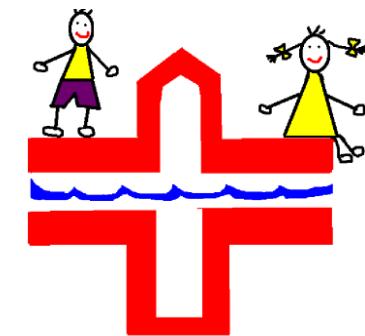




# Imetyks, suoliston mikrobit ja terveysvaikutukset



Erika Isolauri

University of Turku

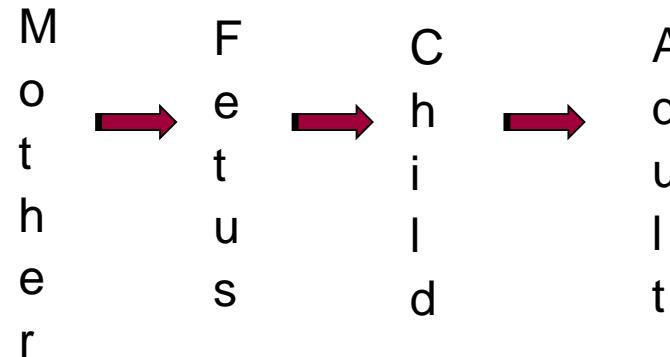
Department of Paediatrics, Turku University Hospital  
Finland



# Terveyden ohjelmoituminen

g  
e  
n  
o  
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## Nutritional Immunological Microbiological PROGRAMMING



High  
risk of  
disease

Manifest,  
chronic  
disease

Low  
risk of  
disease

No  
clinical  
sequelae

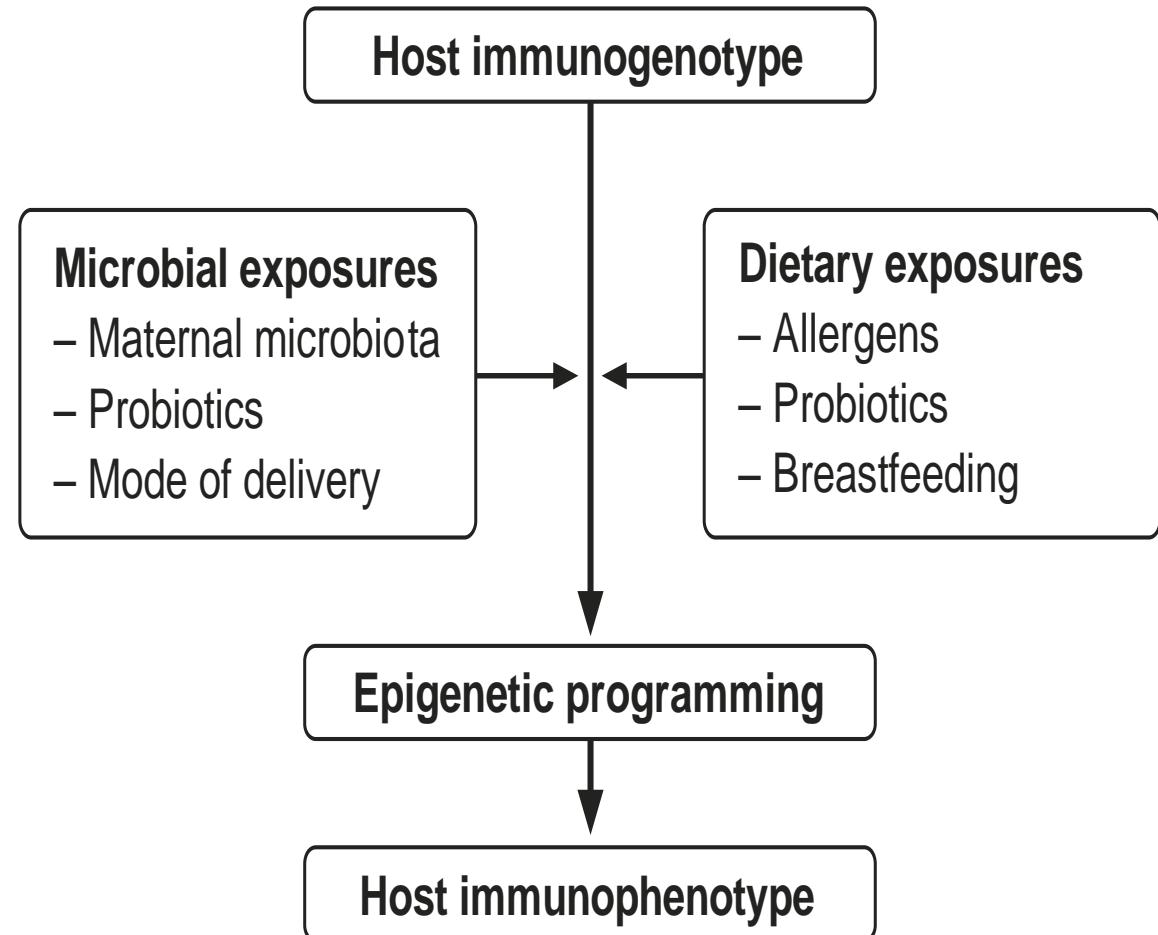
Risk reduction ----- Therapeutic potential

**The developmental origins of health and disease**



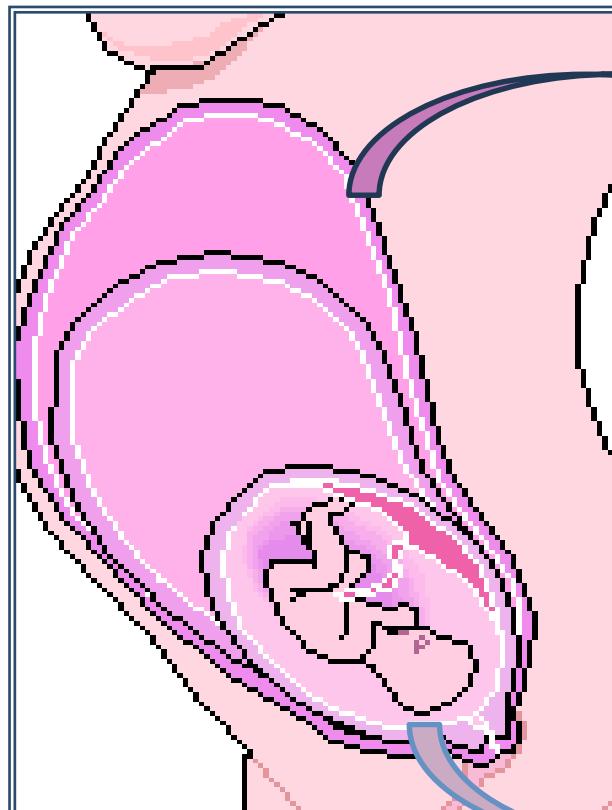
# Key Elements in Immunological Programming

- Pregnancy
- Mode of delivery
- Breast-feeding





# The developmental origins of health and disease



**Intrauteriinen aliravitsemus**  
Sikiön kasvu

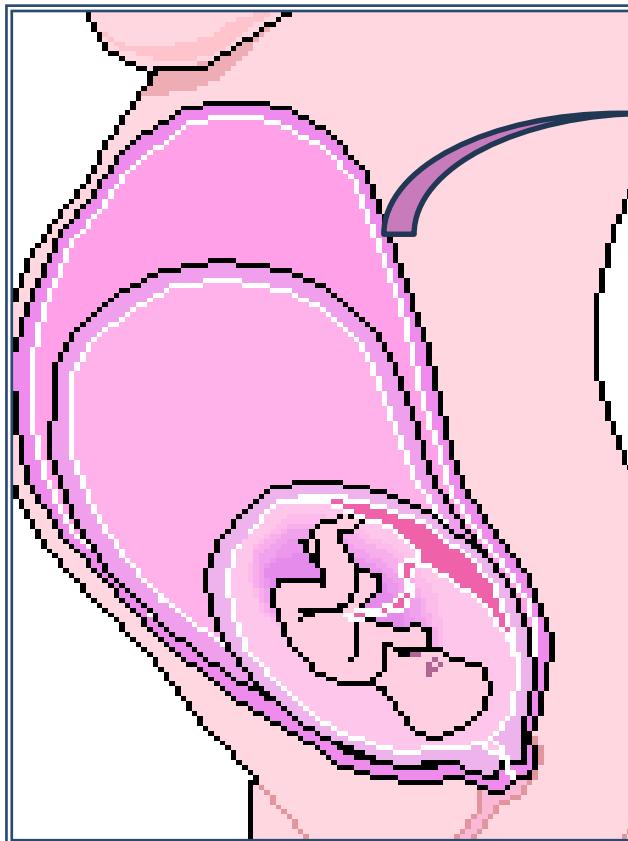


Häiriintynyt  
sokeriaineenvaihdunta  
aikuisena  
MS



Useat tekijät vaikuttavat lapsen immunologiseen/  
metaboliseen kehitykseen...

Mutta kaikki ne vaikuttavat myös mikrobiston  
muodostumiseen- kausaliteetti?



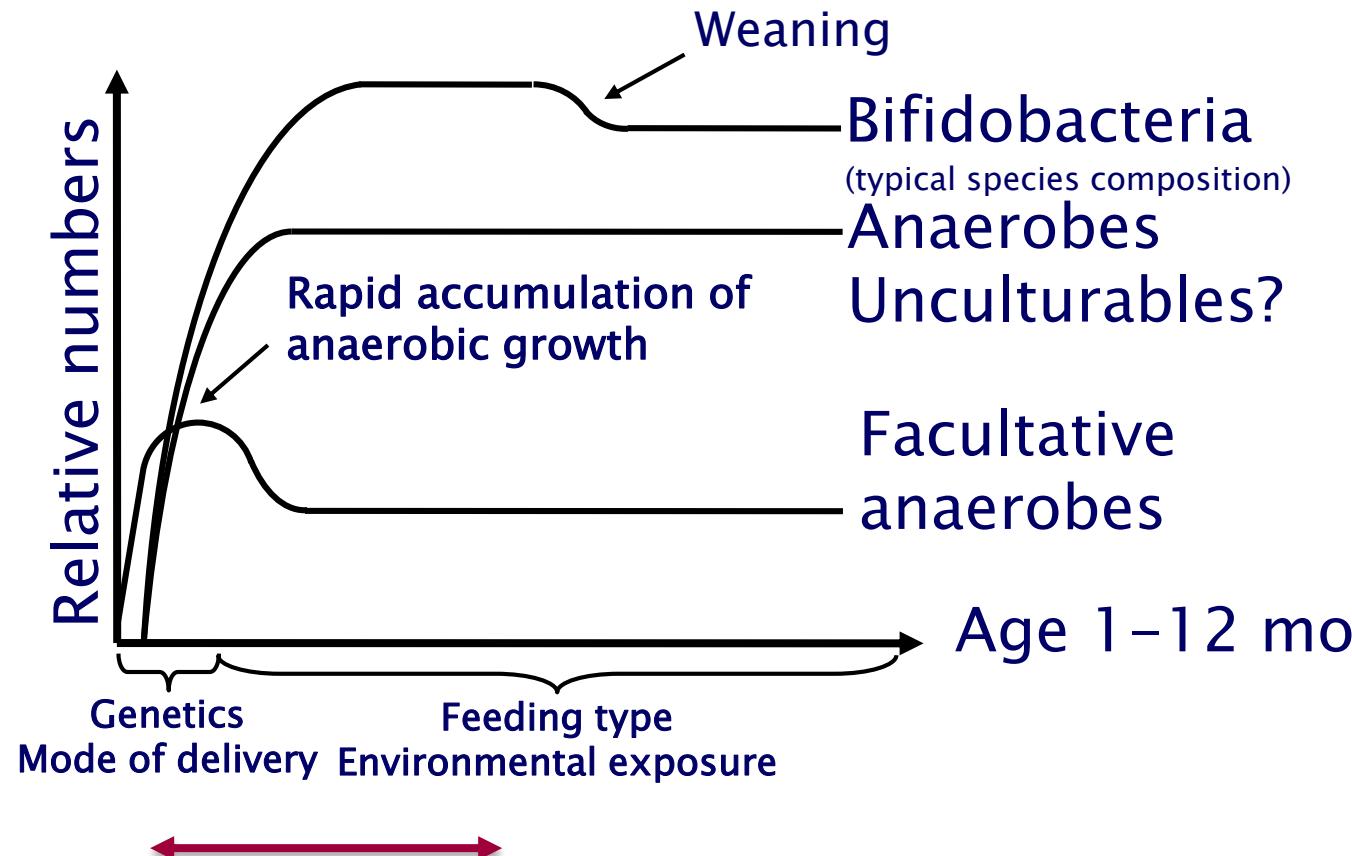
Terveyden  
ohjelmoituminen  
sukupolvelta toiselle

### Runsasenerginen ruokavalio Ylipaino ➔

- GDM
  - Suuri painonnousu
- CS
- Ylipaino 2-4 v/  
Lapsuusajan lihavuus
  - Lihava aikuinen  
(Goldani et al 2011)
  - Astmariski 4x  
(Quinto et al 2011 Lowe et al 2011)
  - T2D riski (Ruchat et al 2013)



# Mikrobiston muodostuminen Postnataalisesti



**The secret of successful programming may be timing**

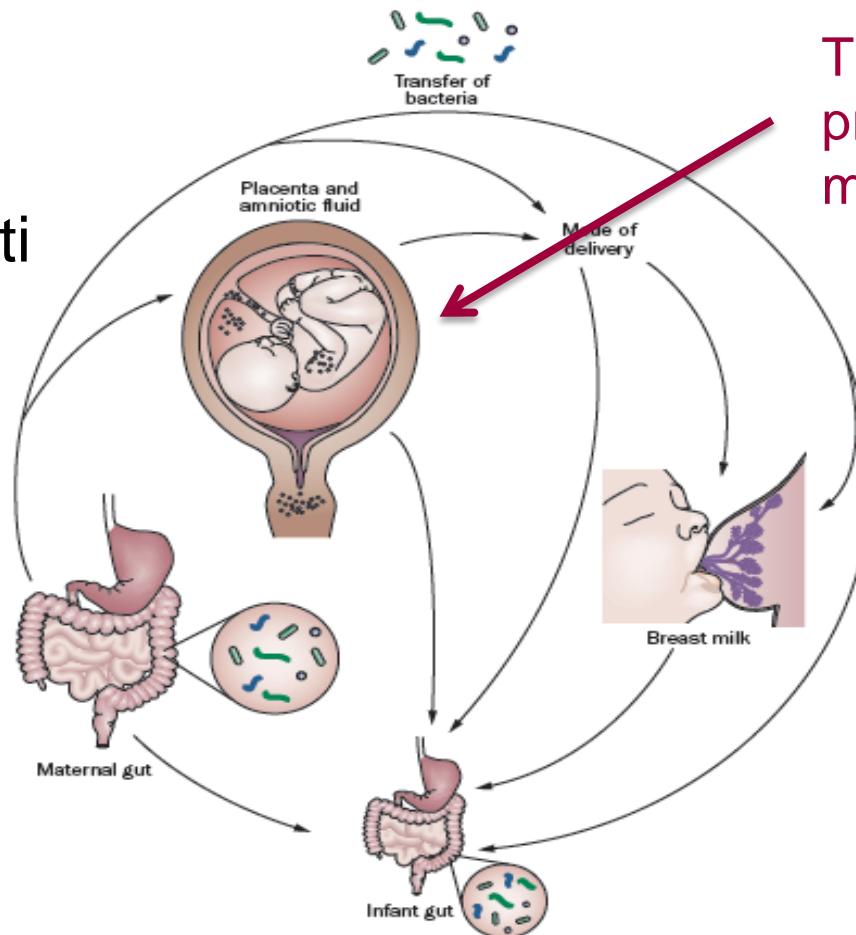


Rautava, S. et al. *Nat. Rev. Gastroenterol. Hepatol.* 9, 565–576 (2012); published online 14 August 2012; doi:10.1038/nrgastro.2012.144

## Microbial contact during pregnancy, intestinal colonization and human disease

Samuli Rautava, Raakel Luoto, Seppo Salminen and Erika Isolauri

Prenataalisesti



The secret of successful  
programming  
may be timing



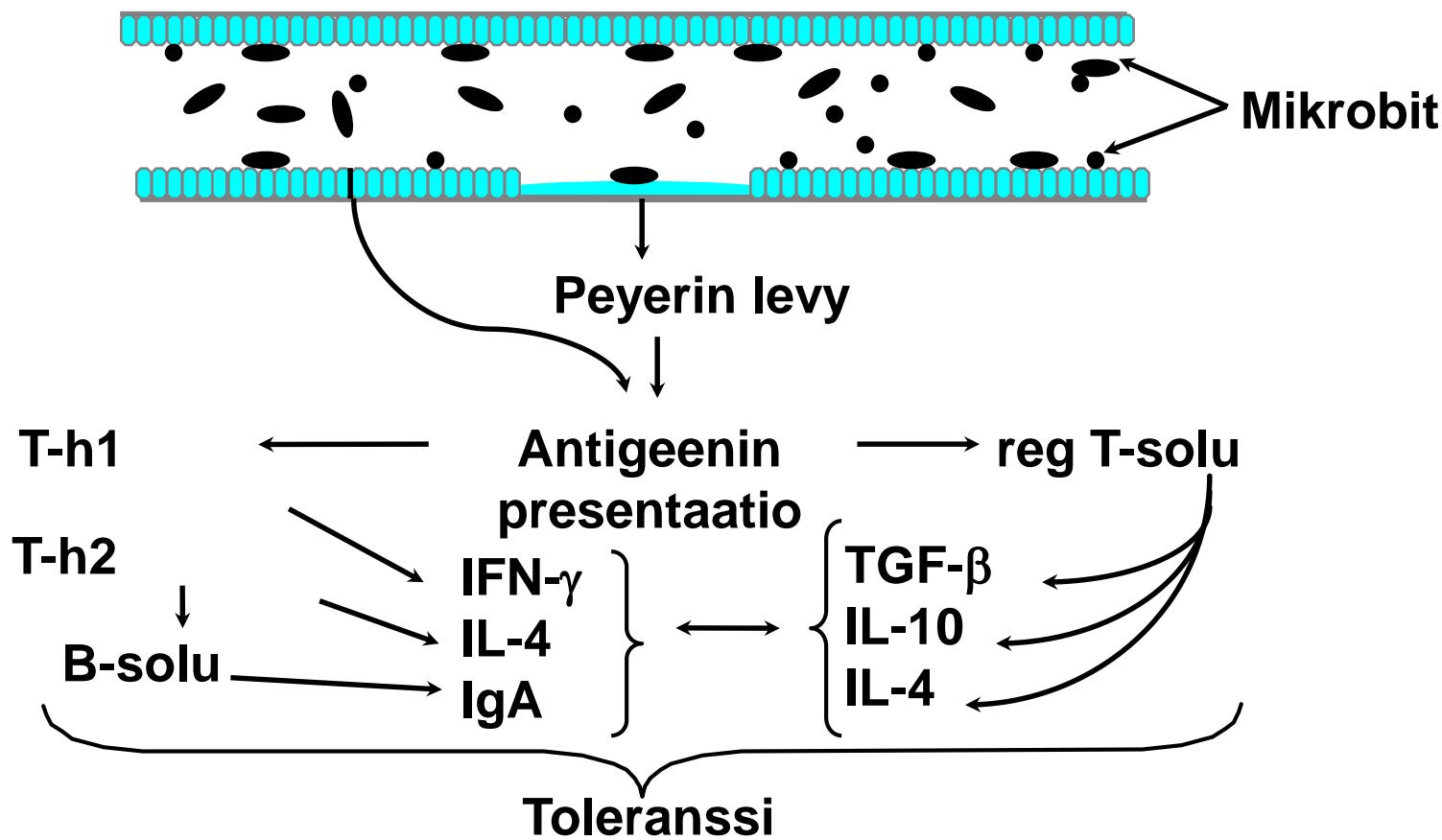
# Muuttuuko käsityksemme mikrobeista?

## 1. Immunologinen tasapaino

“Normaalifloora”

Mikrobi=Patogeeni → infektoriski

Isännän ja mikrobiston vuorovaikutus



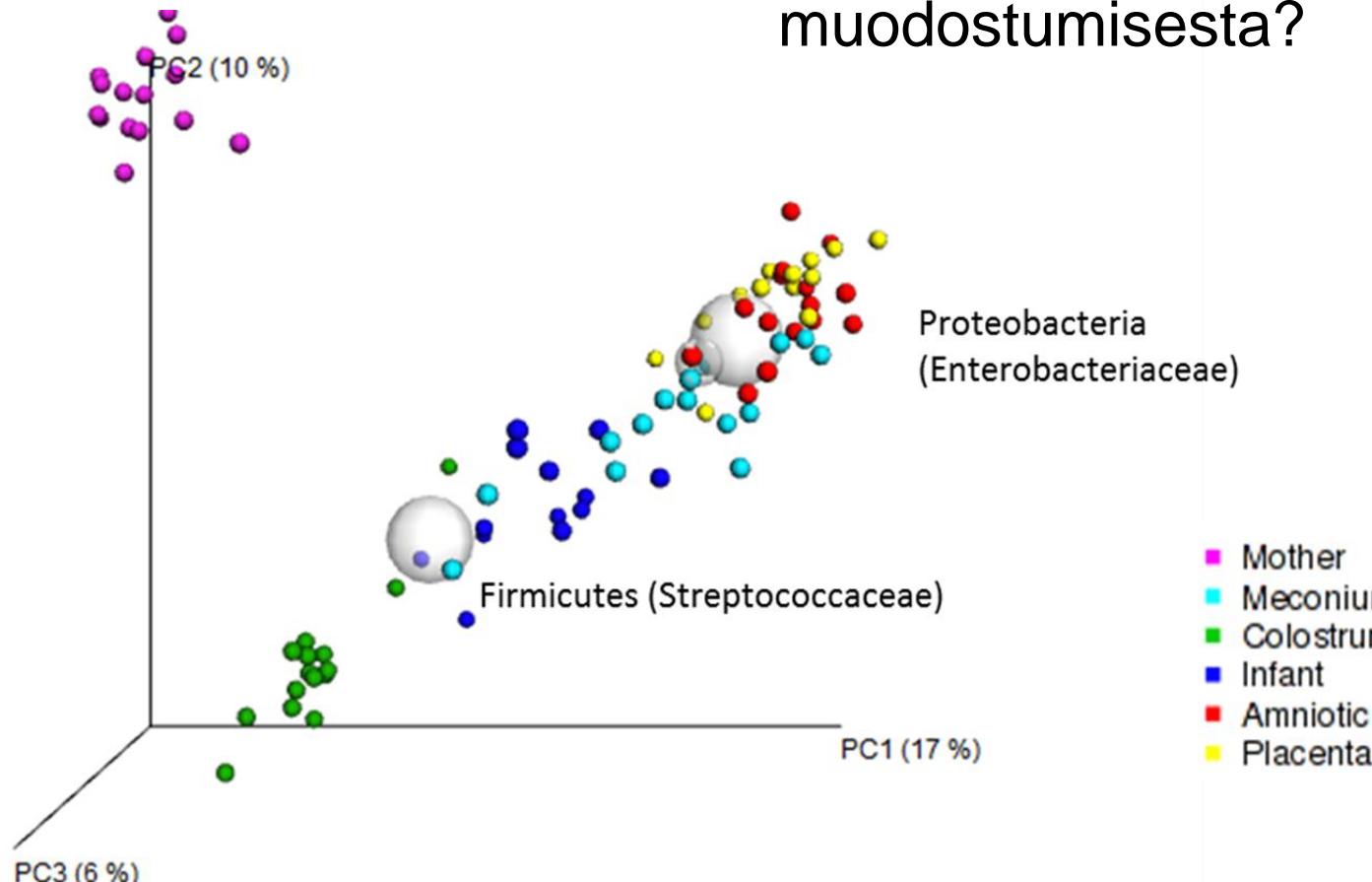
OPEN

## Human gut colonisation may be initiated *in utero* by distinct microbial communities in the placenta and amniotic fluid

Received: 22 October 2015

Accepted: 25 February 2016

Published: 22 March 2016

Maria Carmen Collado<sup>1,2,\*</sup>, Samuli Rautava<sup>3,\*</sup>, Juhani Aakko<sup>1,4</sup>, Erika Isolauri<sup>3</sup> & Seppo Salminen<sup>1</sup>

Muuttuuko käsiteksemme mikrobiston muodostumisesta?



## Normaalipainoiset vs. ylipainoiset naiset

/ erilainen suoliston mikrobisto

raskauden aikana

Collado et al 2008

/ ero heijastuu lapsenpihkaan

Hu et al 2013

/ rintamaidon mikrobistoon

Collado et al 2012

- Bacteroides ja Staphylococcus ryhmän bakteerit yliedustettuna **ylipainoisilla** raskauden aikana.
- Bifidobacterium ryhmän bakteerien määrä suurempi jos **painonousu normaali** raskauden aikana.
- Diabetesäidin lapsen mekonium mikrobistokoostumus muistuttaa aikuisen **DM** mikrobistoa.
- Suuri Staphylococcus ryhmän bakteerien ja pieni Bifidobacterium määrä **ylipainoisten** rintamaidossa.

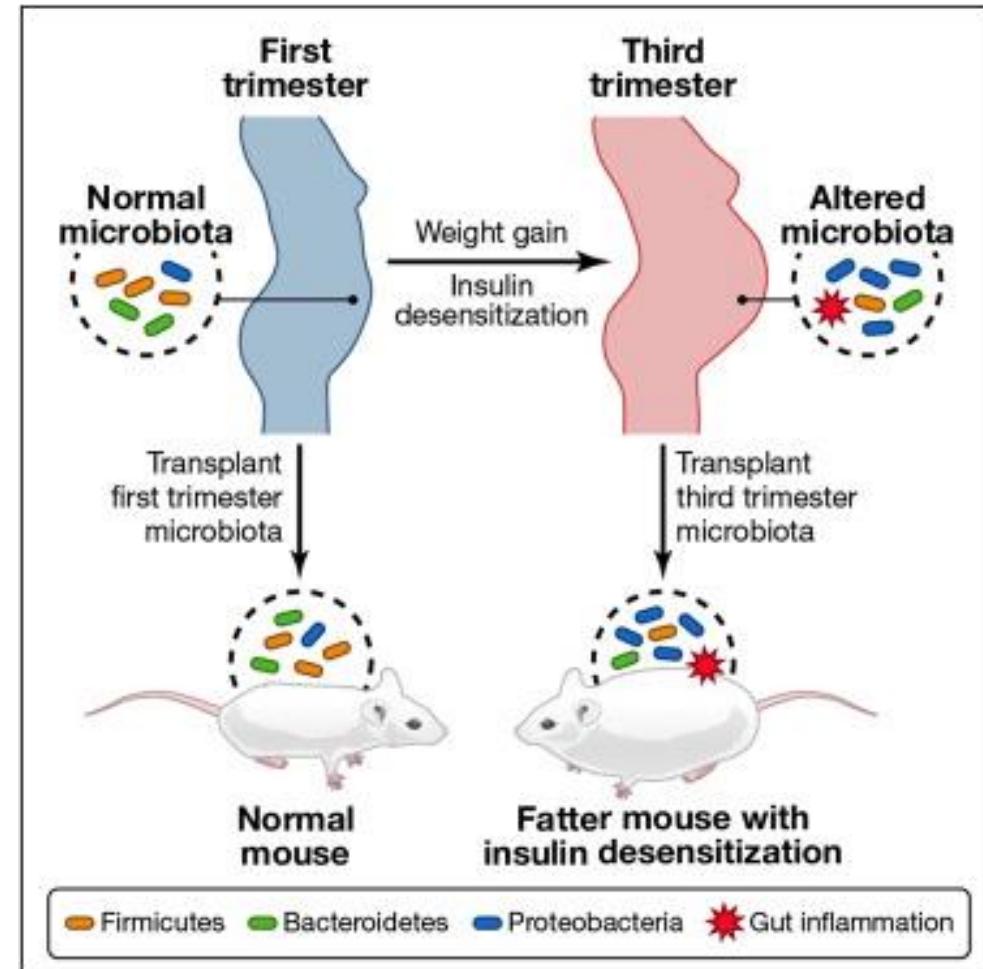


# Host remodeling of the gut microbiome and metabolic changes during pregnancy [Koren et al Cell 2012](#)

Suoliston mikrobisto muuttuu raskauden aikana:

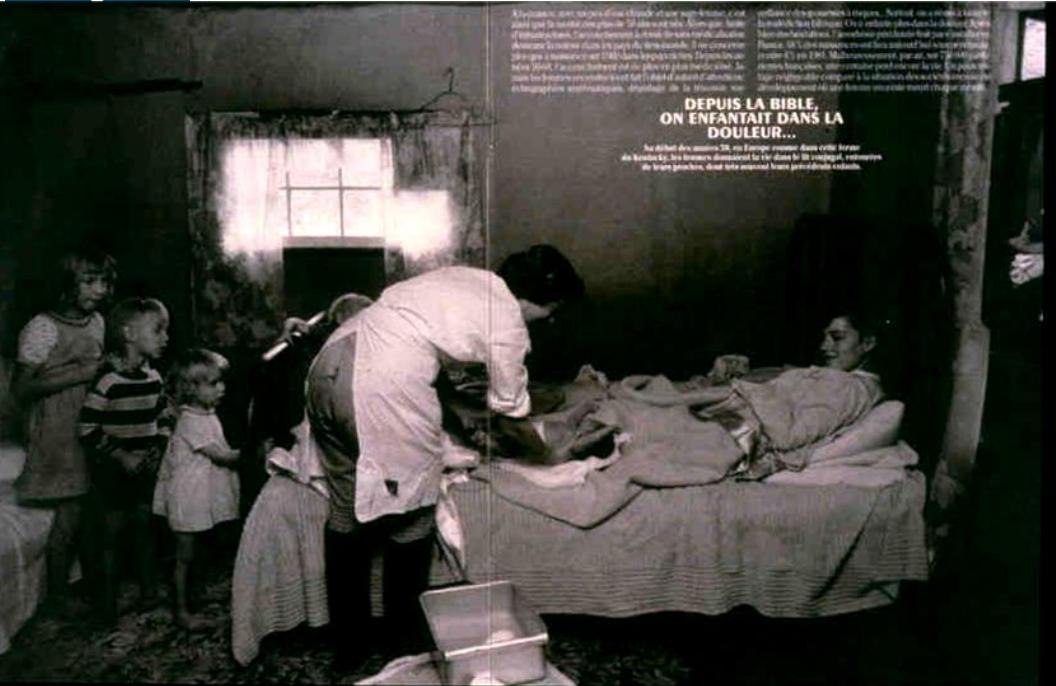
↑ Proteobakteerit  
Actinobakteerit

↓ Mikrobiomin  
monimuotoisuus  
*Faecalibacterium*



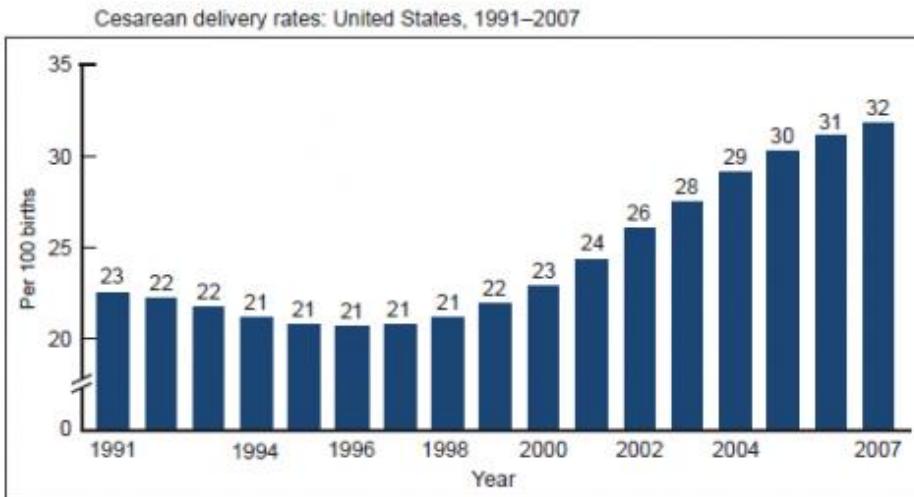


# Synnytystapa vaikuttaa mikrobiston muodostumiseen



Keisarinleikkauksia  
1937-55 3 %

Nyt:  
20-30- 50 %





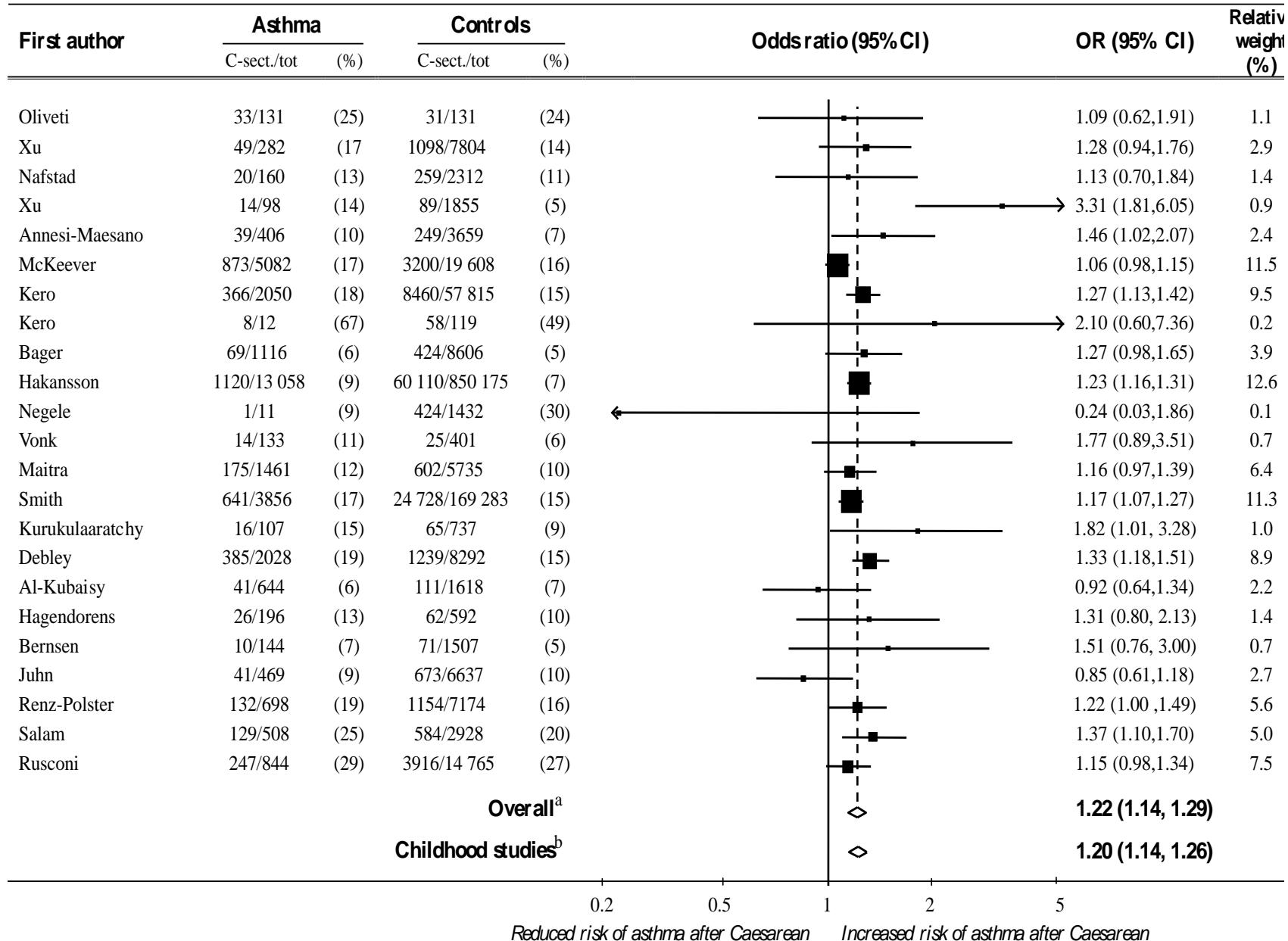
# Syntymä keisarileikkausella kasvattaa ei-tarttuvien tautien riskiä (NCD)

- **Keliakia** (*Decker et al., 2010*)
- **Diabetes DM1** (*Cardwell et al., 2008*)
- **Astma** (*Kero et al., 2002; Thavagnamanan et al., 2008*)
- **Atooppinen ihotuma** (*Thavagnamanan et al., 2008*)
- **Ruoka-allergiat** (*Eggesbo et al., 2003*)

## Sevelsted et al 2015

**TABLE 1** IRRs by Cesarean Delivery in the 35-Year Period 1977–2011 Following 1.9 Million Term Children in the Age Span 0 to 15 Years

	Cases	aIRR (95% Confidence Interval); P	PARF (Cases)
Asthma <sup>a</sup>	103 822	1.23 (1.21–1.25); P < .0001	3.07 (3187)
Asthma >5 y <sup>b</sup>	48 858	1.16 (1.13–1.19); P < .0001	2.19 (1070)
Systemic connective tissue disorders	7498	1.11 (1.04–1.19); P = .0021	1.53 (115)
Juvenile arthritis	6946	1.10 (1.02–1.18); P = .0117	1.34 (93)
Diabetes type 1	6136	1.01 (0.93–1.10); P = .82	— <sup>d</sup>
Inflammatory bowel diseases	2697	1.20 (1.06–1.36); P = .004	2.70 (73)
Immune deficiencies	2589	1.46 (1.32–1.62); P < .0001	6.09 (158)
Celiac disease	1944	0.99 (0.87–1.14); P = .89	— <sup>d</sup>
Leukemia	1631	1.17 (1.00–1.36); P = .048	2.31 (38)
Psoriasis	1306	0.98 (0.81–1.18); P = .81	— <sup>d</sup>
Arm fracture <sup>a,c</sup>	77 490	0.99 (0.96–1.01); P = .19	— <sup>d</sup>



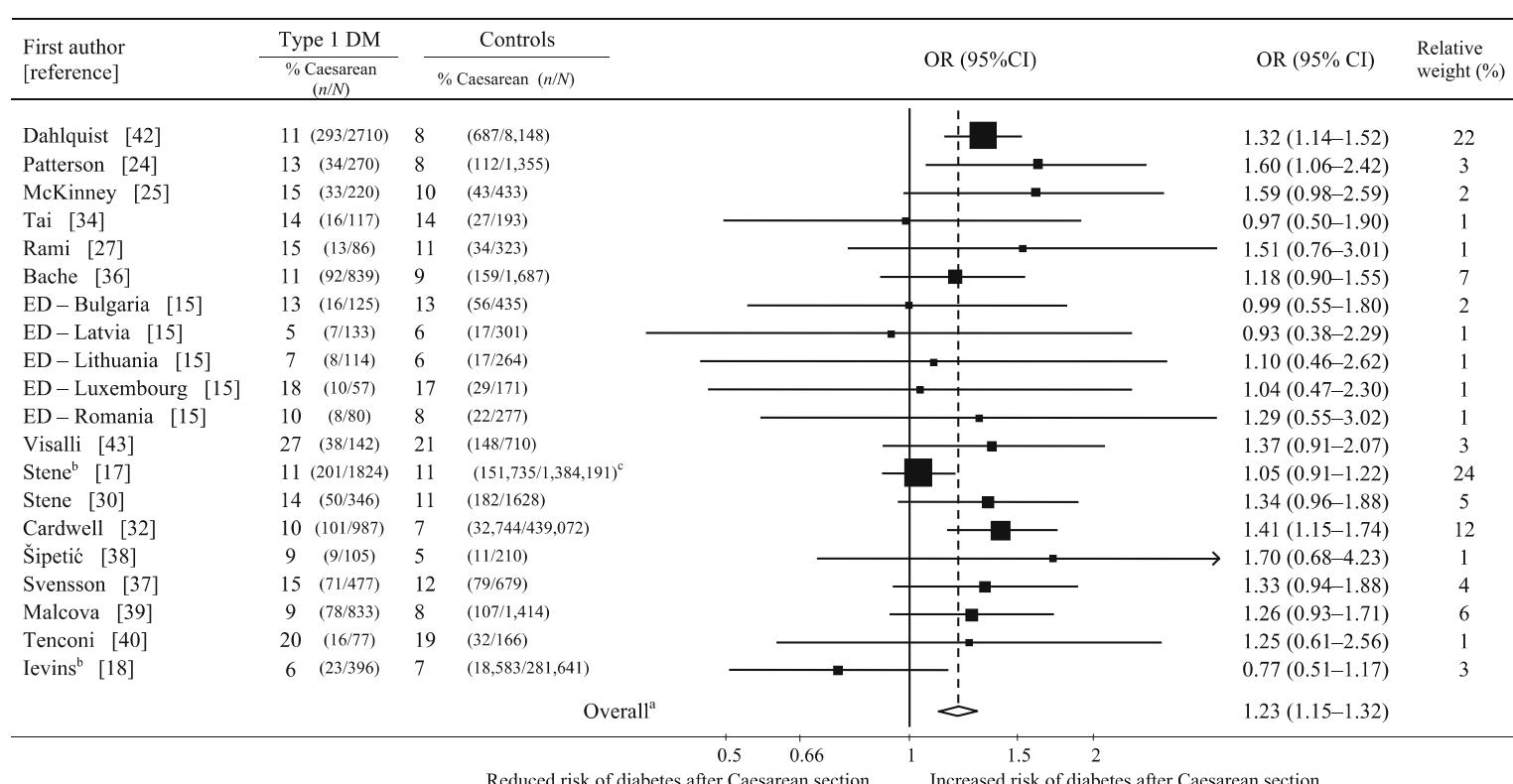


# Caesarean section is associated with an increase risk of childhood-onset diabetes mellitus: a meta-analysis of observational studies

Cardwell et al

Diabetologia (2008) 51:726–735

731





## A birth cohort study, 1978, Brazil

A randomly selected sample (n=2057)

**Obesity BMI>30 at 23-25 y**

**15,2% in CS**

**10,4% in VD**

Prevalence ratio for obesity in subjects aged 23–25 y according to type of delivery obtained by the Poisson regression model

	Prevalence ratio	95% CI	P
Cesarean delivery (nonadjusted)	1.46	(1.15, 1.85)	0.002
Cesarean delivery (adjusted) <sup>1</sup>	1.58	(1.23, 2.02)	<0.001

<sup>1</sup> Adjusted for subject's birth weight, sex, physical activity, smoking, schooling, and income and maternal schooling and smoking during pregnancy.



# Cesarean section and risk of obesity in childhood, adolescence and early adulthood

## Evidence from 3 Brazilian birth cohorts

Barros et al 2012

4 yrs  
11 yrs  
15 yrs  
Not: 23 yrs

50% higher prevalence of obesity in CS vs VD subjects

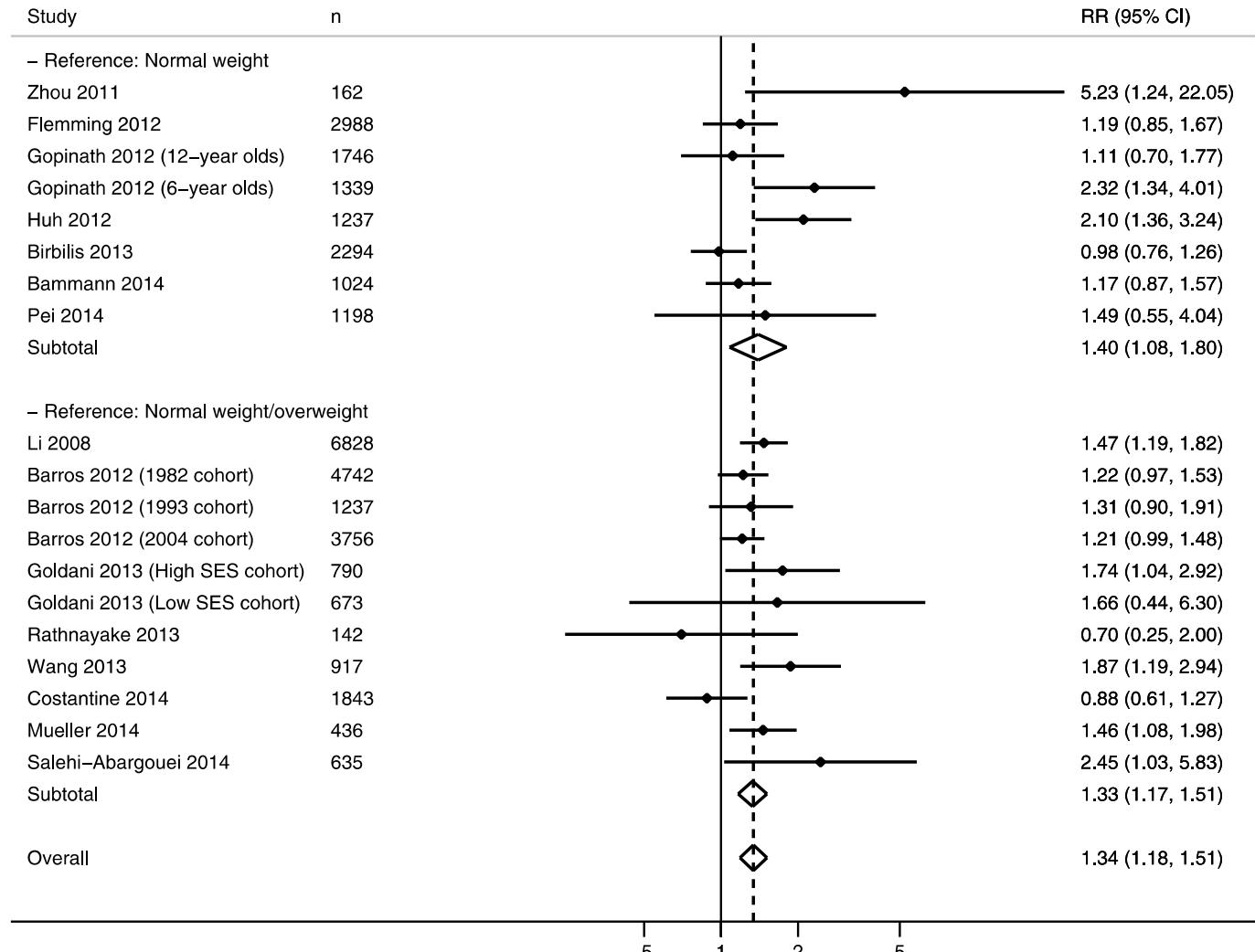
Obesity of individuals born through cesarean section relative to individuals born thro

Follow-up visit/cohort	All			
	Crude	P	Adjusted	P
4 y/1982 cohort ( <i>n</i> = 4742)	1.53 (1.25, 1.87)	<0.001	1.22 (0.97, 1.53)	0.084
4 y/1993 cohort ( <i>n</i> = 1237)	1.80 (1.27, 2.54)	0.001	1.31 (0.90, 1.92)	0.158
4 y/2004 cohort ( <i>n</i> = 3756)	1.52 (1.28, 1.81)	<0.001	1.21 (0.99, 1.48)	0.062
11 y/1993 cohort ( <i>n</i> = 4100)	1.44 (1.22, 1.72)	<0.001	1.06 (0.86, 1.30)	0.575
15 y/1993 cohort ( <i>n</i> = 4349)	1.47 (1.20, 1.79)	<0.001	1.23 (0.98, 1.54)	0.073
23 y/1982 cohort ( <i>n</i> = 4297)	1.10 (0.89, 1.37)	0.374	1.10 (0.87, 1.41)	0.428



# Syntymä keisarileikkausella (CS) kasvattaa lihavuuden riskiä:

Kuhle et al 2015  
Systemaattinen  
katsaus  
Meta-analyysi

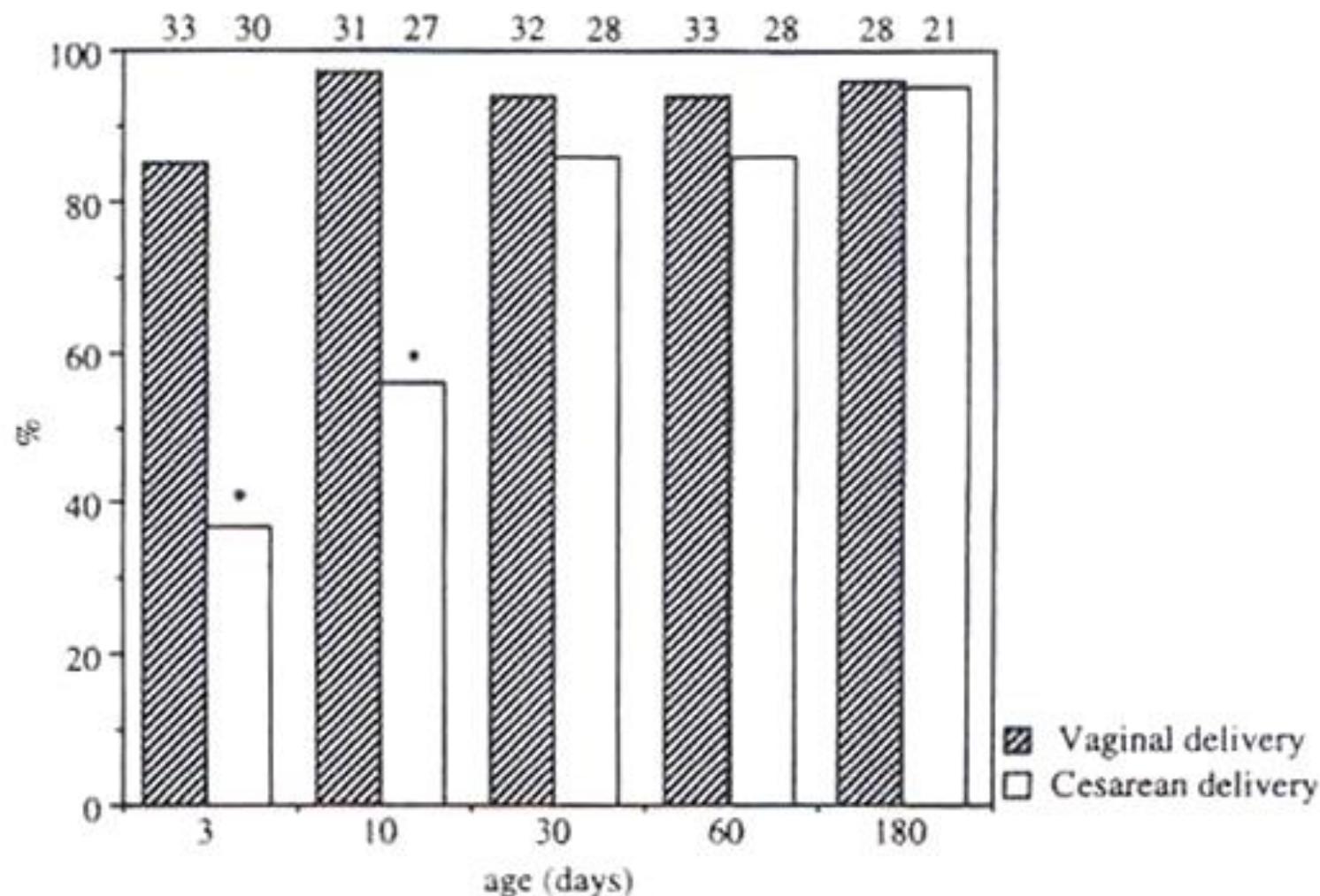


**Figure 2** Forest plot of studies examining the association between caesarean section (compared with vaginal delivery) and offspring obesity. CI, confidence interval; RR, risk ratio; SES, socioeconomic status.



number of infants studied

Grönlund et al- 99



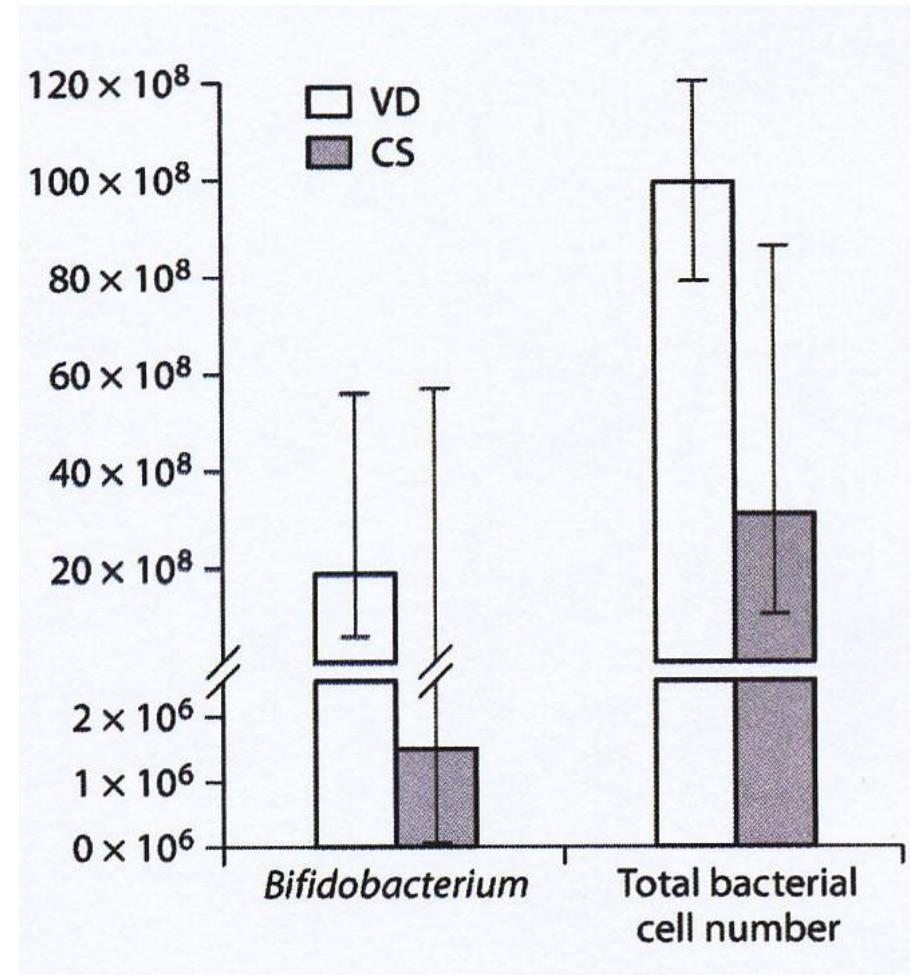
**FIG. 1.** The percentage of *Bifidobacterium*-like bacteria (BLB) colonization in infants aged 3, 10, 30, 60, and 180 days born vaginally and by cesarean delivery. \* $p < 0.001$ .



# Ero synnytystavassa- Ero mikrobistossa

Effects on **Gut Microbiota** and Humoral Immunity  
Huurre et al 2008

- 165 äiti-lapsi paria:  
141 (85%) VD  
24 (15%) CS
- Bifidobakteerit  
ja kokonaismäärä  
1 kk iässä (FISH)





## Imetyksellä vaikuttaa mikrobiston muodostumiseen

Imeväisen ruokinnan  
kultainen standardi:  
terve rintaruokittu  
lapsi

Bifidobakteerit :  
*B.breve*, *B.infantis*,  
*B.longum*  
kolonisoivat lapsen  
suoliston





## Rintamaito:

Antigeniit  
β-lactoglobulin  
Ovalbumin  
Gliadin etc.  
degraded by  
the mother's gut

**Vanha strategia:**  
**Eliminaatiodieetti**



Anti-inflammatoryiset tekijät  
Fatty acids  
Antioxidants, Nucleotides,  
Glutamine, Lactoferrin  
IgA, Cytokines  
Hormones, Growth factors  
Oligosaccharides  
Microbiota

**Uusi strategia:**  
**Aktiiviset yhdisteet**



# Rintamaidon koostumus riippuu... äidin allergiasta:

Maternal breastmilk and intestinal bifidobacteria guide the compositional development of the *Bifidobacterium* microbiota in infants at risk of allergic disease

Grönlund et al 2007

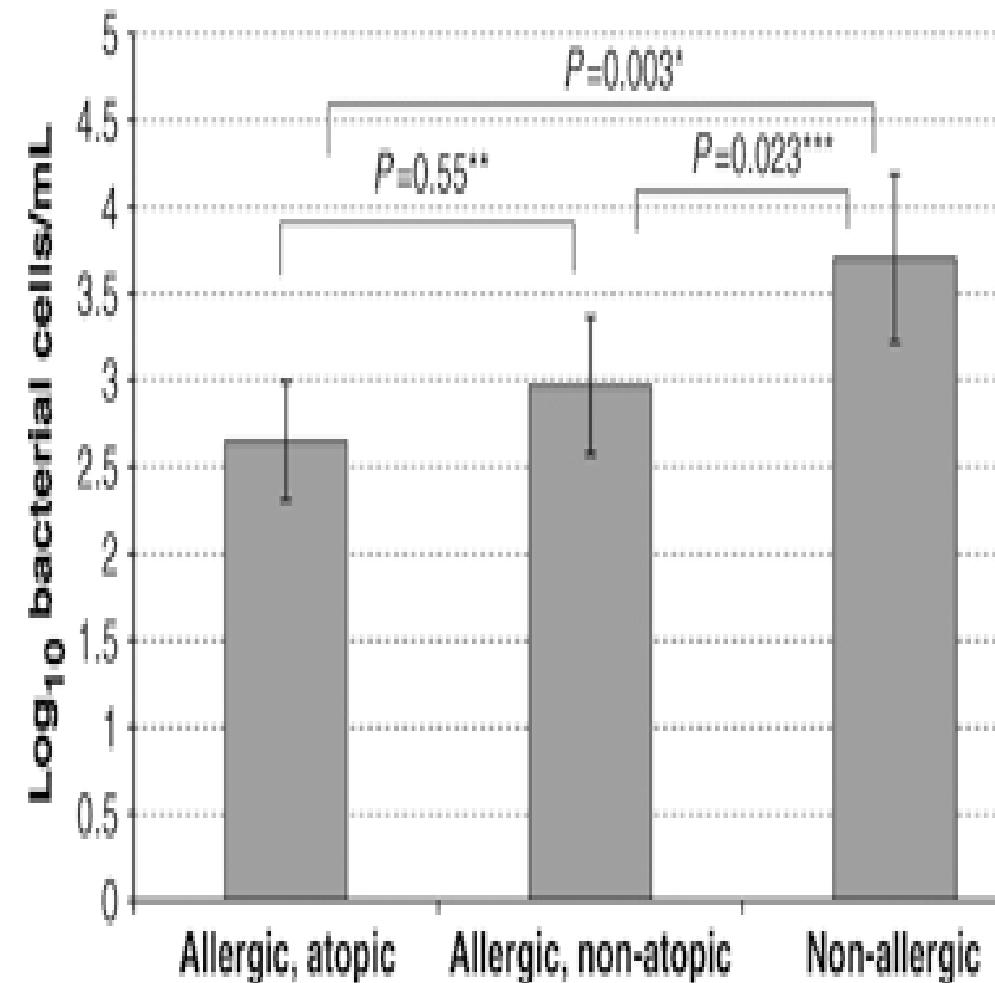
61 äiti-lapsiparia

**Rintamaitonäyte 1 kk**

Kaikki lapset kolonisoituneet bifidobakteereilla,  
paitsi;

1 syntynyt CS

1 saanut antibioottia





## ... äidin painosta ja painonroususta

Distinct composition of **gut microbiota** during pregnancy in normal weight and overweight women

Collado et al 2008

- Bacteroides ja Staphylococcus yleisiä ylipainoisilla
- Bifidobacterium määrit korkoita niillä, joilla normaali painonrousu raskauden aikana



# Maternal weight and weight gain during pregnancy modify the immunomodulatory potential of **breast milk**

Collado et al 2012

- korkeat *Staphylococcus* ja matalat *Bifidobacterium* määärät ylipainoisilla verrattuna normaalipainoisiin
- Matalat TGF- $\beta$ 2 ja sCD14 tasot rintamaidossa ylipainoisilla



... myös lapsi vaikuttaa

## Changes in immunomodulatory constituents of human milk in response to active infection in the nursing infant

Rintamaito  
(n=31)

Tilanteessa kun  
lapsi otettu  
sairaalahoitoon  
kuumeen vuoksi

S1= akuutti vaihe

S2= toipumisvaihe

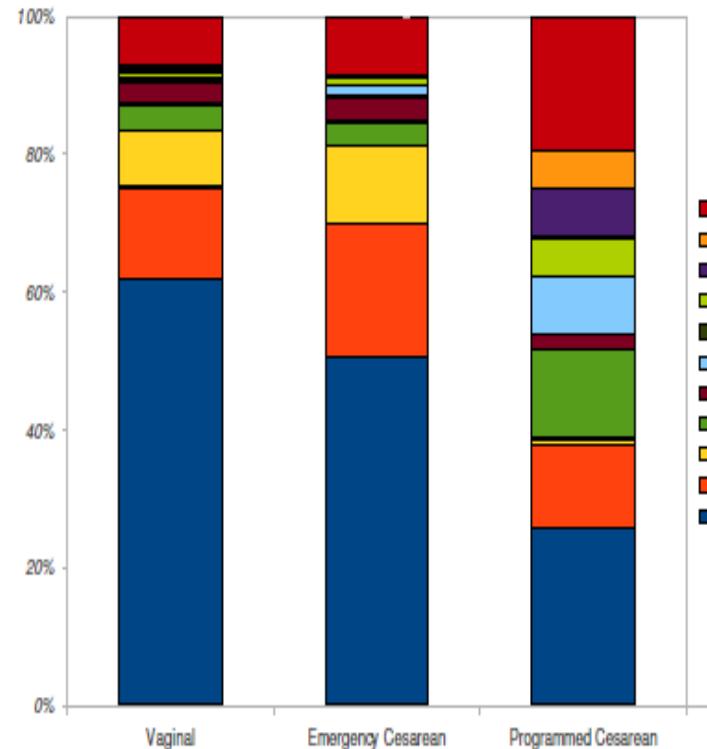
	CD45+	Mothers of sick infants who were not ill themselves (N) (n = 20)		<i>P</i> value
		S1	S2	
		6,078 (2,226; 18,955)	2,462 (717; 11,508)	<b>0.014<sup>a</sup></b>
		2,279 (389; 4,090)	730 (184; 3,167)	0.104 <sup>a</sup>
	Neuroph/ml	1,246 (877; 9,933)	986 (261; 4,328)	<b>0.045<sup>a</sup></b>
	Macroph/ml	1,365 (325; 3,834)	321 (100; 2,155)	<b>0.006<sup>a</sup></b>
		64.0 (32.0; 122.0)	58.0 (29.0; 149.0)	0.167 <sup>a</sup>
	Lactoferrin Mg/ml	0.79 (0.52; 1.33)	0.50 (0.41; 0.59)	0.072 <sup>b</sup>
		0.63 ± 0.23	0.58 ± 0.20	NS <sup>d</sup>
	TNF- $\alpha$ pg/ml	3.92 ± 1.80	3.09 ± 1.74	0.108 <sup>d</sup>



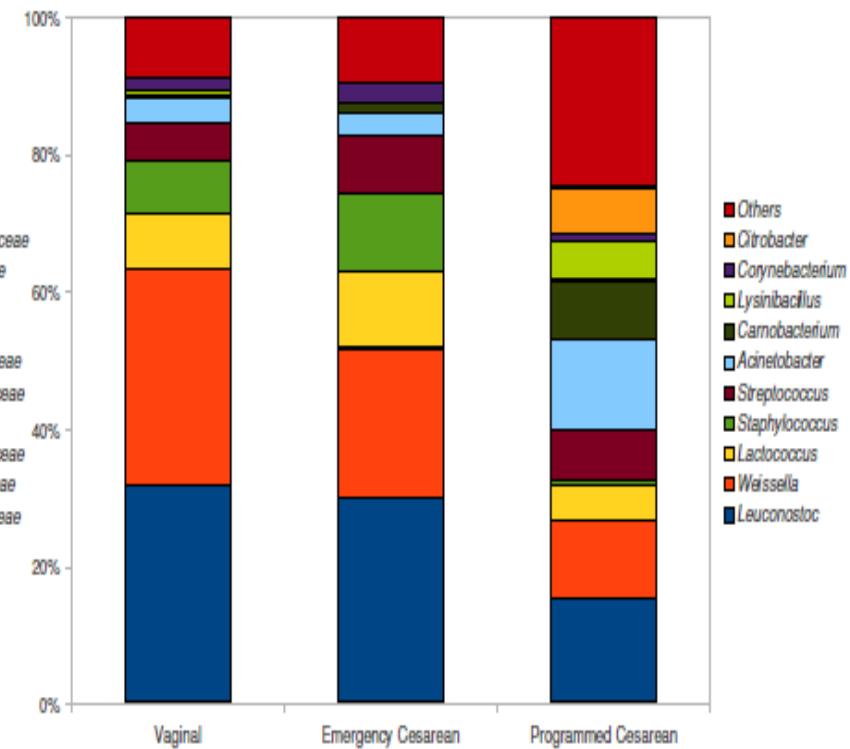
... synnytystapa vaikuttaa myös rintamaidon mikrobistoon

## MICROBIOTA COMPOSITION

Colostrum



Mature milk (at 6 mo)

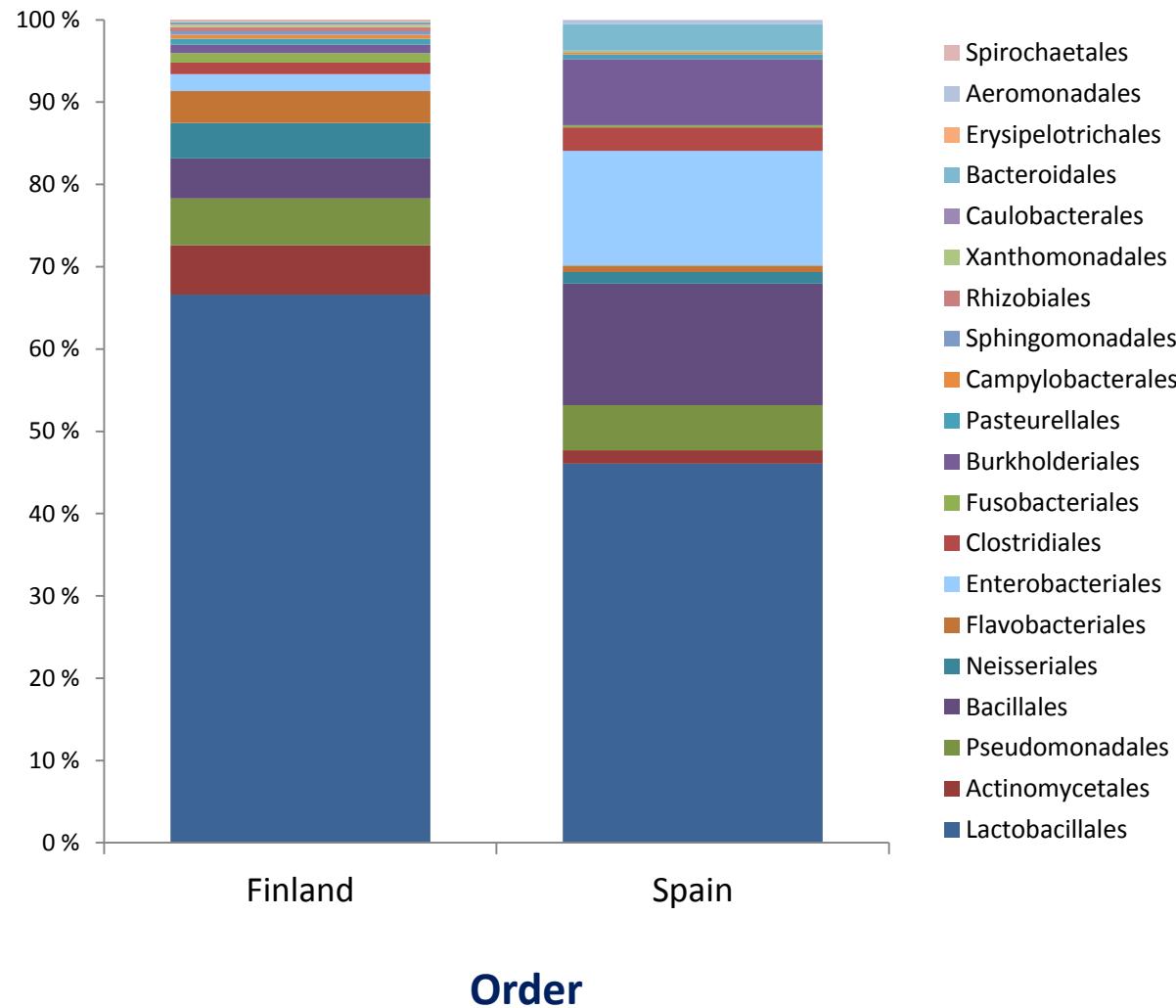


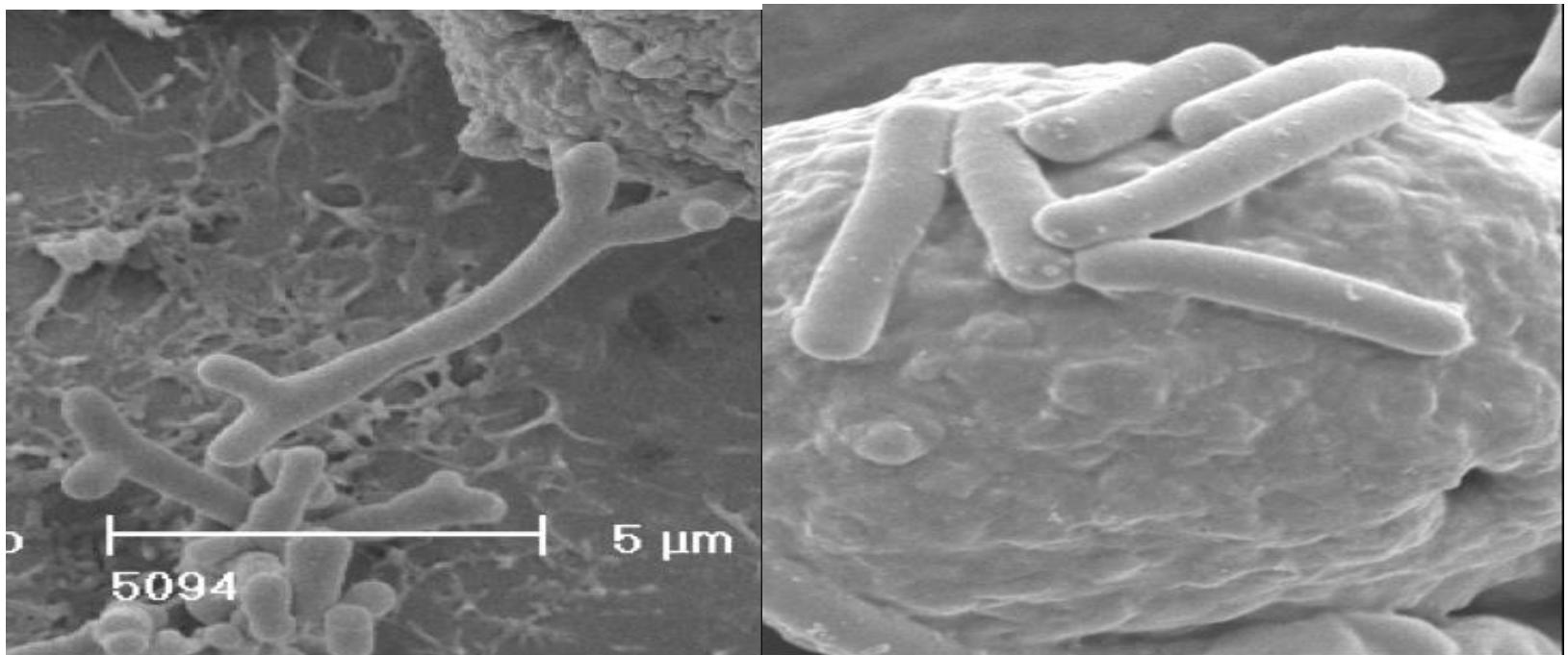
Mode of delivery

MC Collado 2012



# ... sekä maantiede





## Voisiko hoito spesifeillä probioottikannoilla pienentää ei-tarttuvien tautien riskiä?

1. Epidemiologinen näyttö
2. Immunologinen/ mikrobiologinen näyttö
3. Kokeellinen näyttö
4. Kliininen näyttö



# Ajattelu ennen: Allergiariski

Allergia kehittyy kosketuksesta  
herkistäviin aineisiin

Allergisten sairauksien syntyä ei tunneta tarkkaan. Tiedetään kuitenkin, että yliherkkyys kehittyy samanlaisen tapahtumasarjan seurauksena kuin vastustuskyky taudinaiheuttajille muodostuu: kun elimistöön tulee bakteereja ja viruksia, se alkaa muodostaa niitä tuhoavia vastaaineita. Tähän perustuu vauvojen rokotus tavallisimpia tauteja vastaan. Kun lapsen istutetaan vaarattomaksi tehtyjä

taudinaiheuttajia, hän on neljän–kuuden viikon kuluttua täysin tai osittain immuuni tuolle taudille.

Kun allergiatapumuksen perintyvä lapsi saa elimistöönsä allergeeneja, hänenä kehittyy jonkin ajan kuluttua myös näille vasta-aineita. Mutta tässä tapauksessa nuo vasta-aineet saavat aikaan allergian kehityksen ja allergisia oireita aina, kun lapsi joutuu uudelleen kosketukseen herkistäjän kanssa.





The New York Times

25.5.2000

# What Do You Mean, 'It's Just Like a Real Dog'?

As Robot Pets and Dolls Multiply, Children React in New Ways to Things That Are 'Almost Alive'



By KATHY SEIFER

In a country where the television personality *David Letterman* is known for his love of talking to robots, and where the *Alvin and the Chipmunks* sing chipmunk songs, it's not surprising that children are getting interested in talking to their electronic pets. And it's not surprising that they're getting attached to them. In fact, it's almost expected. After all, the *Toy Story* movies have introduced millions of children to the idea that toys can be more than just objects of fun.

But what's new is the way children are responding to their electronic pets. Instead of being satisfied with a simple pet that can bark and wag its tail, many children are demanding that their pets be more lifelike. They want their pets to be able to respond to their commands, to play games with them, and even to learn new tricks.

And they're getting what they want. As the market for electronic pets grows, so does the variety of products available. From simple barking dogs to complex robots that can walk, run, and even jump over obstacles, there are now many different types of electronic pets to choose from.

One trend in particular seems to be growing: the "virtual pet."

These are electronic pets that don't have physical bodies. Instead, they are controlled by a computer program that allows children to interact with them through a keyboard or a mouse.

The popularity of virtual pets is growing fast, especially among girls. And that's good news for companies like Hasbro, Mattel, and Fisher-Price, which are introducing new lines of virtual pets every year.

The positive side of virtual pets is that they are easy to care for. They don't need food, water, or attention. They also don't cost much money, making them a great choice for parents who are looking for a low-cost gift for their children.

However, there are some negative aspects to virtual pets. For one thing, they can be expensive. A typical virtual pet costs between \$50 and \$100. And they require electricity, which means that they need to be charged regularly. This can be inconvenient, especially if you live in a place where power outages are common.

Another downside of virtual pets is that they can be addictive. Children often spend hours playing with them, which can lead to a lack of interest in other activities.

But despite these negatives, virtual pets are becoming increasingly popular. And as more companies introduce new models, it's likely that the market for virtual pets will continue to grow.

So if you're looking for a gift for your child, consider a virtual pet. It may not be a traditional toy, but it's sure to bring a smile to your child's face.

—Kathy Seifer is a reporter for The New York Times.



# Ratkaisu?

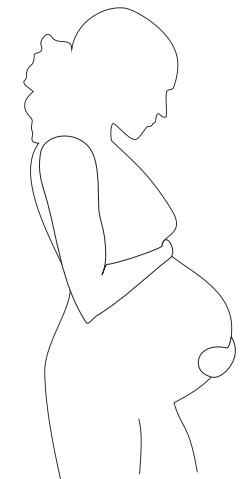


## Ratkaisu 2: Eliminaatiodieetti

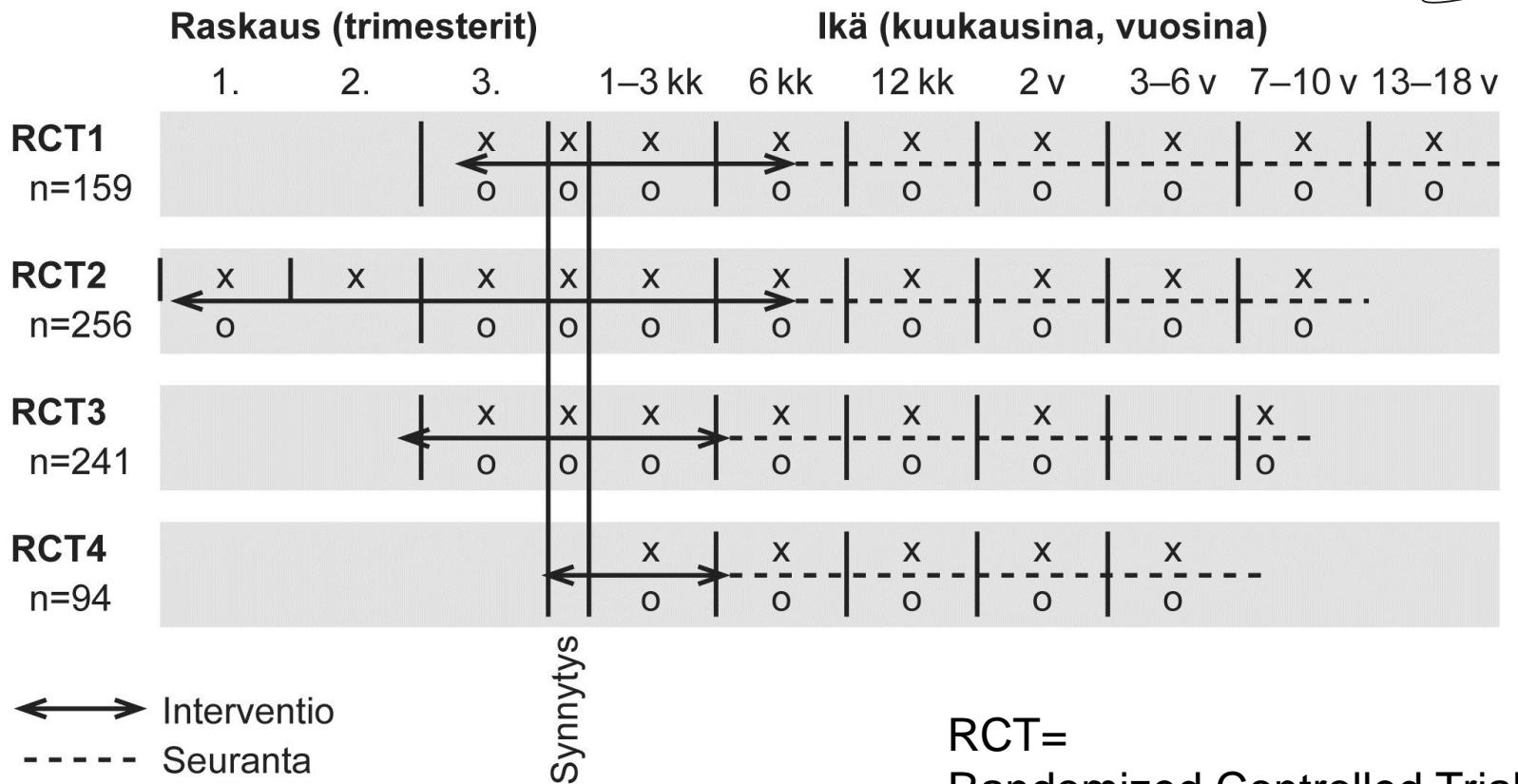




# Nutrition, Allergy, Mucosal immunology, Intestinal microbiota (NAMI) ohjelman interventiotutkimukset 1997-



## Probiootti vs. Placebo



RCT=  
Randomized Controlled Trial

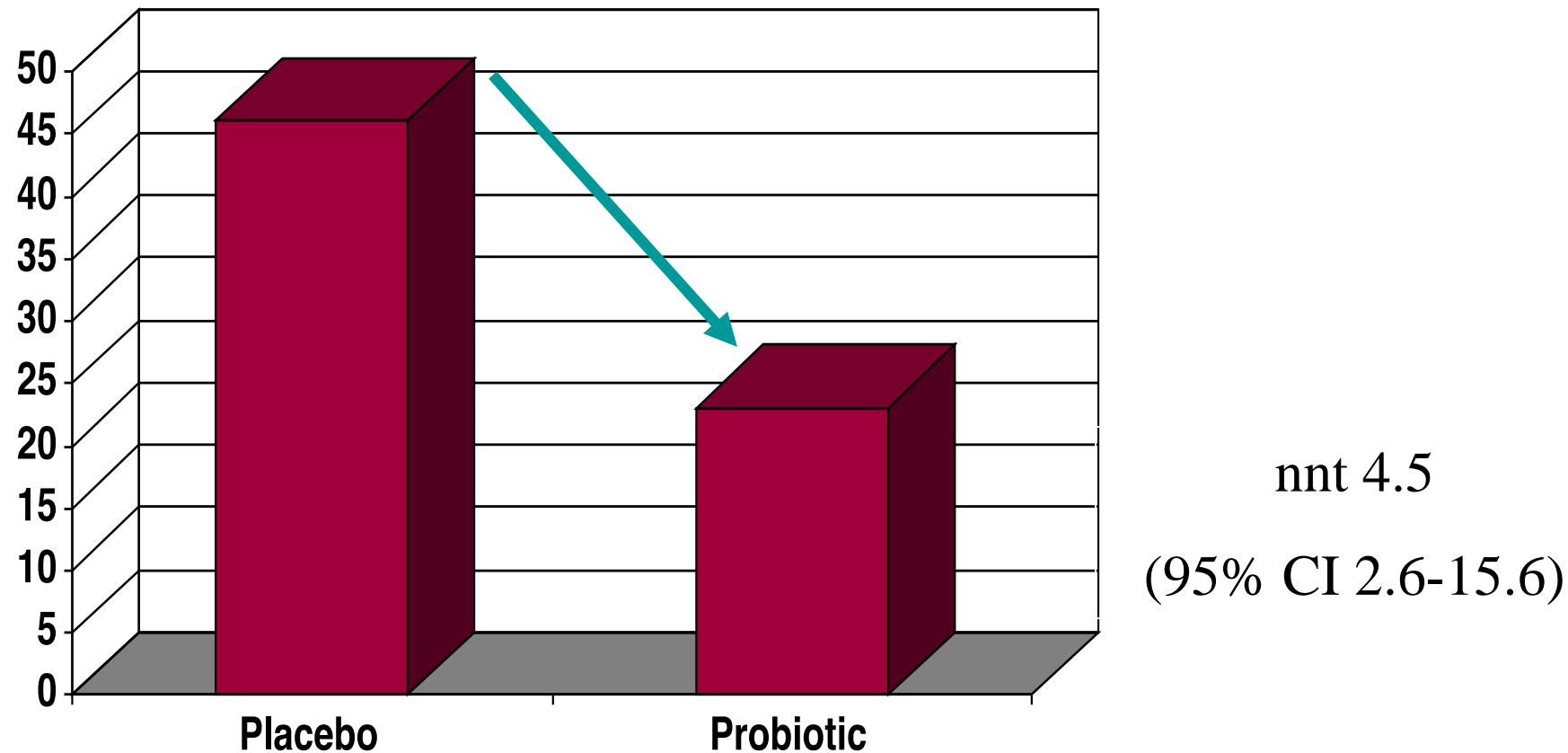


# Vaikutus atooppisen ihottuman riskiin merkitsevä:

Kalliomäki et al Lancet -2001, 2003; JACI 2007..

Rautava et al JACI 2002; 2012..

Tutkimus toistettu muissa populaatioissa muiden tutkimusryhmien toimesta





# Maternal atopy and specific probiotics during pregnancy – infant sensitization

**Probiotic combination (B. lactis + L. GG)  
had a protective effect in high risk infants**

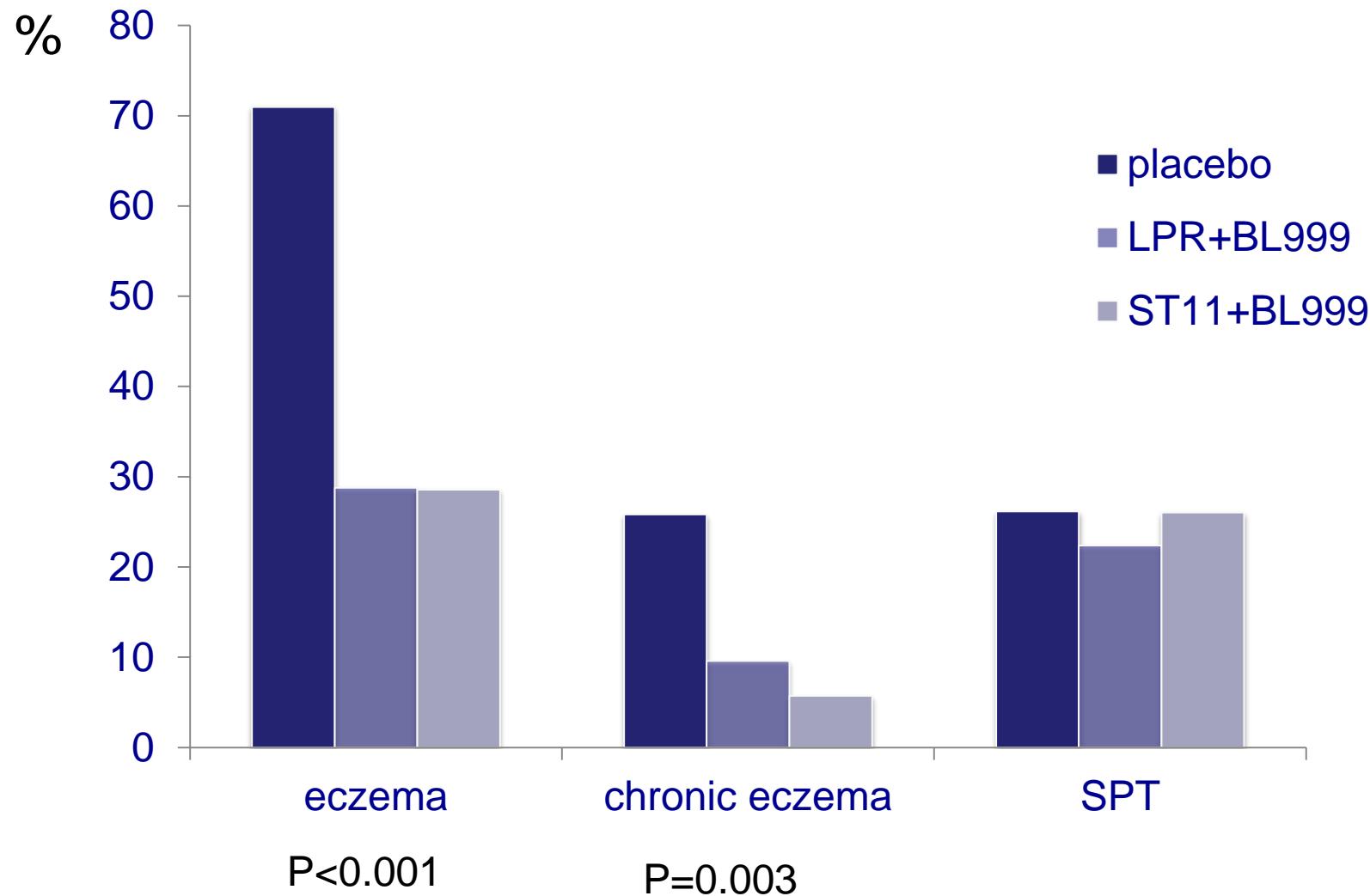
**26% probiotic group**  
vs.  
**50% placebo group**  
(OR 0.34, p=0.023)

{ Skin prick test +



# Maternal probiotic supplementation during pregnancy and breast-feeding reduces the risk of eczema in the infant

Rautava et al J Allergy Clin Immunol 2012





# Käsityksemme allergiapreventiosta on muuttunut:

Fiocchi et al. *World Allergy Organization Journal* (2015) 8:4  
DOI 10.1186/s40413-015-0055-2



**POSITION ARTICLE AND GUIDELINES**

**Open Access**

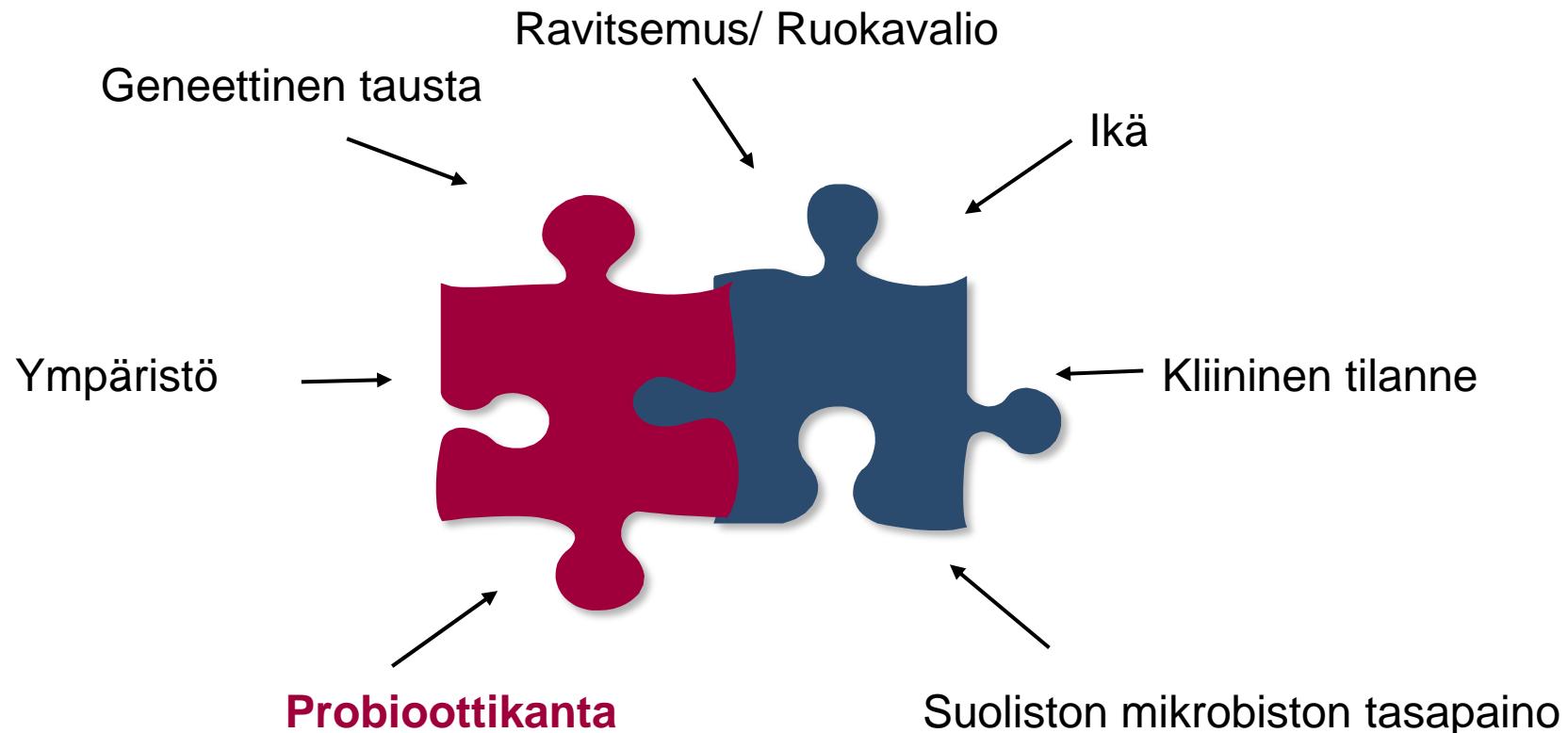
## World Allergy Organization-McMaster University Guidelines for Allergic Disease Prevention (GLAD-P): Probiotics

Alessandro Fiocchi<sup>1†</sup>, Ruby Pawankar<sup>2†</sup>, Carlos Cuello-Garcia<sup>3,4</sup>, Kangmo Ahn<sup>5</sup>, Suleiman Al-Hammadi<sup>6</sup>, Arnav Agarwal<sup>3,7</sup>, Kirsten Beyer<sup>8</sup>, Wesley Burks<sup>9</sup>, Giorgio W Canonica<sup>10</sup>, Motohiro Ebisawa<sup>11</sup>, Shreyas Gandhi<sup>3,7</sup>, Rose Kamenwa<sup>12</sup>, Bee Wah Lee<sup>13</sup>, Haiqi Li<sup>14</sup>, Susan Prescott<sup>15</sup>, John J Riva<sup>16</sup>, Lanny Rosenwasser<sup>17</sup>, Hugh Sampson<sup>18</sup>, Michael Spigler<sup>19</sup>, Luigi Terracciano<sup>20</sup>, Andrea Vereda-Ortiz<sup>22</sup>, Susan Waserman<sup>21</sup>, Juan José Yepes-Nuñez<sup>3</sup>, Jan L Brožek<sup>3,21\*</sup> and Holger J Schünemann<sup>3,21</sup>



# Probioottihoido suojaa Allergialta

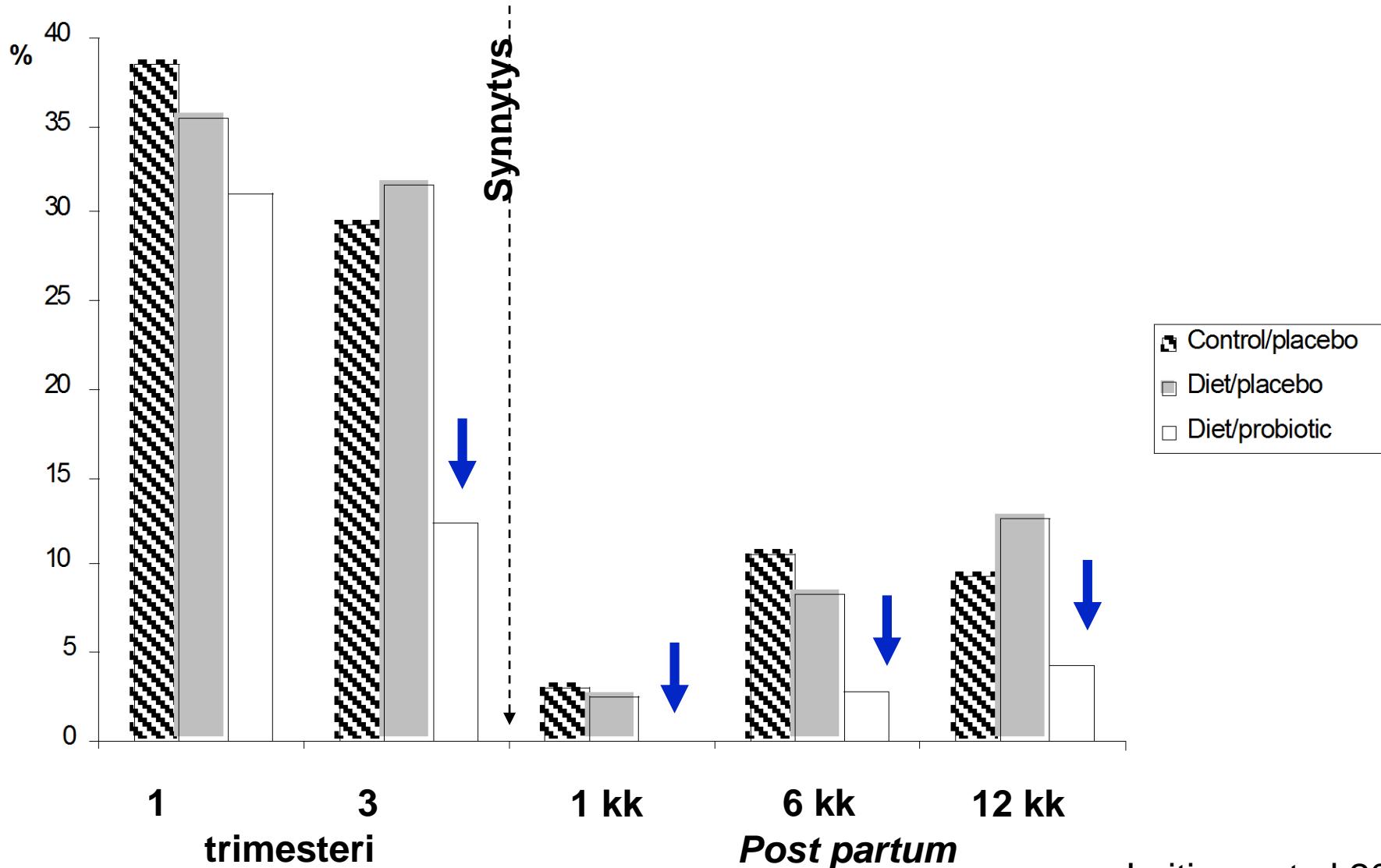
## ... Mutta





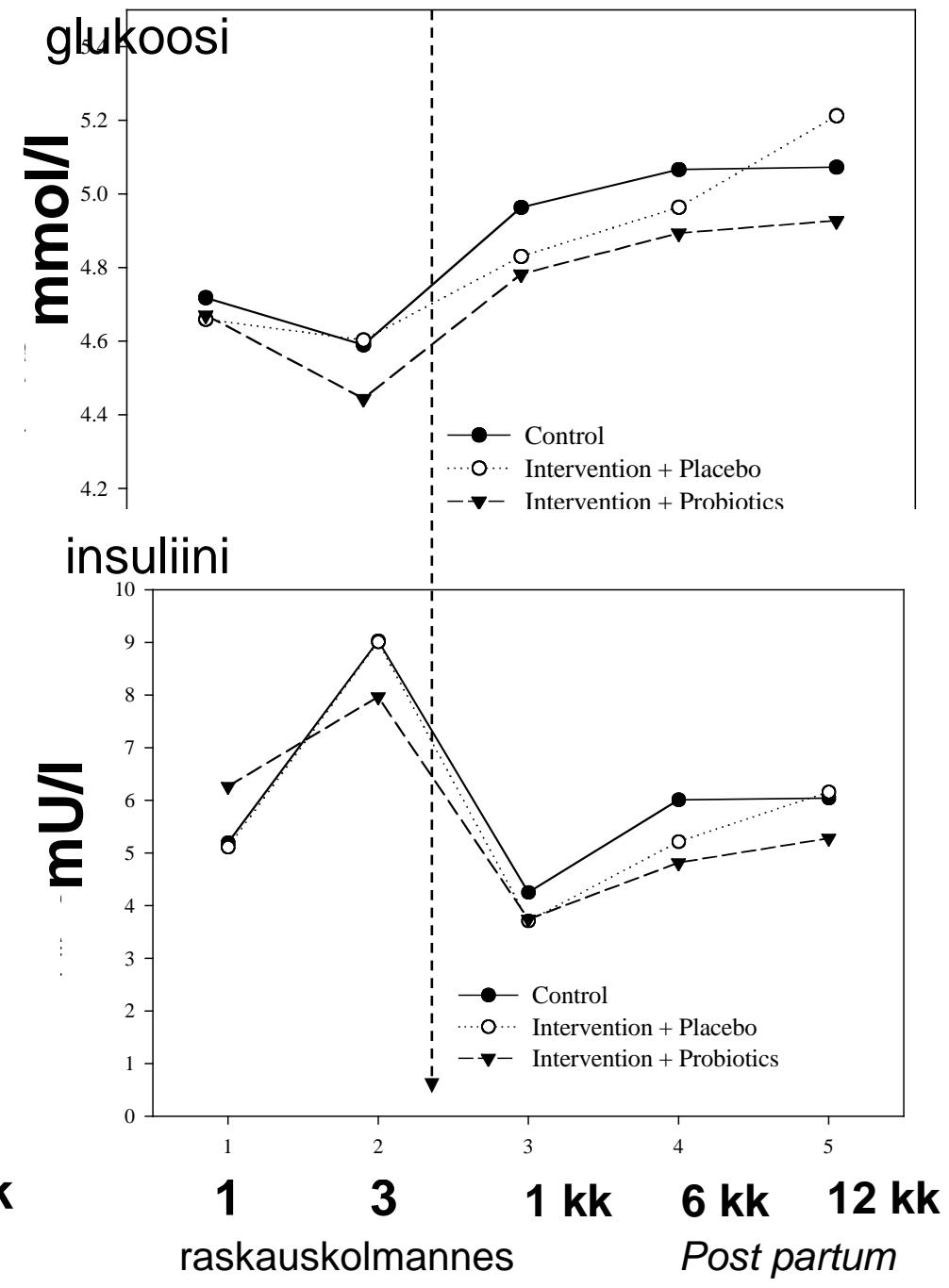
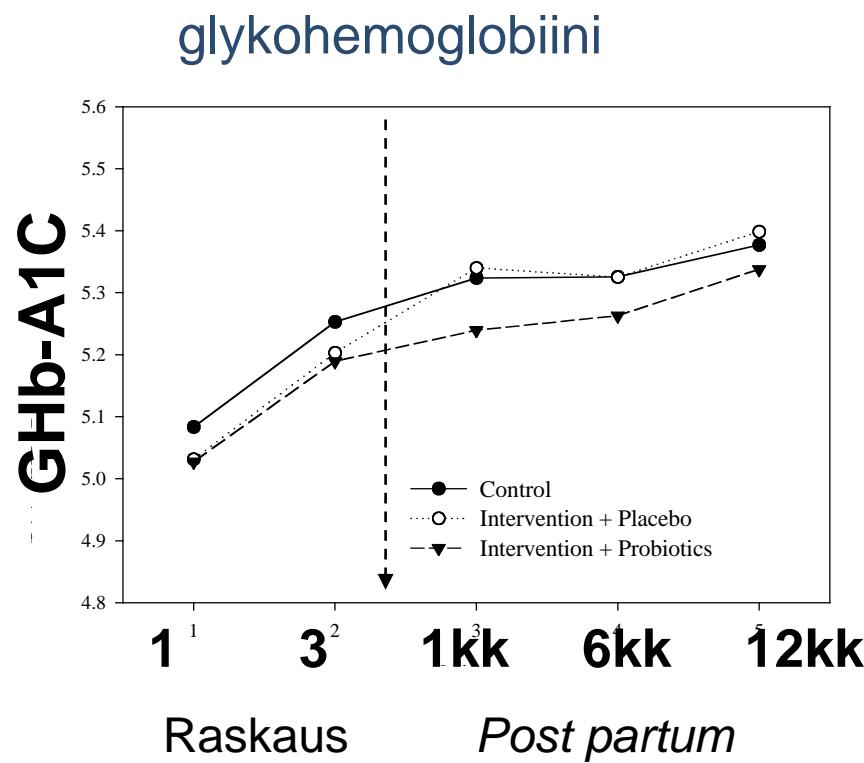
Vaikutus äitiin: Probioottihoito (*B. lactis* + *L. GG*) raskauden ja imetyksen ajan:

Naiset joilla korkea veren sokeriarvo raskauden aikana ( $\geq 4.8 \text{ mmol/l}$ ) ja sen jälkeen ( $\geq 5.6 \text{ mmol/l}$ )





# Probiootti-intervention vaikutus sokeriaineenvaihduntaan



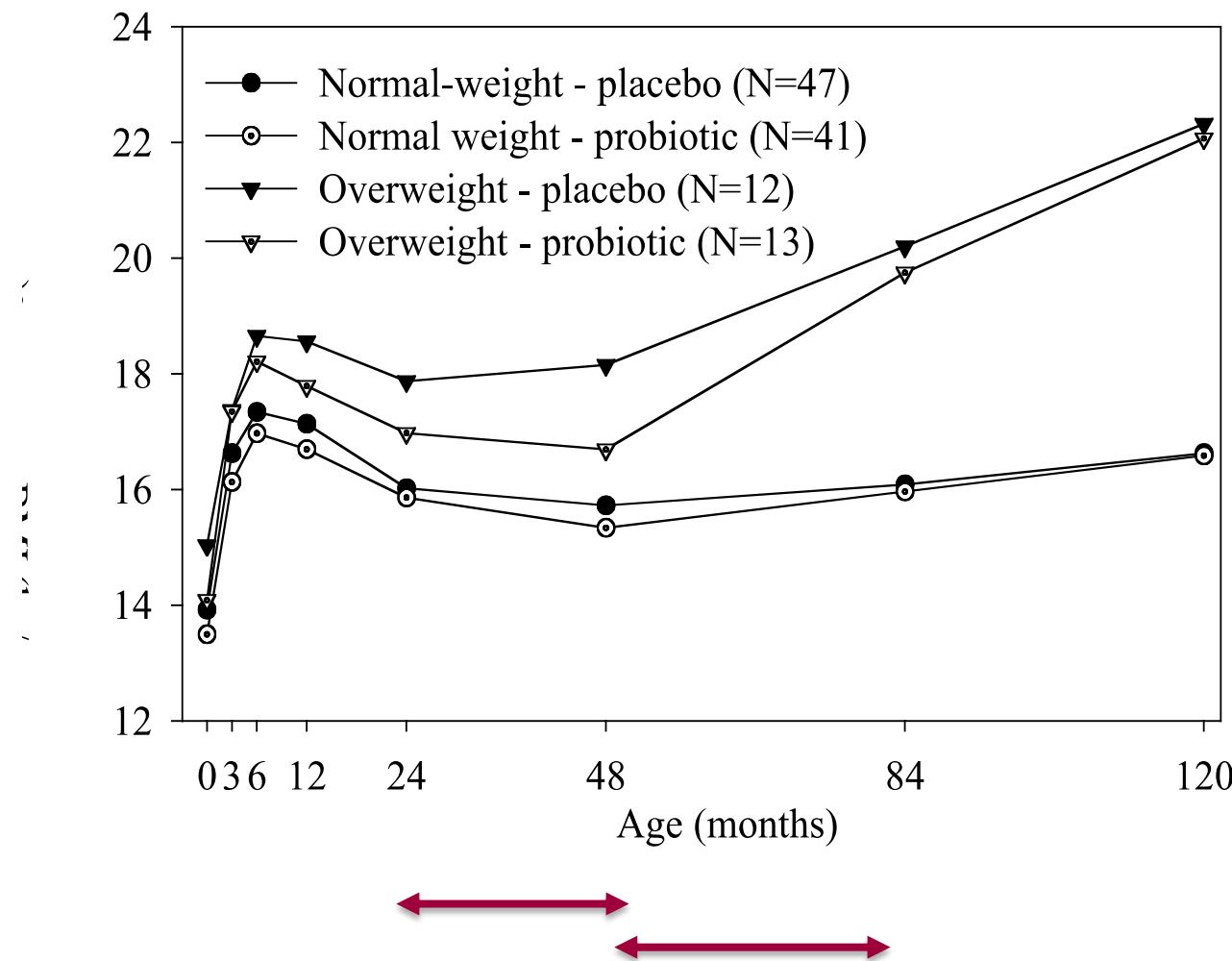


# Ravitsemusneuvontaan yhdistetty probiootti-interventio pienensi raskausdiabeteksen riskiä

- Probiootti → GDM ↓ ( $P=0.002$ ) Luoto et al 2010
  - 13% ravitsemusneuvonta + probiootti
  - 36% ravitsemusneuvonta + lumevalmiste
  - 34% verrokkiryhmä (lumevalmiste)
- Yksilöllinen ravitsemusneuvonta → makrosomian riski GDM raskauksissa ↓ ( $P<0.05$ )
- Ja äidin ylipainon riskiä:
  - 37 %:lla ylipaino 12kk synnytyksestä
  - Yksilöllinen ravitsemusneuvonta + probiootti-interventio → Vyötärölihavuuden ( $> 80$  cm) riski ↓  $P < 0.05$ ; NNT=4
- Mekanismi?



# Vaikutus lapsen varhaisen lihavuuden riskiin:



Critical age for obesity and  
MS development Liem et al 2013



# Placebo vs Lactobacillus rhamnosus GG (single or in combinations) 10-15 yrs follow-up

	Placebo	LGG
Asthma (questionnaire), n (%)	18 (15.8)	10 (10.4)
Asthma (ISAAC)	17 (12.1)	12 (9.2)
Any allergy	79 (56.4)	59 (44.4)
Obesity/ overweight state	21 (18.6)	17 (18.5)



# Mikrobisto ja Metabolinen terveys

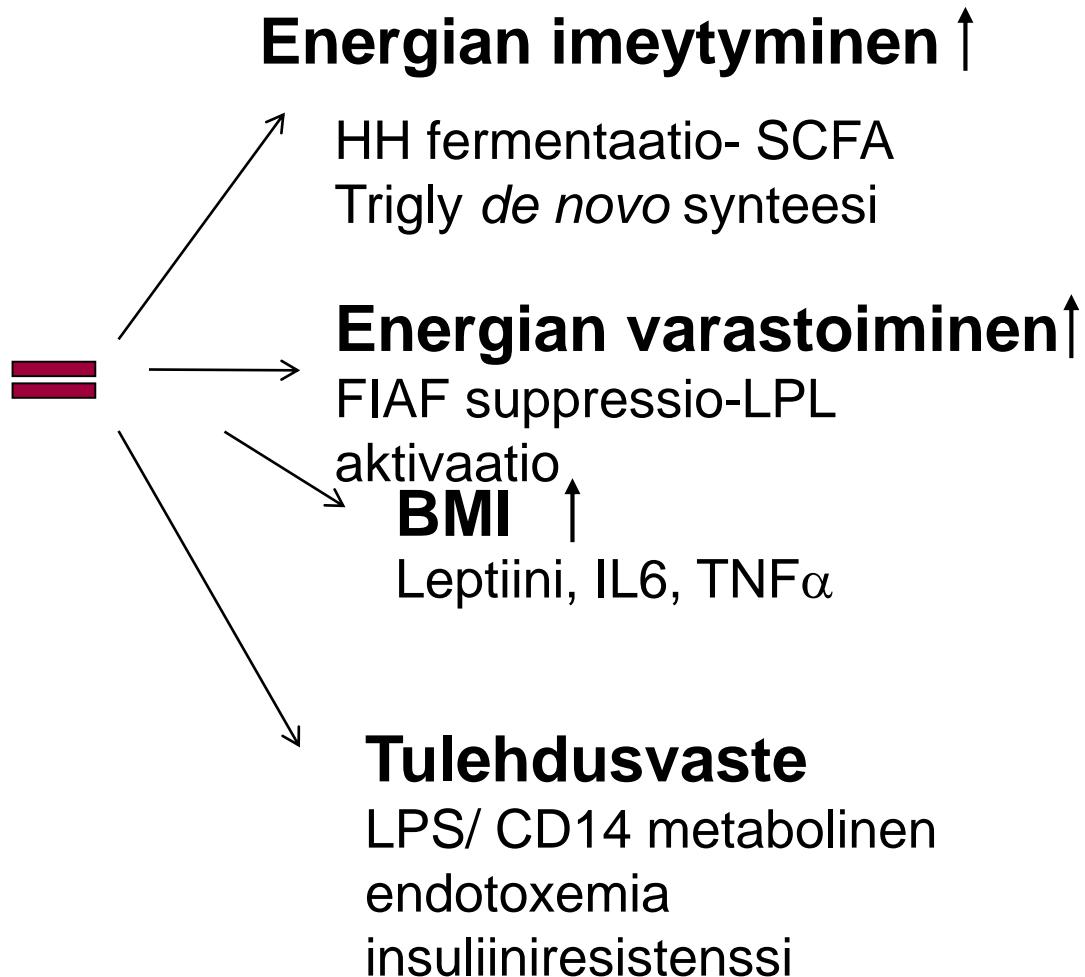
- Normaalipainoisten ja lihavien suoliston mikrobiston koostumus on erilainen (Ridaura et al 2013)
- Poikkeava mikrobiston koostumus suolistossa edeltää lihavuuden kehittymistä (Kalliomäki et al 2008)
- Poikkeava mikrobisto varhaisessa imeväisiässä- riski lihavuudelle
- Matala-asteinen krooninen tulehdus liittyy lihavuuteen, dysbioosi liittyy tulehdustilaan ja lihavuuteen, mutta mikä on syy ja mikä on seuraus?



# Kokeellinen näyttö

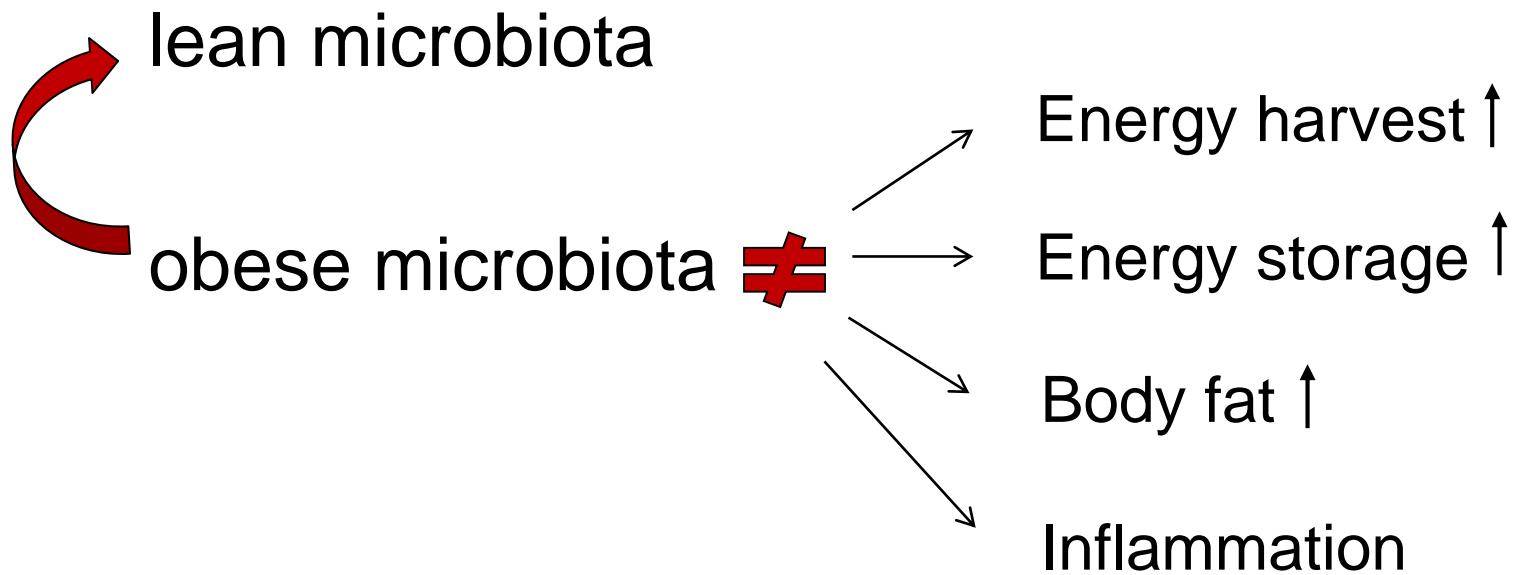
Bäckhed, Gordon et al 07; Cani, Delzenne 2009

## Obesogeninen mikrobisto





# Reprogramming option – probiotics, synbiotics..





Oct 17-18, 2015 NY TIMES

# Overselling breast-feeding

BREAST-FEEDING, FROM PAGE 7

tion to breast-feed exclusively for six months if you are a stay-at-home mom with a breadwinning partner. In a country where the average working mother returns to work six weeks after having a baby, and nearly 30 percent of new mothers take no maternity leave at all, breast-feeding for any length of time is very hard to do.

The effect of the moral fervor surrounding breast-feeding goes beyond mere shaming. It also reflects, and rein-

terventions that punish poor women who do not breast-feed. This isn't just the unobtrusive little "nudge" in the right direction. It's more like a shove, with a kick for good measure.

Middle-class women primarily experience breast-feeding advocacy in the form of education campaigns and limits on their access to formula in hospitals. Poor women are vulnerable to more explicit coercion. The Special Supplemental Nutrition Program for Women, Infants and Children, known as WIC,

feeding is the measure of our moral worth, it isn't long before the idea of a mother not breast-feeding her child summons the familiar tropes of bad parenting and irresponsible citizenship that we have long deployed against poor women and minorities.

Does all this mean that women should stop breast-feeding? No. If you want to, if it's easy for you, if you are healthy, if your baby is thriving on breast milk, then by all means do it. If I had to do it all over again, I probably would. But it



## Breastfeeding does not improve IQ, study finds

Major research by Goldsmiths, University of London, suggests breastfeeding has no impact on the intelligence of a child



It is known that breastfeeding lowers the risk of allergies, ear infections and admission to hospital in babies and it has been linked to better health overall into adulthood Photo: Alamy

The Telegraph 2015

Reference: von Stumm& Plomin PLOS One 2015



# Imetyks ja terveysvaikutukset: monen tekijän summa

## Esimerkki: Allergia

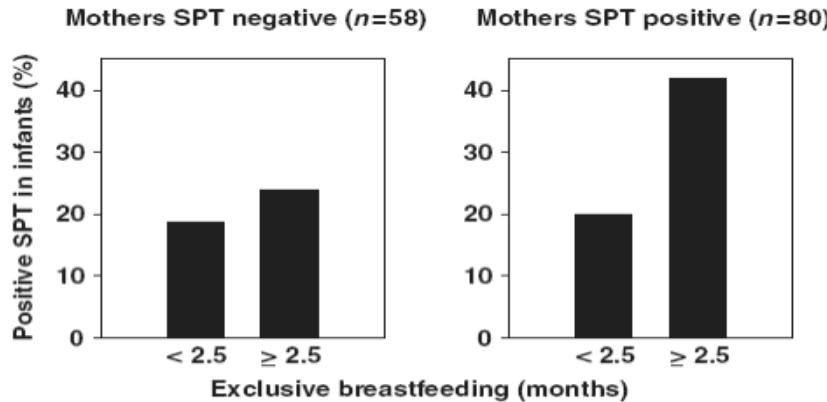
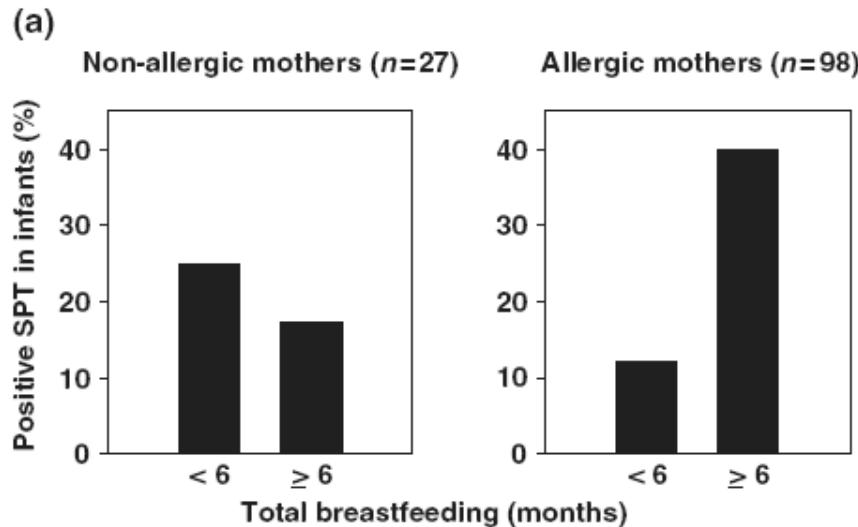


Fig. 1. (a) Positive SPT (%) in infants according to the allergy and SPT status of mother and duration of total breastfeeding. (b) Positive SPT (%) in infants according to the allergy and SPT status of mother and duration of exclusive breastfeeding. SPT, skin prick test.



Huurre A et al 2008

Ravitsemus  
Terveys

Rintamaito

Imettävä  
äiti

Lapsen  
terveys

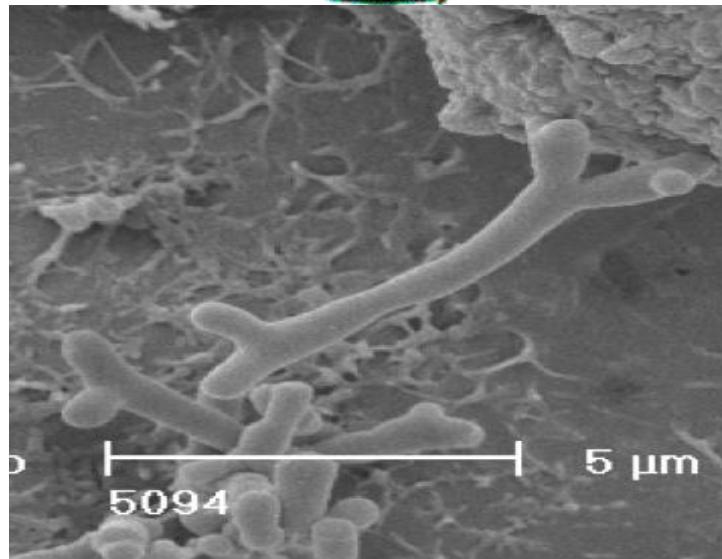
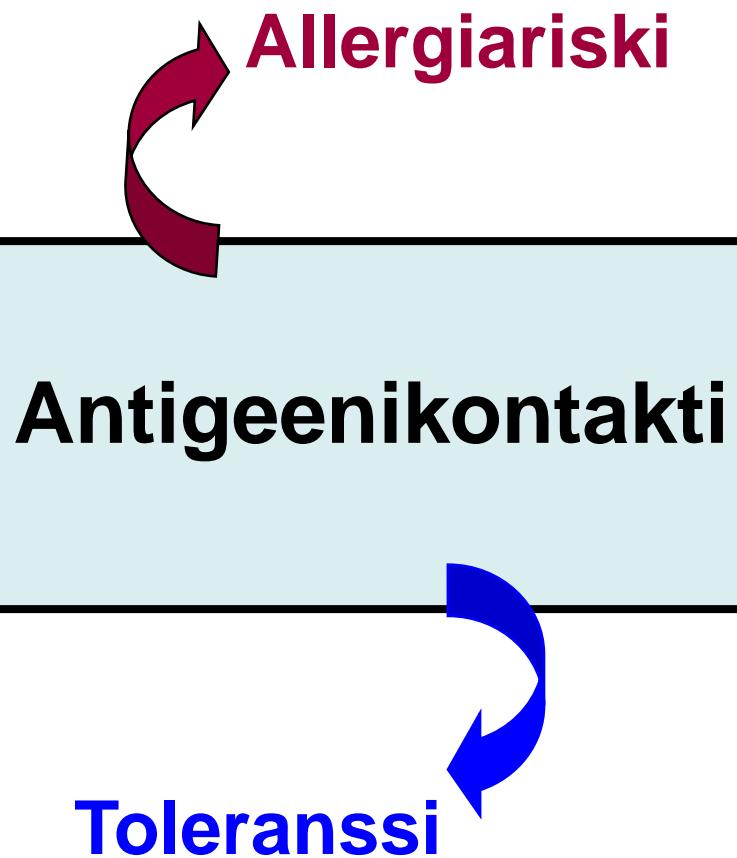
Kehon koostumus  
BMI



Käsityksemme allergiasta muuttui

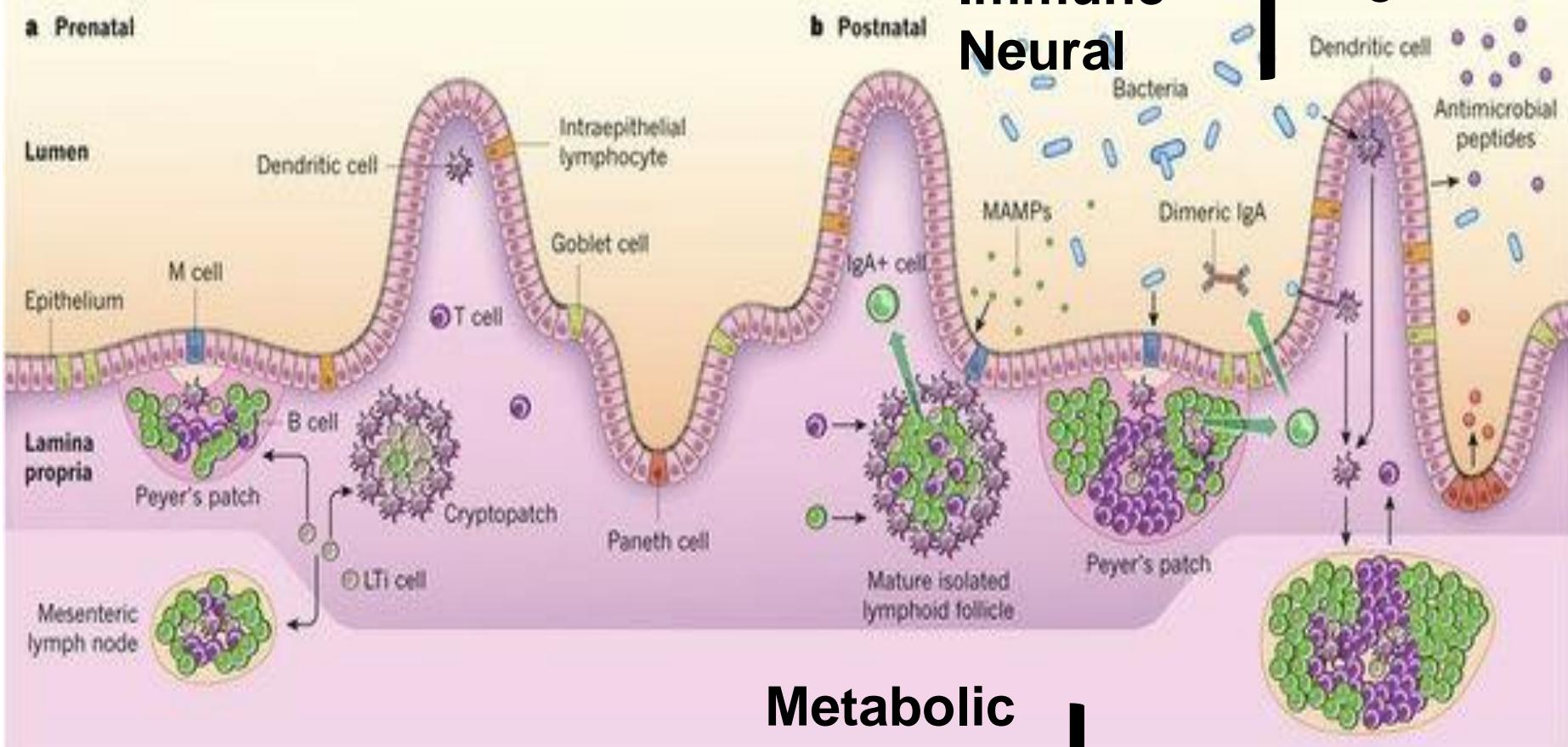
Vanha strategia: **välttäminen**

Uusi strategia: **aktiiviset yhdisteet-ravitsemushoito**





# Käsityksemme mikrobeista on muuttunut....



Targets in

**Metabolic  
Immune  
Humoral  
Neural**

Pathways

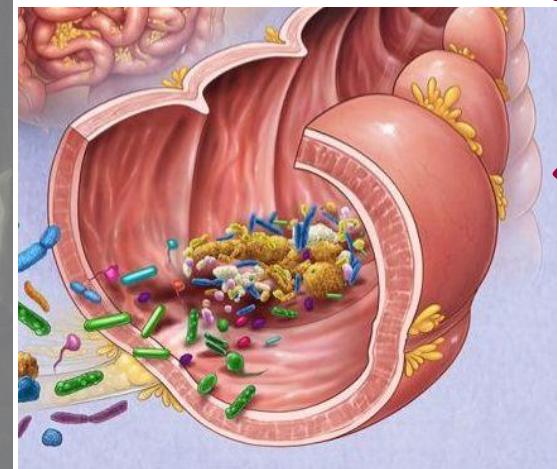


There are in fact two things, science and opinion;  
the former begets knowledge, the latter ignorance. Hippocrates

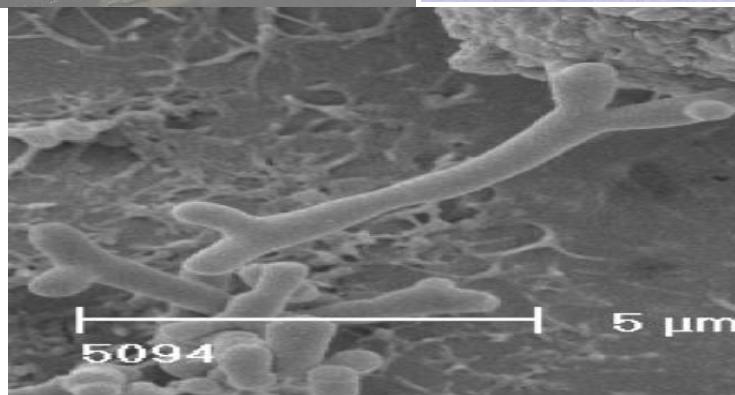


Anatomy lesson of  
Dr. Nicolaes Tulp Rembrandt  
1632

New organ detected



Clinical impact





# Kliininen käytäntö- spesifit probiootit

Acute gastroenteritis +

Antibiotic-associated diarrhoea +

Food allergy- infants with atopic eczema +

IBD: relapses of pouchitis

NEC +

Obesity risk



# Safety documentation– available for specific probiotics

- Epidemiological data
- Clinical data
  - Intervention studies in rotavirus diarrhoea, cow milk allergy, atopic eczema, colic, preterm infants
  - Meta-analyses
- Long-term follow-up (with clinical+growth, immunological, microbiological assessments)
  - Probiotics pre-, peri- and postnatally: 5-10-15 yrs of follow-up
- Documentation of clinical practice
  - Preterm infants Luoto R et al. Clin Infect Dis 2010; 50: 1327-8.
- Demonstrations on mechanisms





# Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer

Maria G Dominguez-Bello<sup>1,2</sup>, Kassandra M De Jesus-Laboy<sup>2</sup>,  
Nan Shen<sup>3</sup>, Laura M Cox<sup>1</sup>, Amnon Amir<sup>4</sup>, Antonio Gonzalez<sup>4</sup>,  
Nicholas A Bokulich<sup>1</sup>, Se Jin Song<sup>4,5</sup>, Marina Hoashi<sup>1,6</sup>,  
Juana I Rivera-Vinas<sup>7</sup>, Keimari Mendez<sup>7</sup>, Rob Knight<sup>4,8</sup> &  
Jose C Clemente<sup>3,9</sup>

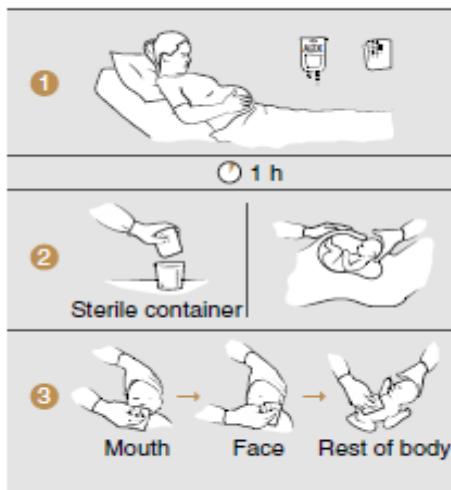
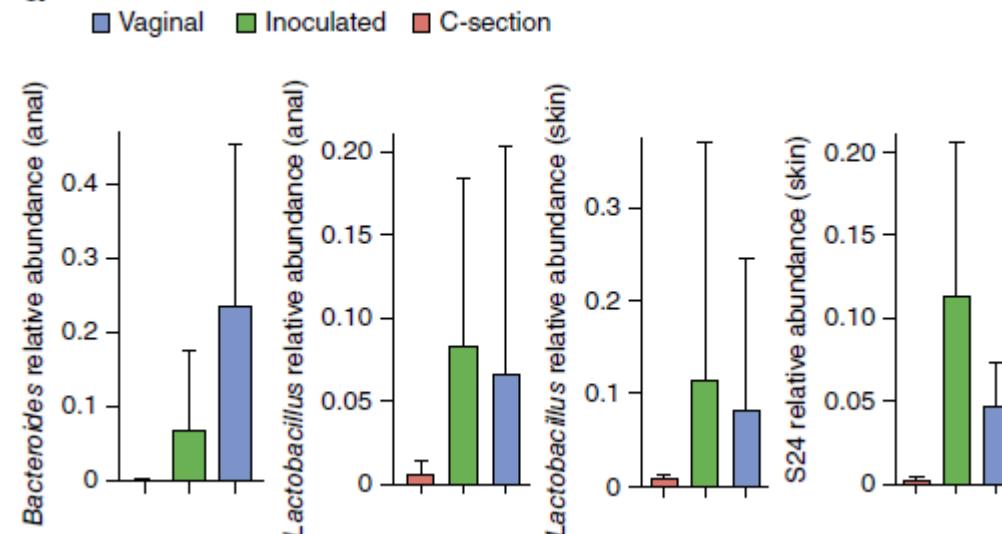
**a**

Image: M.J. Schoen

**d**

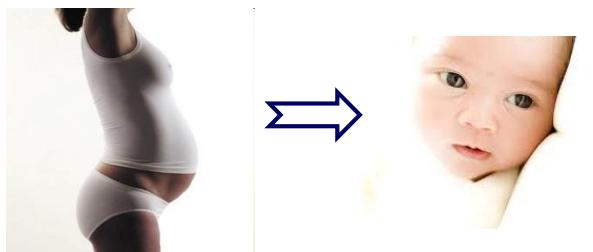
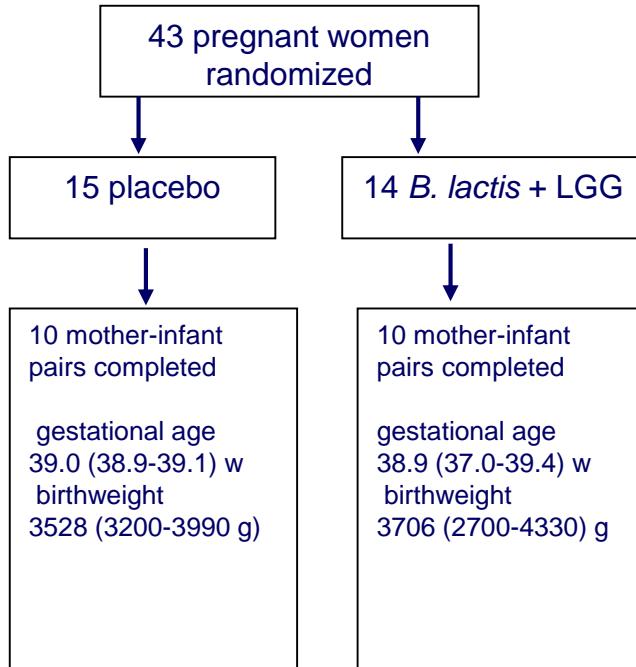
Yhteensä 18 vastasyntynyt ja heidän äitinsä:

- 7 alateitse syntynyt lasta, 11 elektiivisellä sektiolla syntynyt, joista 4 pyyhittiin synnytyksen jälkeen.
- Äideistä kenelläkään ei ollut GBS-kantajuutta tai muuta synnytyksen aikaista paikallista infektiota.

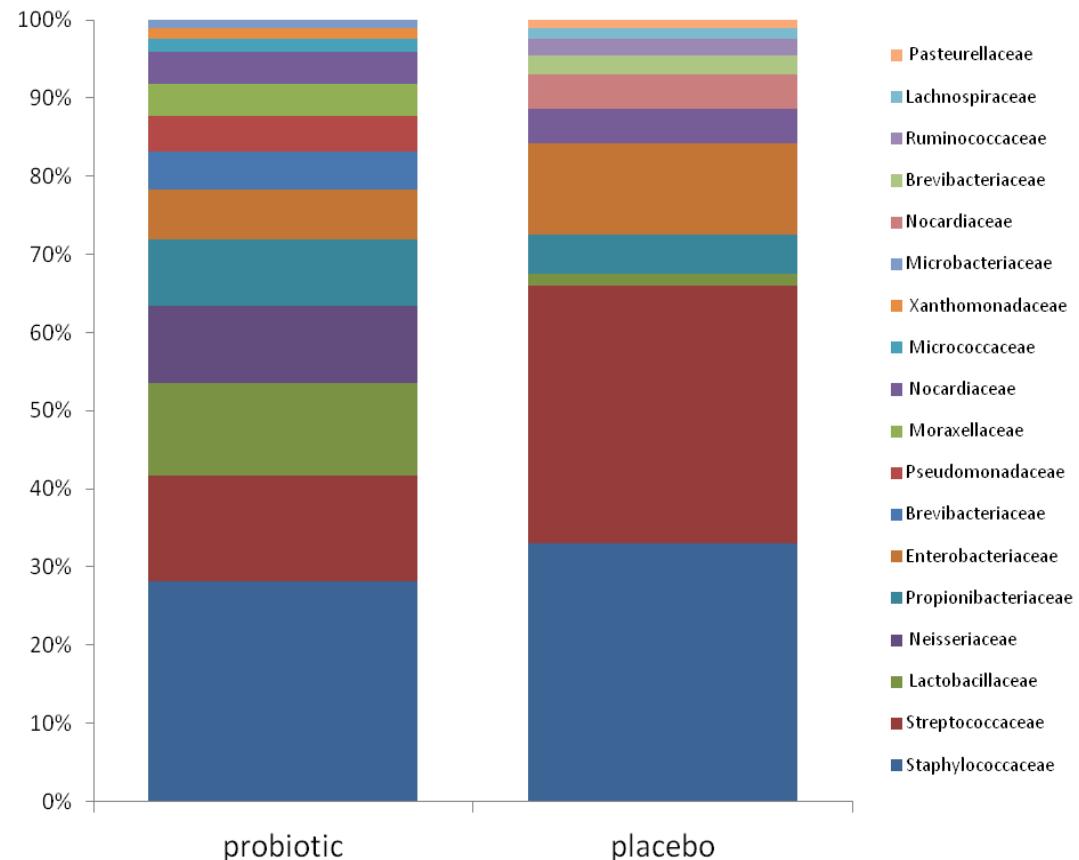


# Fetomaternal immune interface –intervention target?

## Elective C-Section



## MILK MICROBIOTA





# Allergic Sensitization - Allergic Disease Hygiene Hypothesis



**The newborn:  
Immunologically immature  
canvas**

early microbial  
stimulation

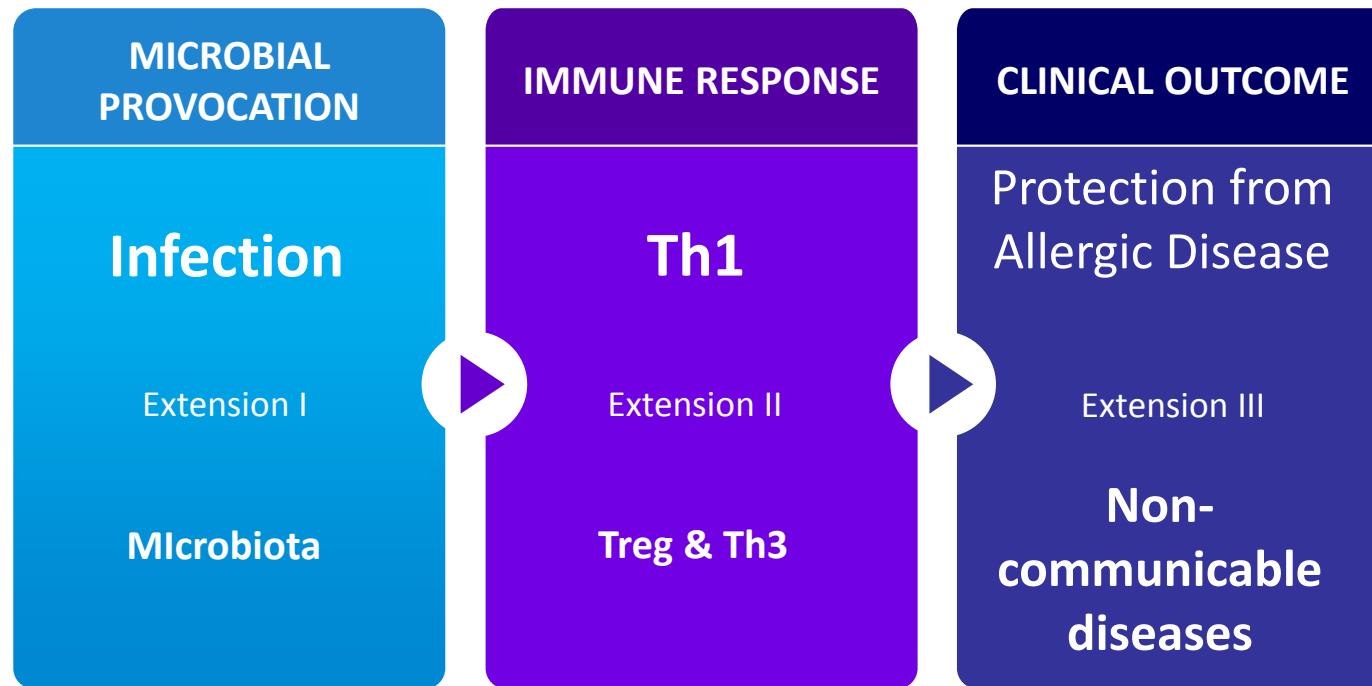


aberrant immune  
responses to antigens  
later in life





# The extended hygiene hypothesis



Probiotics: new applications in extended populations  
Isolauri 2002, Rautava et al 2005