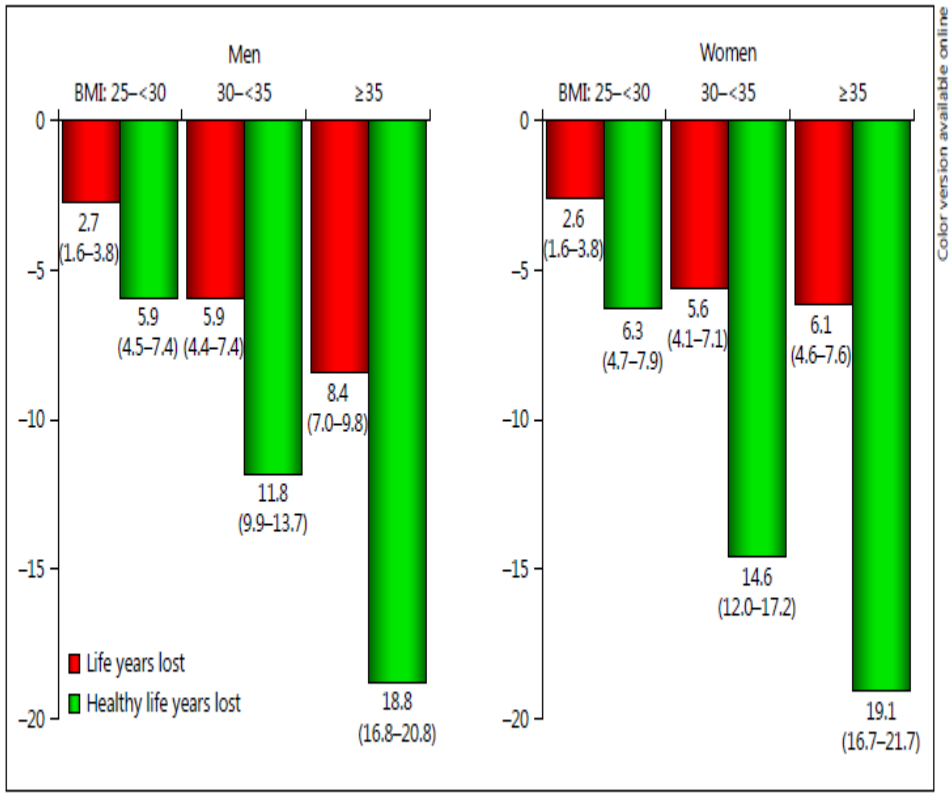


Fig. 1. The high disease burden of different degrees of overweight and obesity is apparent from the loss of life years and of disability adjusted life years (healthy life years) in affected people aged 20–39 years. Drawn from data of [5].

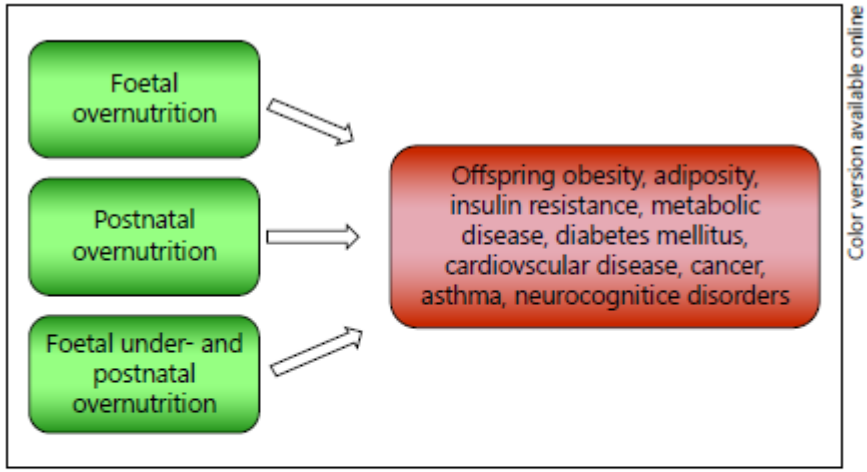
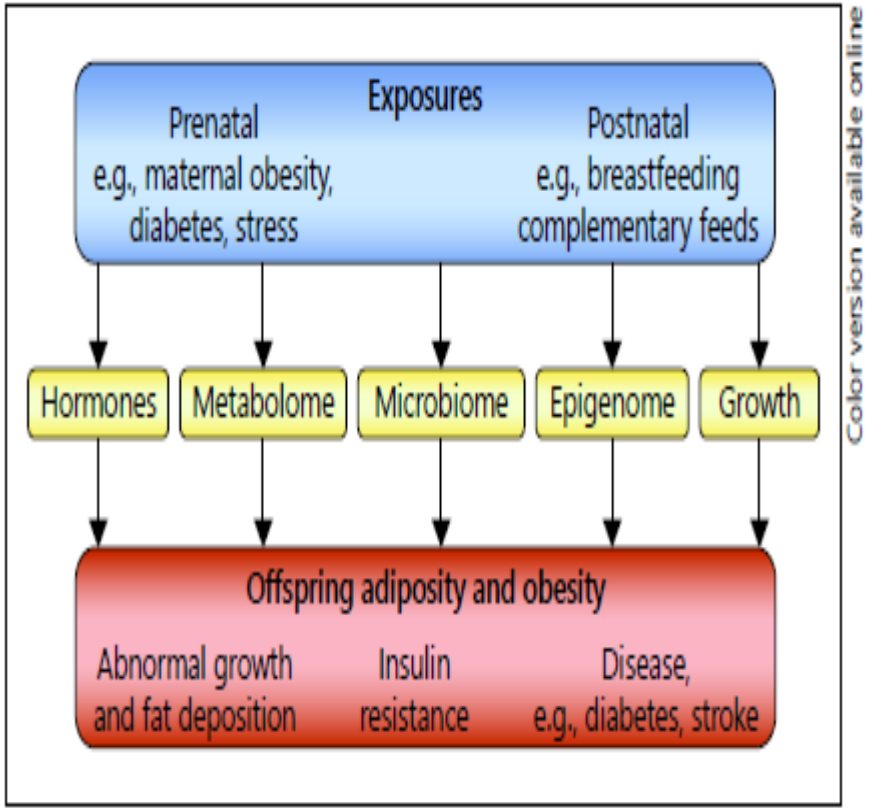


Fig. 2. The workpackages of the Early Nutrition Research Project are designed to jointly test 3 key hypotheses on early life origins of adiposity and associated disorders with different and complementary methodological approaches, that is, the fuel mediated in utero hypothesis, the accelerated postnatal growth hypothesis, and the mismatch of pre- and postnatal growth trajectories hypothesis.

Grover et al., 2015; Koletzko et al., 2017



2212 grávidas com sobrepeso
Intervenção: ↓ açúcar e gordura saturada
↑ atividade física
Resultados:
Tendência ↓ risco para GIG (p=0,24)
↓ número de PN > 4000g (p=0,04)

Grávidas obesas:
3 – 6 x → RNs > 4000g

Dobra o risco de obesidade futura

Yu et al., 2011; Koletzko et al., 2017

Table 2. Subscapular skinfold thickness in infants aged 6 months is reduced by an antenatal lifestyle intervention in obese pregnant women to improve maternal diet (glycemic load and saturated fat intake) and physical activity (UPBEAT trial, 342 intervention, 356 control). Modified from [12]

Skinfolds	Z-score (95% CI)	*p* value
Triceps	−0.14 (−0.38 to 0.10)	ns
Subscapular	−0.26 (−0.49 to −0.02)	<0.001

ns, not significant.

1555 grávidas obesas
Intervenção: 6 sessões dieta/AF
Resultados:
DMG e GIGs: NS
Aos 6 m: ↓ prega subescapular

Sobrepeso/obesidade materna

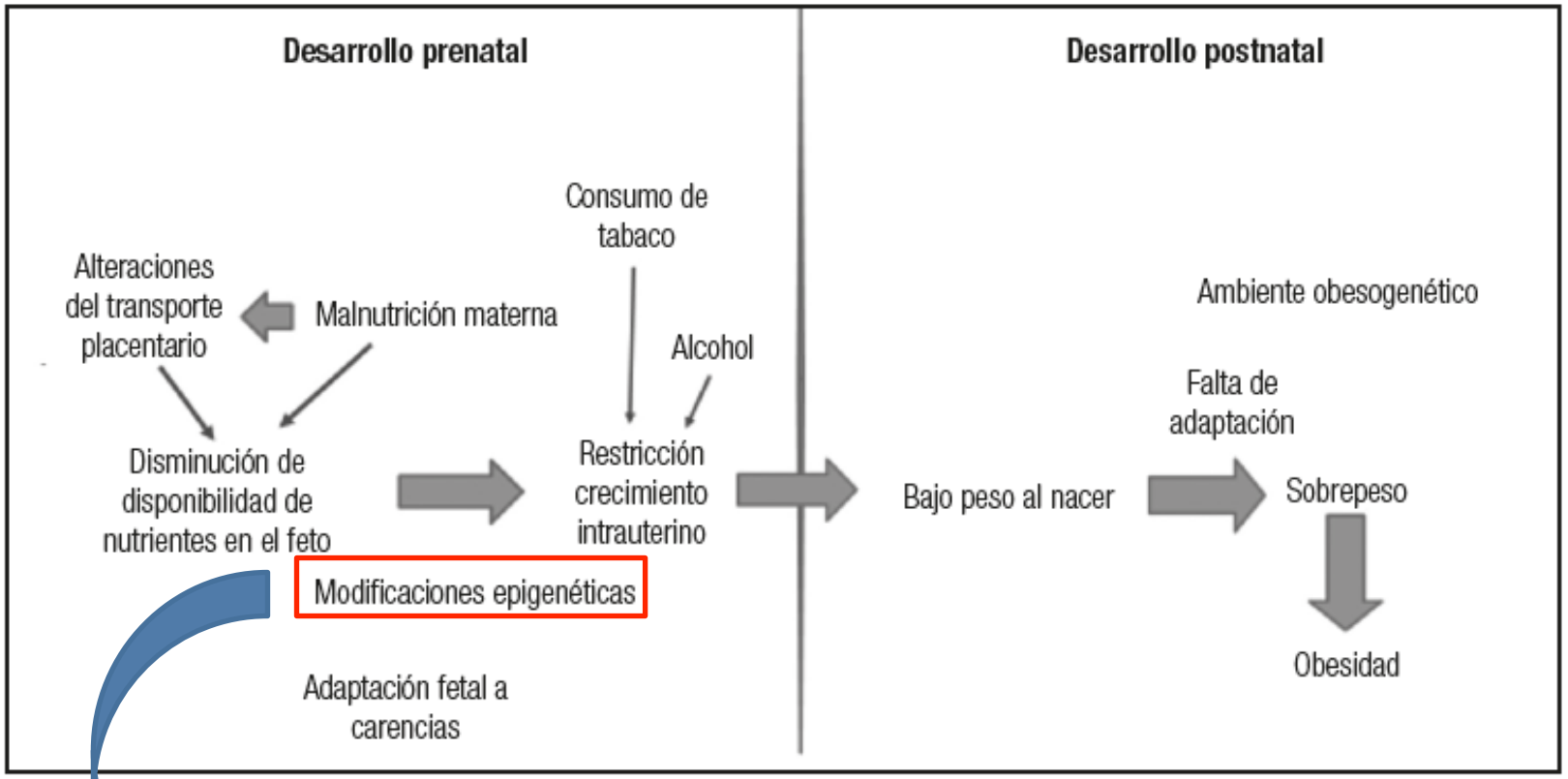
- Massa gorda nas 1as. h de vida
- Sobrepeso na infância
- Obesidade no adulto

DMG

- Macrossomia
- Adiposidade fetal
- Risco de obesidade

Hanley et a., 2010; Pacce et al., 2016
Patel et al., 2012; Koletzko et al., 2017

Influências epigenéticas



Exposição a dietas
Restrições maternas de nutrientes
Zinco, selênio, ferro e Vit. C

U

Hanley et al., 2010; García et al., 2017

Table 2. Summary of human studies evaluating non-nutritive sweetener (NNS) exposure during pregnancy and obesity-related outcomes in offspring.

Study, Year	Setting, Year of Study Enrollment/Baseline Intake, Study Name	*n*	Timing of Prenatal NNS Exposure	Duration of Follow Up	NNS Type, Measure, Method of Assessment	Confounders/Covariates Considered, and Comparators for RCTs	Outcomes in Offspring	Main Finding
Randomized Controlled Trials								
Nakai et al., 2008 [50]	Japan, unspecified	107 pregnant women	6th month of pregnancy to 9 months postpartum	13 months	Xylitol gum, 1 pellet at least 4x/day	Maternal age, oral examination (DMFT); child birthweight, sex. Comparator: no gum	Birth weight (examined as a covariate)	**No association** of infant birth weight and daily maternal xylitol gum
Maslova et al., 2013 [49]	Denmark, 1996, DNBC	60,466 pregnant women	Prenatal; 25th week pregnancy	7 years	ASB, servings, validated FFQ	Maternal BMI, total energy intake, parity, smoking, exercise, gestational weight gain, education and occupation, breastfeeding duration; child gestational age, sex	Birth weight (examined as a covariate)	**No association** of infant birth weight with maternal ASB intake
Prospective Cohort Studies								
Azad et al., 2016 [29]	Canada, 2009, CHILD	2686 pregnant women	Prenatal exposure	1 year	ASB, servings, validated FFQ	Maternal BMI, total energy intake, diet quality, age, education, smoking, diabetes; infant gestational age, sex, birth weight; breastfeeding duration, timing of solid food introduction	BMI z-score, overweight	**Higher** infant BMI and risk of overweight with daily maternal ASB consumption (males only)
Gillman et al., 2017 [51]	USA, 1999, Project Viva	1078 pregnant women without gestational diabetes	Prenatal exposure	6.6–10.9 years	ASB, servings, validated FFQ	Maternal BMI, age, race, education, smoking, parity; household income; child age, sex	Adiposity (BMI z-score, fat mass index, skinfolds), central adiposity (skinfold ratio, WC)	**No association** of child adiposity with maternal ASB intake
Zhu et al., 2017 [30]	Denmark, 1996, DNBC	918 pregnant women with gestational diabetes	Prenatal exposure	7 years	ASB, servings, validated FFQ	Maternal BMI, energy intake and diet quality, age, employment level, smoking, physical activity; infant sex, breastfeeding duration; child ASB/SSB consumption, physical activity	Large-for-gestational age (LGA), BMI z-score, overweight/obesity	**Higher** BMI and risk of LGA and overweight with daily maternal ASB intake (effect larger in boys)

Studies sorted by year of publication. Abbreviations: ASB, artificially-sweetened beverage; BMI, body mass index; CHILD, Canadian Healthy Infant Longitudinal Development; DMFT, decayed, missing, and filled teeth; DNBC, Danish National Birth Cohort; FFQ, food frequency questionnaire; GA, gestational age; NNS, non-nutritive sweetener; SES, socioeconomic status; SSB, sugar-sweetened beverage. **Bold** text indicates main direction of association between NNS exposure and obesity-related outcome.

2686 mães consumo ASB gestação
↑ 0,2 DP IMC com 1 ano de idade
2 x risco de sobrepeso
Independente das condições maternas

918 mães com DMG consumo diário ASB
aumento 0,59 DP (7 anos de idade)
1,9 x risco obesidade/sobrepeso

Efeito maior em meninos

3 estudos: sem associação

Lactação: resultados incertos (animais)

Azad et al., 2016; Zhu et al., 2017
Archibald et al., 2018

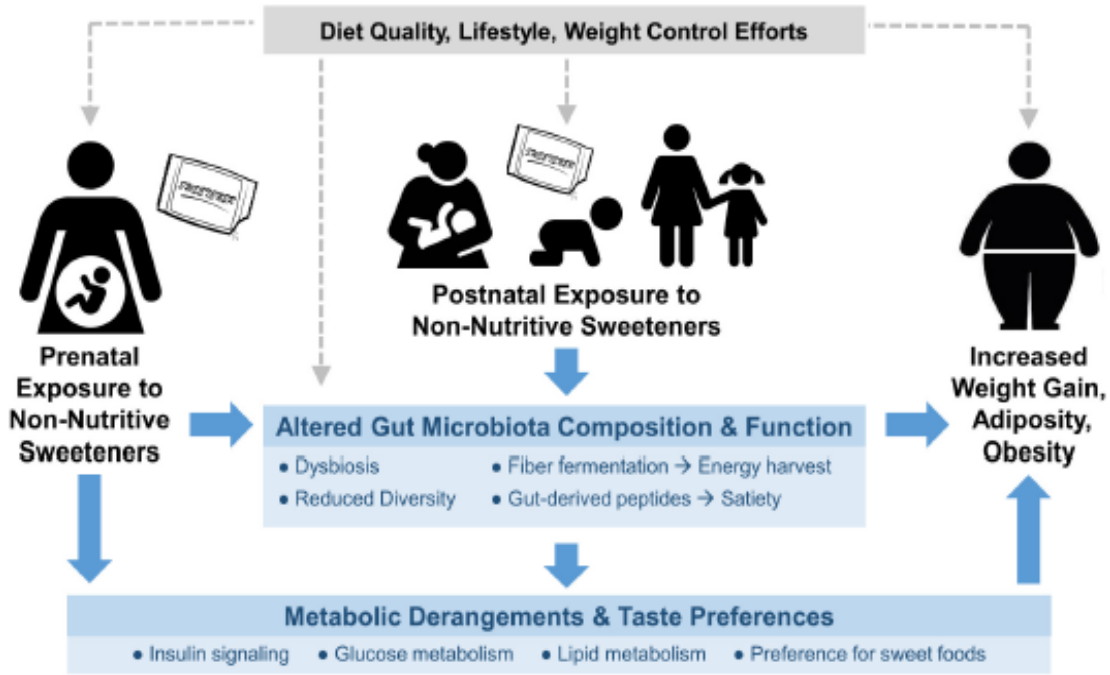


Figure 1. Conceptual framework for the impact of early-life exposure to non-nutritive sweeteners (NNS) on obesity-related outcomes later in life. Potential causal mechanisms are shown in blue; potential confounding factors are shown in grey. NNS exposure occurring in utero, through lactation, or via direct feeding may affect the developmental programing of metabolism, taste preferences, and gut microbiota, ultimately influencing weight gain, adiposity and obesity.

Archibald et al., 2018

SGA: 85 – 90% catch-up até 4 a

SGA – obesidade
Proporção de SGA nos obesos?
Prevalência de obesidade nos SGA?

Catch-up:
excesso de peso nos adultos
altera a composição corporal

Table 1. Summary of general risk factors for childhood obesity

General risk factors	Relative risk
Birth weight (per 100 g)	1.1
Maternal smoking (over 20 cigarettes)	1.8
Parental obesity (body mass index >30 kg/cm^2)	10.4
Catch-up growth	2.2
Catch-down growth	0.2
Early childhood weight (at 8 mo)	3.1
Adiposity rebound	
Late (>61 mo)	1.0
Very early (<43 mo)	15.0

Data adapted from the study by Reilly et al.[40]

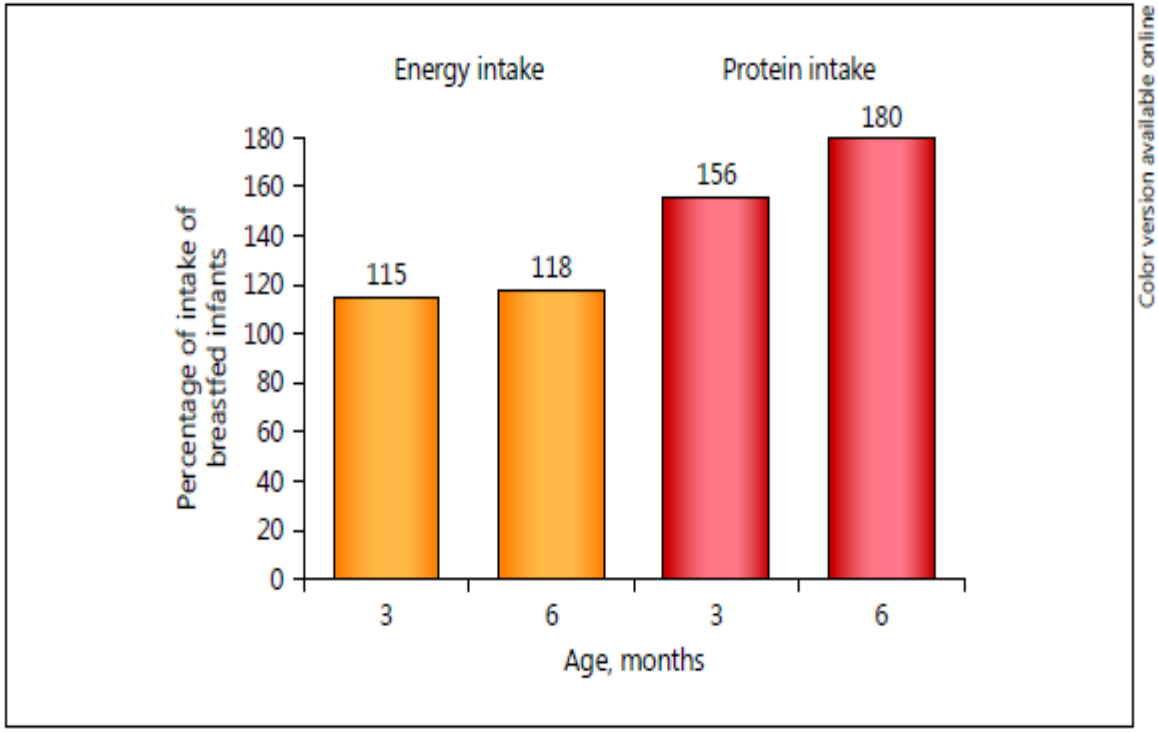
Catch-up rápido:
"rebote precoce de adiposidade"
(5 - 7 anos)

4431 crianças (2 – 47 m)
- Massa magra: SGA < LGA
- SGA: > proporção massa gorda
- SGA: > massa gorda abdominal

Mecanismo: incerto
Compensação na ghrelina? Leptina?
↑ Leptina no catch-up de SGA
↑ Ghrelina (infusão de glicose): ↑ peso excessivo

Rolland-Cachera et al. 1984;
Nam, Lee; 2018

Fórmulas convencionais comparadas ao LM

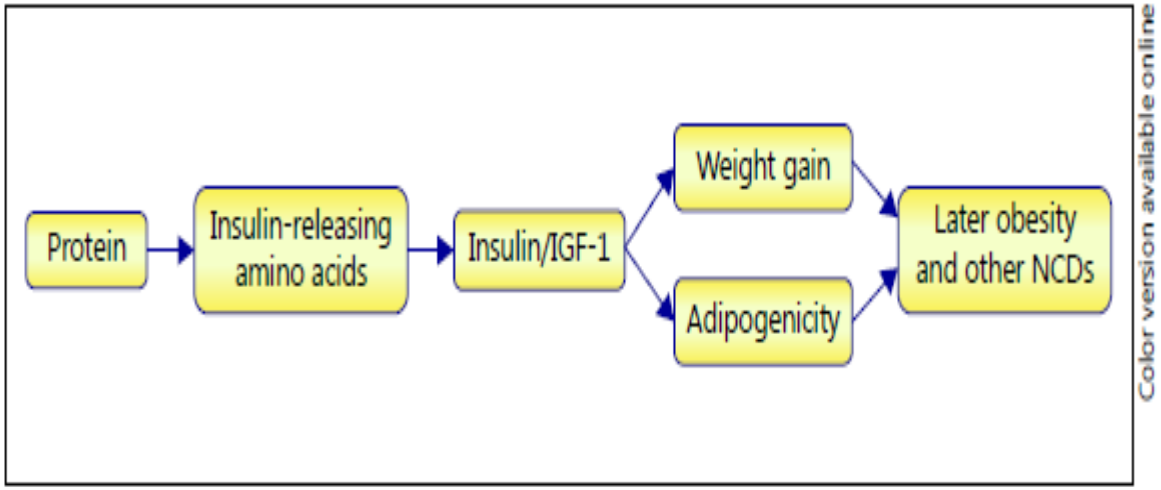


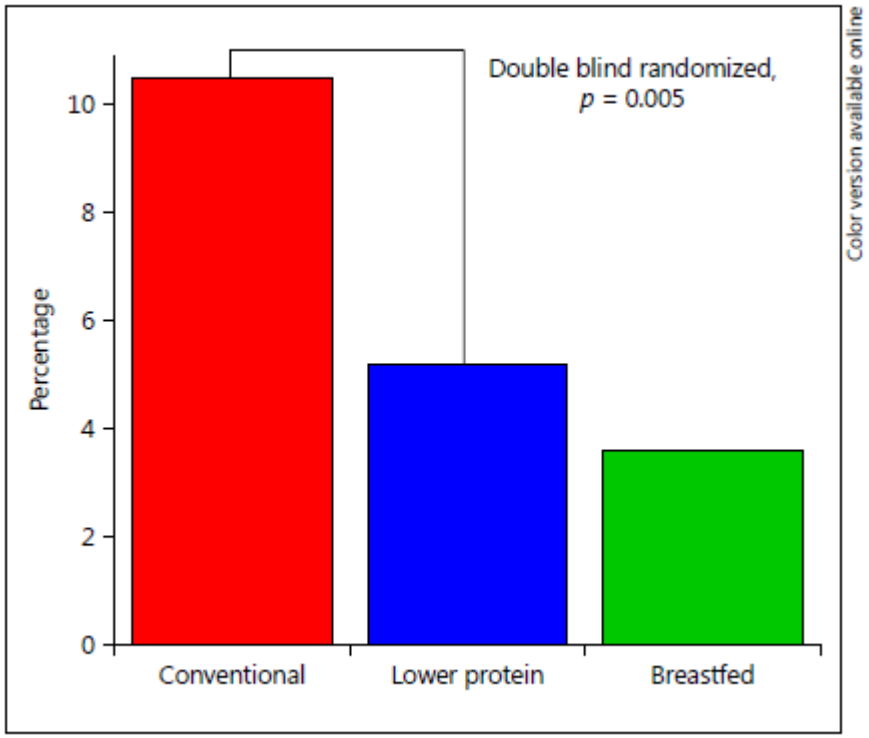
Ingestão de proteína: considerando ingestão de N

- 25% do N LM não é protéico
- Parte da proteína do LM resiste à digestão

Koletzko et al., 2005; 2016; 2017

“Early protein hypothesis”





1678 RN normais AIG

Resultados:

- ↓ aa essenciais
- ↓ insulina e IGF-I
- IMC normal aos 2 anos

Aos 6 anos, obesidade:

3,6% LM

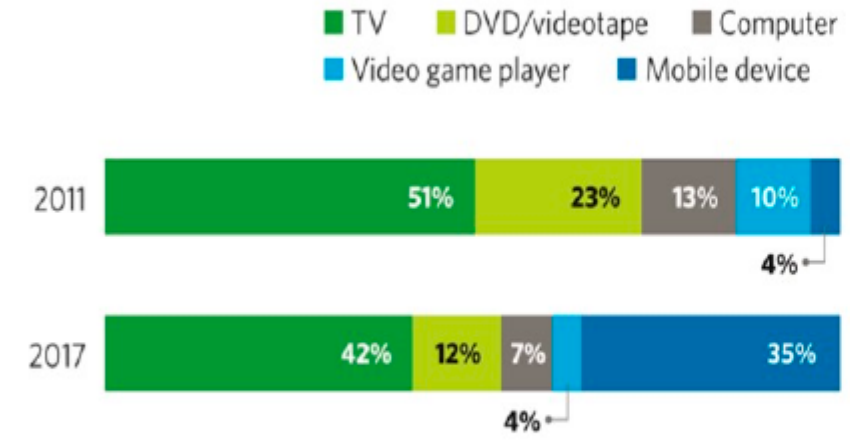
10,5% fórmula convencional

5,2% fórmula ↓ proteína

Koletzko et al., 2009; 2016; Weber et al., 2014

Screen media use, by device, 2011 and 2017

Among 0- to 8-year-olds, proportion of screen time spent with each device



Note: *Video game player* includes console and handheld players. *Mobile device* includes smartphone, tablet, iPod Touch, or similar device.

(a)

Screen media use, by device and age, 2017

Among 0- to 8-year-olds, average amount of screen time spent daily with each device (hours: minutes)

Device	All	Child's age		
	0 to 8	Under 2	2 to 4	5 to 8
Television set	:58	:29[a]	1:09[b]	1:04[b]
DVD/videotape	:17	:06[a]	:23[b]	:18[b]
Mobile device	:48	:07[a]	:58[b]	1:02[b]
Computer	:10	*[a]	:05[b]	:20[c]
Video game player	:06	*[a]	:04[b]	:12[c]
Total screen media	**2:19**	**:42[a]**	**2:39[b]**	**2:56[b]**

*Less than one minute but more than zero.

Note: Superscripts (a,b,c) are used to denote whether differences between groups are statistically significant ($p < .05$). Items with different superscripts differ significantly. Items that do not have a superscript, or that share a common superscript, do not differ significantly.

(b)

50% dos pais: ajuda no aprendizado
50% dos adolescentes: sentem-se adictos

Rideout, 2017; Wolf et al., 2018

> 1,5 h/dia: fator de risco para obesidade

a cada h (aos 2 a): ↑ IMC

a cada h adicional (aos 2 a e 5 m): ↓ 13% AF e ↑ 5% IMC

> 1h (jardim da infância): ↑ risco em 52% de sobrepeso

Table 1. Current daily screen time recommendations 0–5 years [7].

Age	American Academy of Pediatrics Recommendation
0–18 months	No screen time except video chatting
18–24 months	High quality programming/apps with active adult interaction
2–5 years old	One hour of quality programming/apps co-viewed with an adult
	No screens during meals
	No screens at least 1 h before bedtime
	Turn off television and other devices when not in use

De Jong et al., 2013; Wen et al., 2014
Peck et al., 2015

Childhood BMI in relation to microbiota in infancy and lifetime antibiotic use

K. Korpela[1*], M. A. C. Zijlmans[2], M. Kuitunen[3], K. Kukkonen[4], E. Savilahti[3], A. Salonen[1], C. de Weerth[2] and W. M. de Vos[1,5]

↑ *Firmicutes* ↓ bifidobactérias: preditor de obesidade, ↑ adiposidade

162 crianças normais/PN AIG
Aos 3 m: microbiota
Tratamentos com ATBs
Aos 5 -6 anos: IMC

→

Aos 3 m: ↑ *Firmicutes*
↑ IMC os 5 – 6 a (se ATB)

↑ *Streptococcus* e ↓ bifidobactérias:
↑ IMC (mais forte se **ATB**).

Exposição mínima: associação desaparece

Korpela et al., 2017