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Timing and tempo of
first year growth
in relation to cardiovascular
and metabolic risk profile
in early adulthood

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Metabolic and cardiovascular profile at 21 years

- **Introduction**
- **Influence of low birth weight**
- **Influence of preterm birth**
- **Influence of postnatal growth**
- **Conclusions**



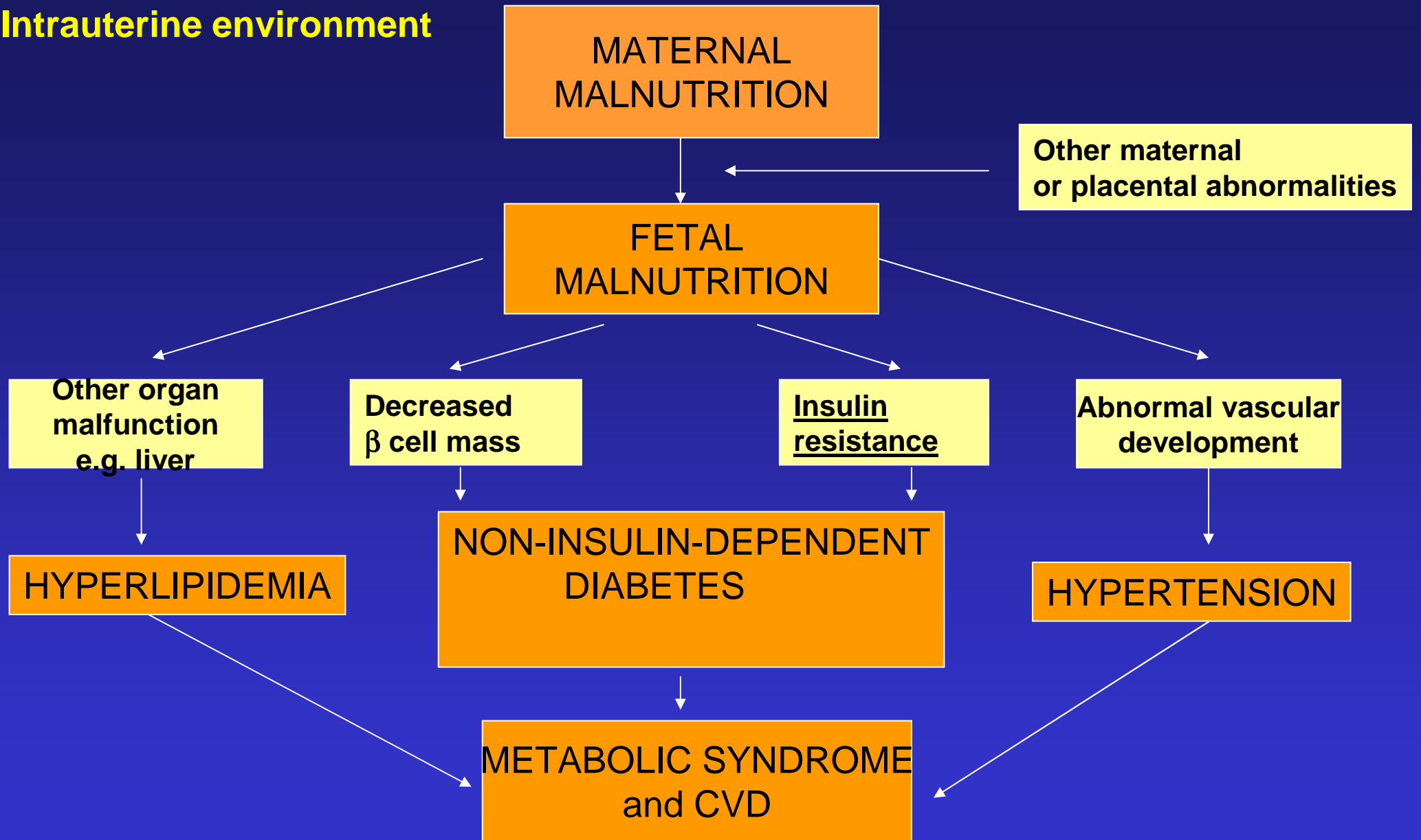
3641 men born in Helsinki 1924 -1933

Resident in Finland in 1971

High death rates from coronary heart disease:

- * low birth weight**
- * relative low placenta weight**
- * caught up in weight after birth**

Intrauterine environment



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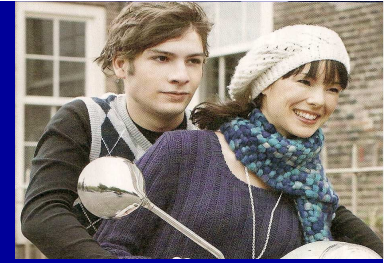
PROGRAM STUDY in young adults 18-24 yrs



Started in 2002

- **345 born at term (> 36 wks GA)**
- **oversampling of subjects born SGA**

Inclusion criteria and measures

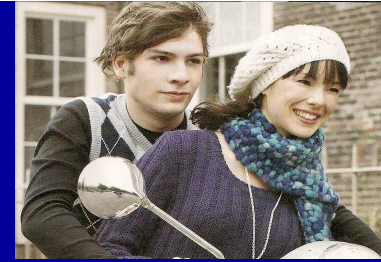


Healthy young adults (18-24 years)

Born singleton, at term, Caucasian

- Anthropometry, body composition by DXA scan,
- Blood pressure and carotis intima media thickness (cIMT)
- Frequent Sampling IV Glucose tolerance test with Tolbutamide
- Serum lipids, hormones, adipocytokines
- Family history, questionnaires
- Health records and growth during first years after birth

Is birth weight related to insulin sensitivity?

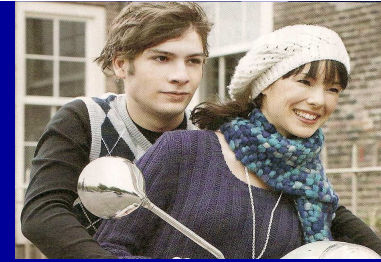


Variables	Insulin sensitivity*	
	β	P-value
Birth weight SDS	0.146	0.049

Adjusted for age, gender, SES, birth length SDS and adult height SDS

* Log transformed

Is birth weight related to insulin sensitivity?

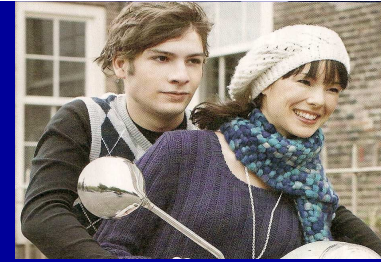


Variables	Insulin sensitivity*		Insulin sensitivity*	
	β	P-value	β	P-value
Birth weight SDS	0.146	0.049	0.115	0.098
Adult weight SDS			-0.199	<0.001

Adjusted for age, gender, SES, birth length SDS and adult height SDS

* Log transformed

Is birth weight related to insulin sensitivity?

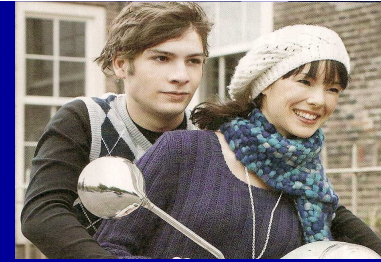


Variables	Insulin sensitivity*		Insulin sensitivity*		Insulin sensitivity*	
	β	P-value	β	P-value	β	P-value
Birth weight SDS	0.146	0.049	0.115	0.098	0.083	0.210
Adult weight SDS			-0.199	<0.001		
Fat mass (kg)					-0.044	<0.001
Lean body mass (kg)					-0.002	0.840

Adjusted for age, gender, SES, birth length SDS and adult height SDS.

* Log transformed

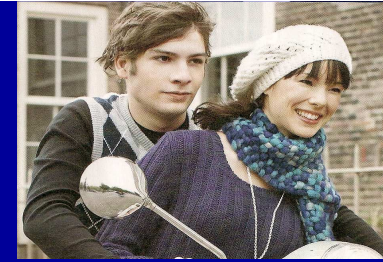
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Fat accumulation during childhood is related to insulin sensitivity in early adulthood

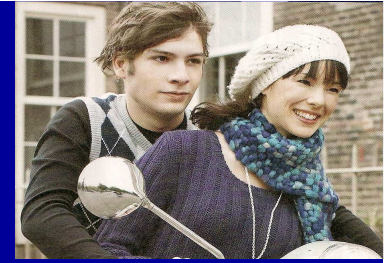
Metabolic profile in early adulthood



Dependent variable	Birth weight SDS (p-value)	Fat mass (p-value)
Insulin sensitivity	0.210	<0.001 (-)
Cholesterol	0.733	0.013 (+)
Chol/HDL ratio	0.086	0.065 (+)
HDL	0.100	0.962 (+)
LDL	0.371	0.045 (+)
Apo A1	0.668	0.665 (+)
Apo B	0.157	0.016 (+)
Triglycerides	0.239	0.004 (+)
Systolic blood pressure	0.273	0.004 (+)
Diastolic blood pressure	0.594	0.011 (+)
cIMT	0.506	0.478 (+)

Adjusted for age, gender, SES, birth length SDS and adult height SDS

CONCLUSION



- Not prenatal growth, reflected by birth size, but **postnatal weight gain during childhood** is related to determinants of CVD and DMII in early adulthood
- Weight gain during childhood can be specified as **fat accumulation**

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Young adults born preterm



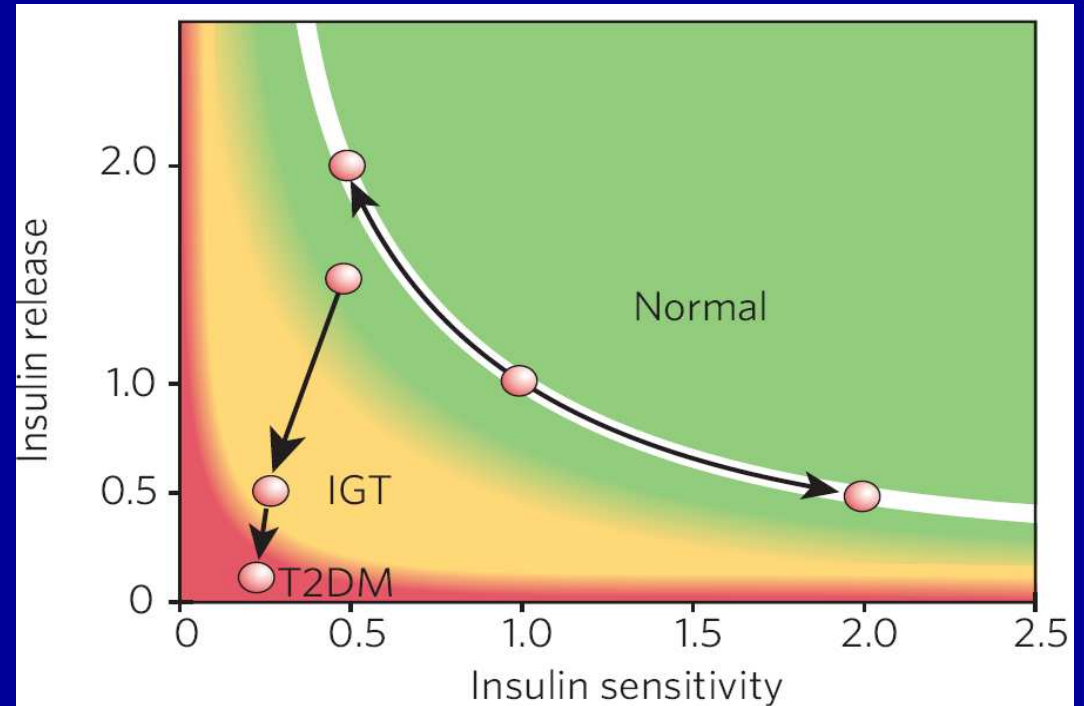
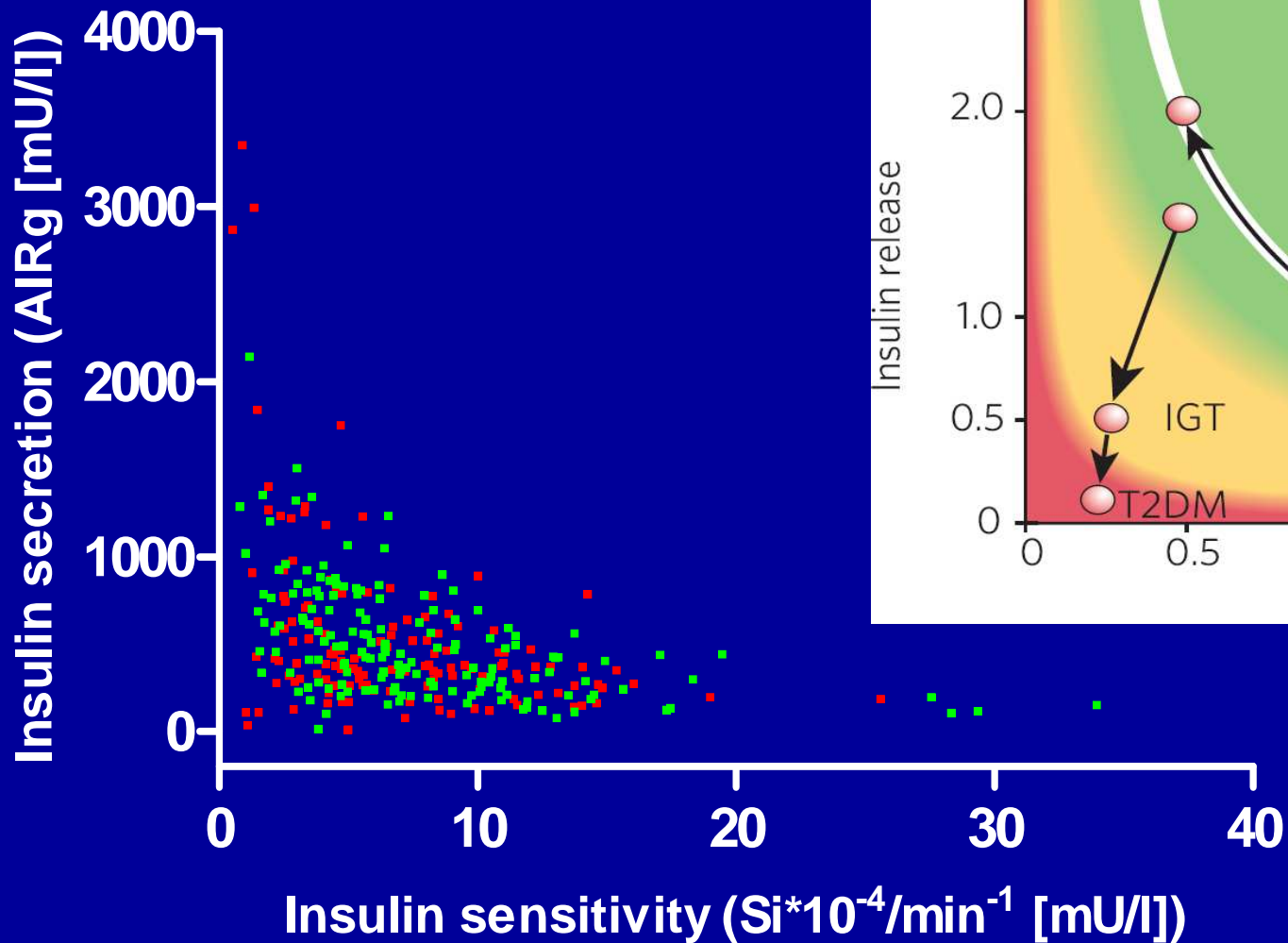
- Background
 - One report suggested a lower insulin sensitivity in children born premature → higher risk for development diabetes?
 - It is unknown whether this reduced insulin sensitivity persists into adulthood
 - In 2005 , 12.7% of all babies was born preterm

Young adults born preterm / term

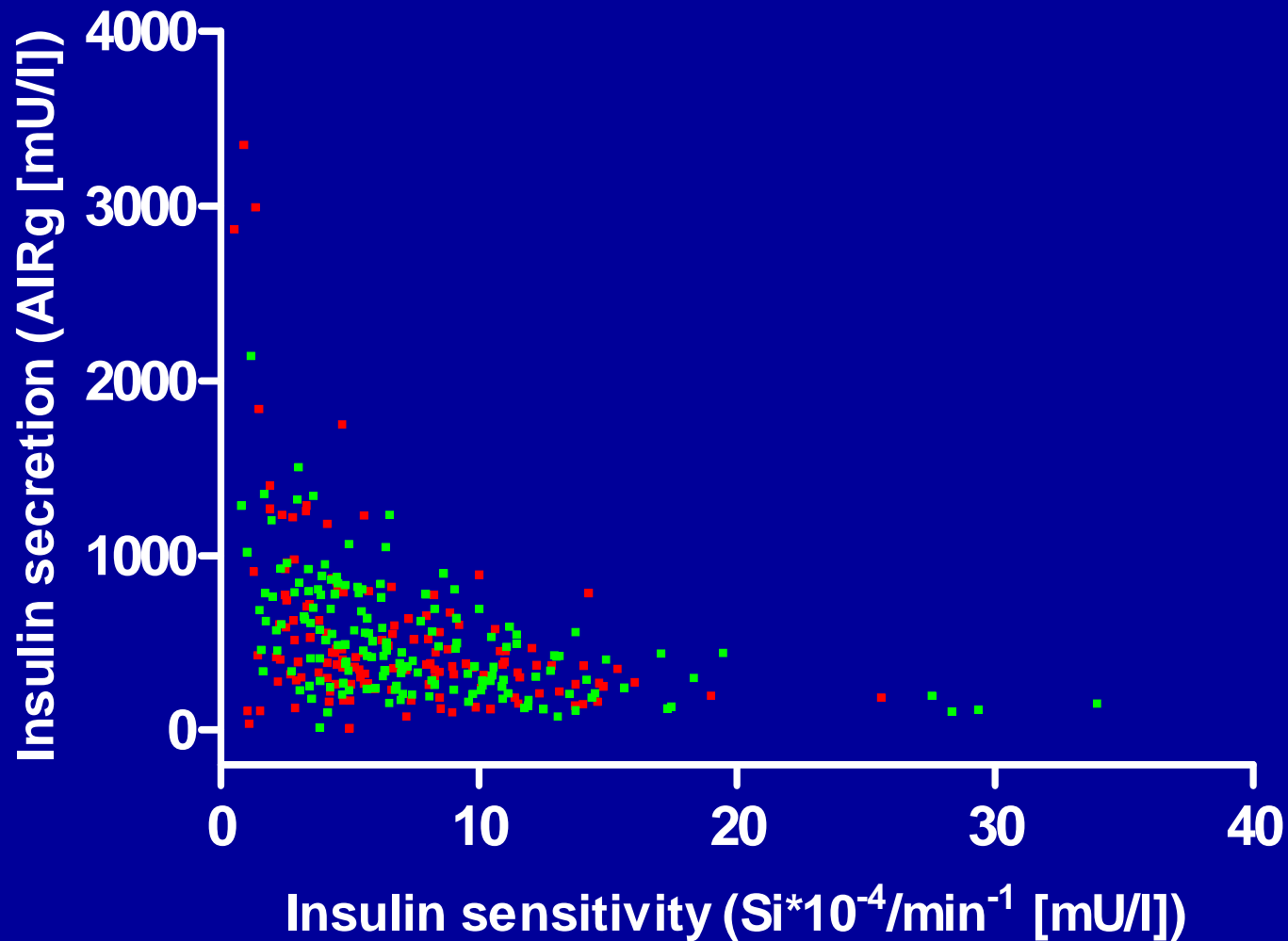


- **Subjects**
 - 305 young adults (18-24 yr): 169 born premature and 136 term
- **Measurements**
 - **Insulin sensitivity by FSIGT**
 - **Body composition by DXA**
 - **cIMT**
 - **Lipids, adipocytokines**
 - **Athropometrics**

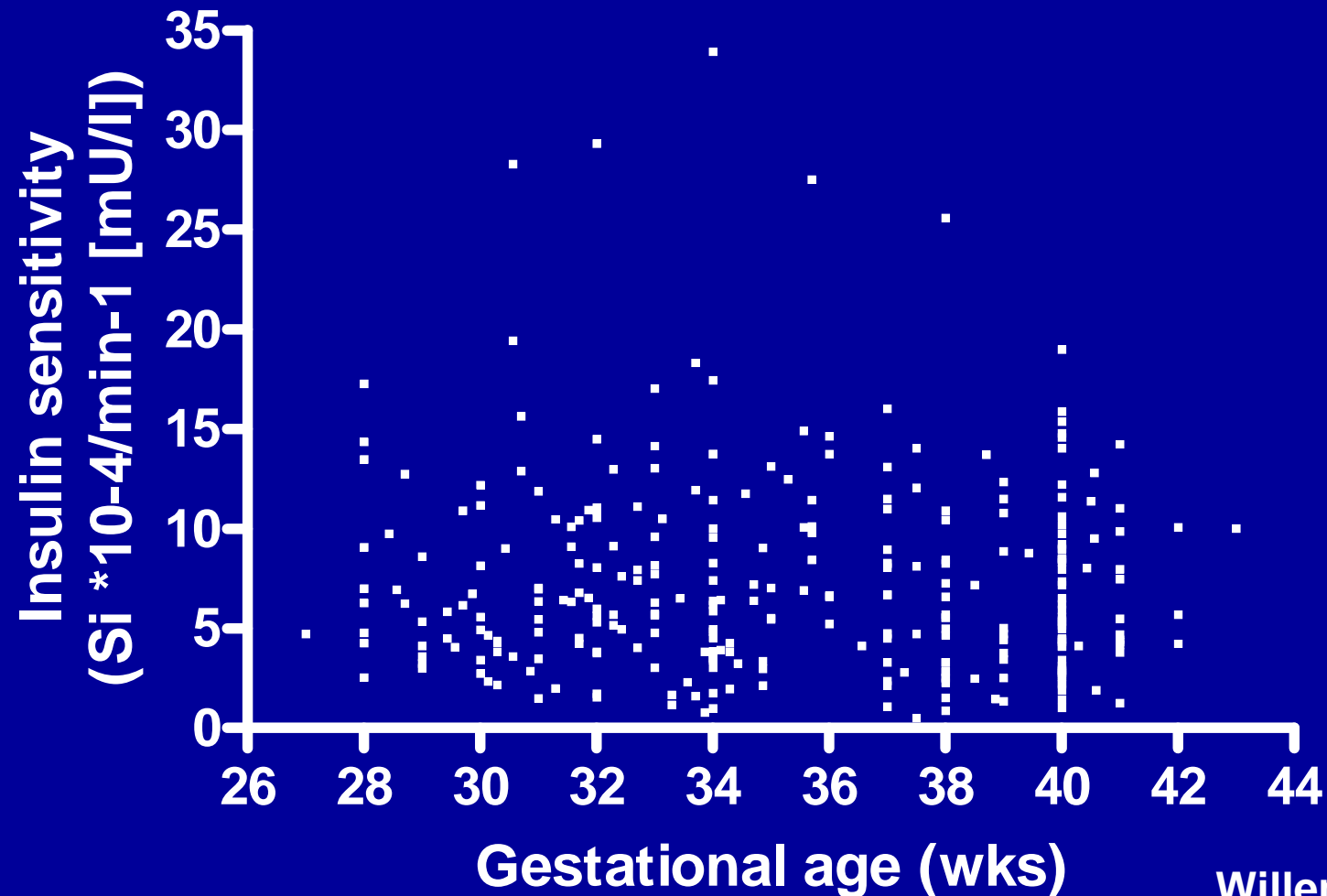
Young adults born preterm vs term



Young adults born preterm / term

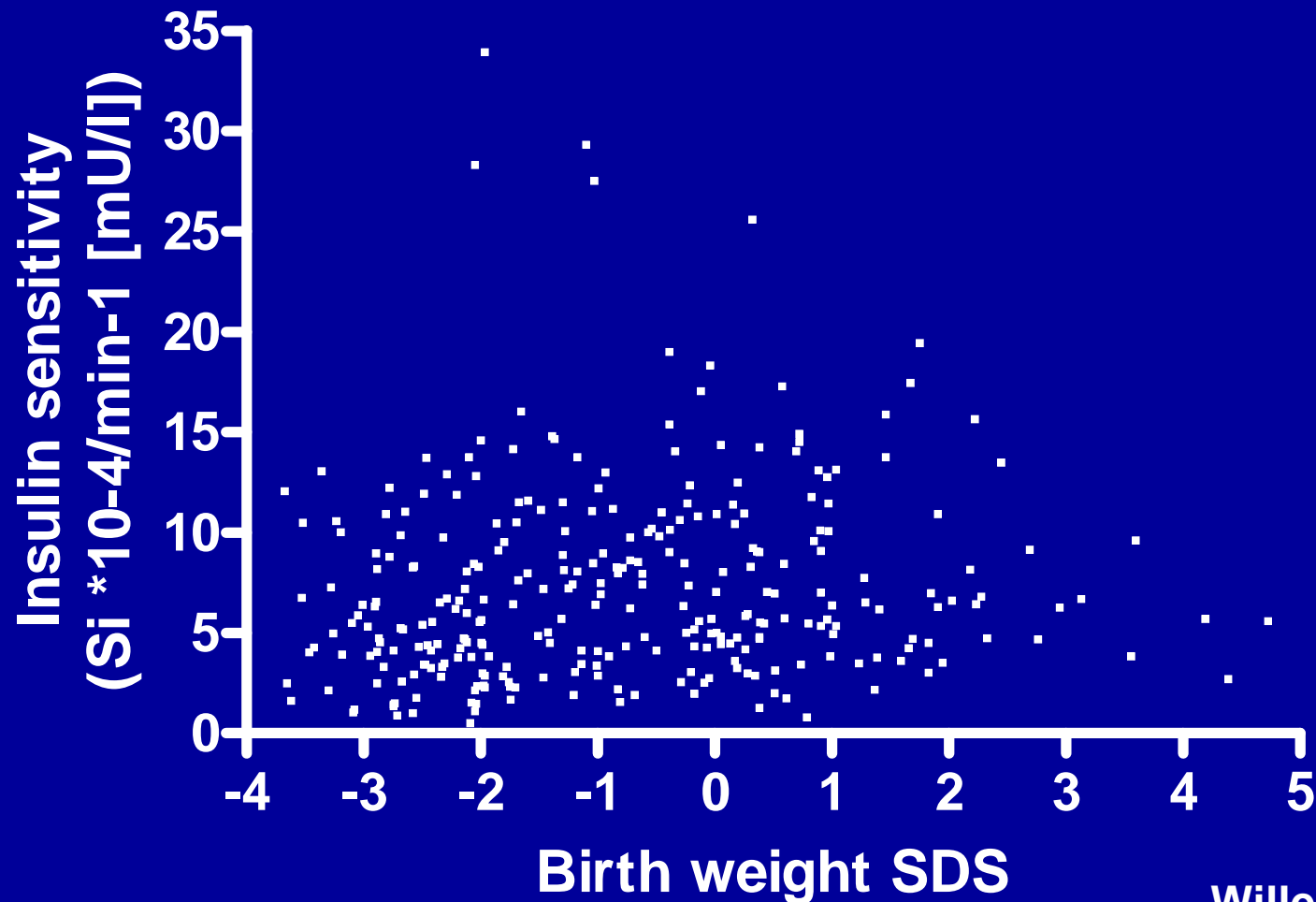


Insulin sensitivity vs gestational age



Willemssen R. JCEM 2009

Insulin sensitivity vs birth weight



Willemsen R. JCEM 2009

Insulin sensitivity



	Model A*		Model B*	
	Beta	P-value	Beta	P-value
GA (wks)	0.004	0.95	-0.001	0.99
BW SDS	0.17	0.07	0.12	0.18
OC-use	-0.18	0.03	-0.17	0.03
Height SDS	0.37	<0.0005	0.20	0.02
Weight SDS	-0.44	<0.0005		
Fat mass (kg)			-0.52	<0.0005
Lean mass (kg)			-0.03	0.81
Adjusted R²	0.23		0.33	

* Adjusted for age, gender, birth length SDS, BL*AH

Insulin sensitivity



	Model A*		Model B*		Model C*	
	Beta	P-value	Beta	P-value	Beta	P-value
GA (wks)	0.004	0.95	-0.001	0.99	-0.009	0.88
BW SDS	0.17	0.07	0.12	0.18	0.11	0.19
OC-use	-0.18	0.03	-0.17	0.03	-0.17	0.02
Height SDS	0.37	<0.0005	0.20	0.02	0.20	0.02
Weight SDS	-0.44	<0.0005				
Fat mass (kg)			-0.52	<0.0005		
Lean mass (kg)			-0.03	0.81	-0.04	0.76
Trunk FM (kg)					-0.57	<0.0005
Limbs FM (kg)					0.07	0.66
Adjusted R ²	0.23		0.33		0.34	

* Adjusted for age, gender, birth length SDS, BL*AH

Conclusions

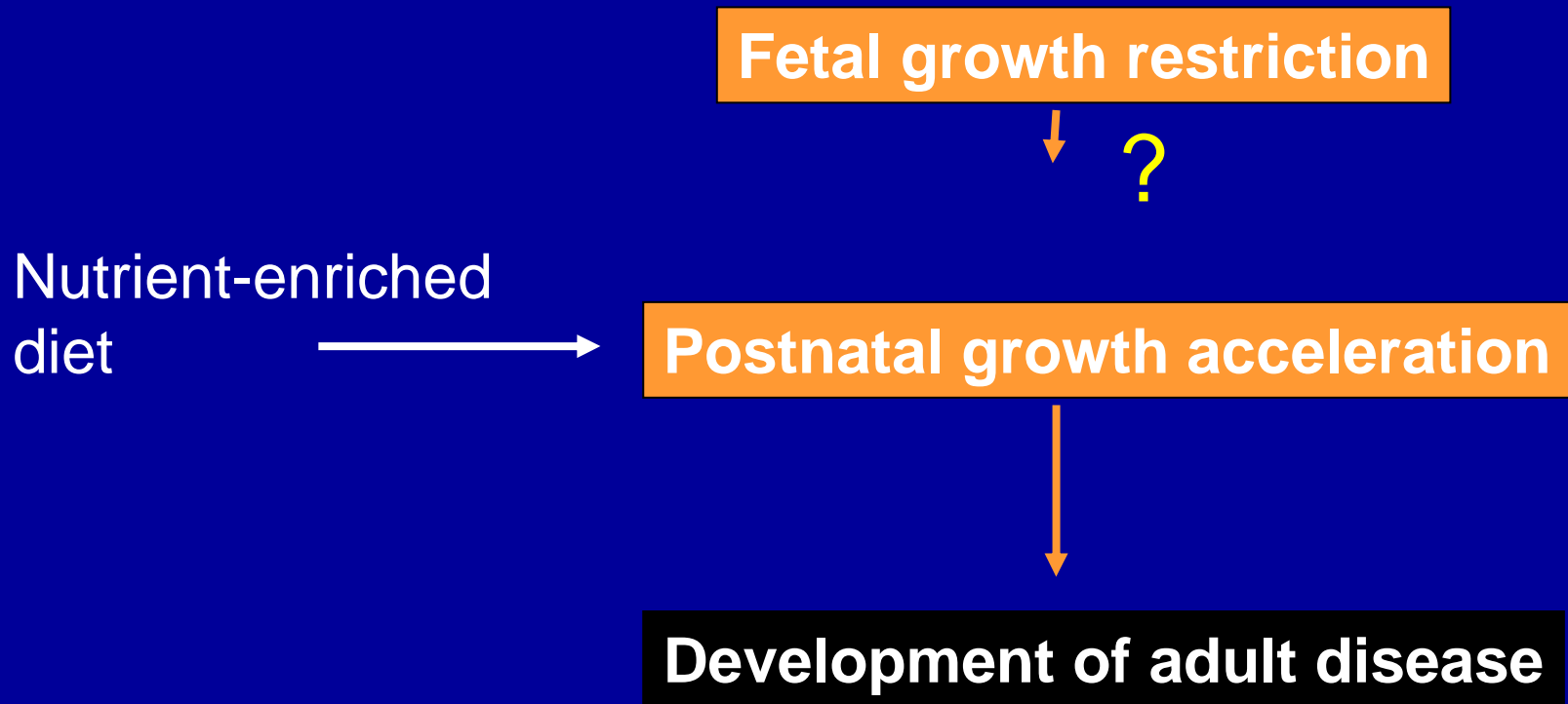


- **Prematurity** is **not** associated with reduced insulin sensitivity in young adulthood
- Most important predictors for a low insulin sensitivity are **fat percentage** and oral contraceptive use in women

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Growth acceleration hypothesis



Fat accumulation hypothesis

Postnatal growth acceleration



Fat accumulation



Development of adult disease

Which postnatal period is critical ?



RESULTS



Increased weight gain in the **first 3 months of life**



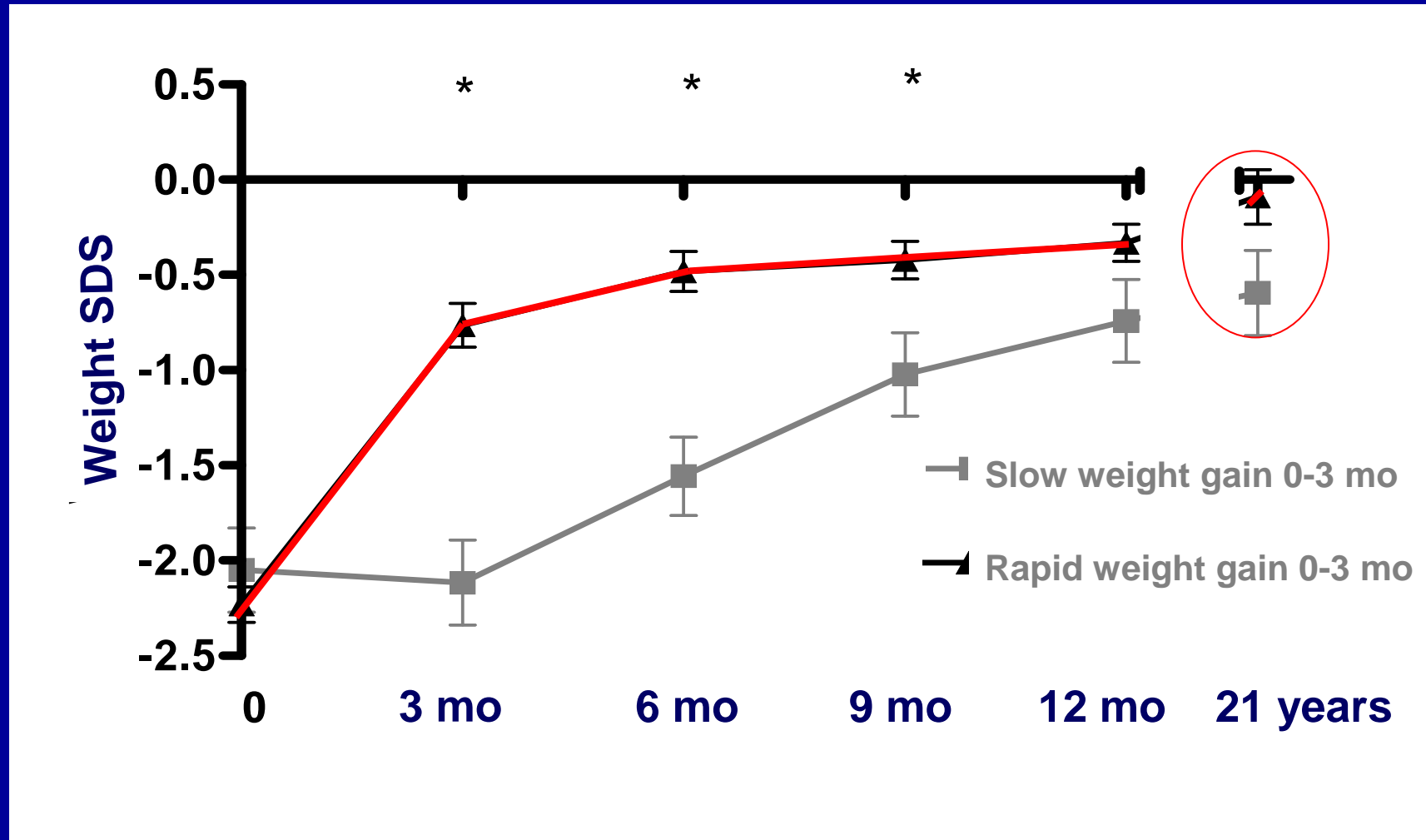
- **Reduced insulin sensitivity**
- **Reduced HDL levels**
- **Higher cholesterol/HDL ratio**
- **Higher triglyceride levels**
- **Increased fat mass %**
- **Increased abdominal circumference**
at 21 years

Is there a difference between Rapid catch-up and Slower catch up?

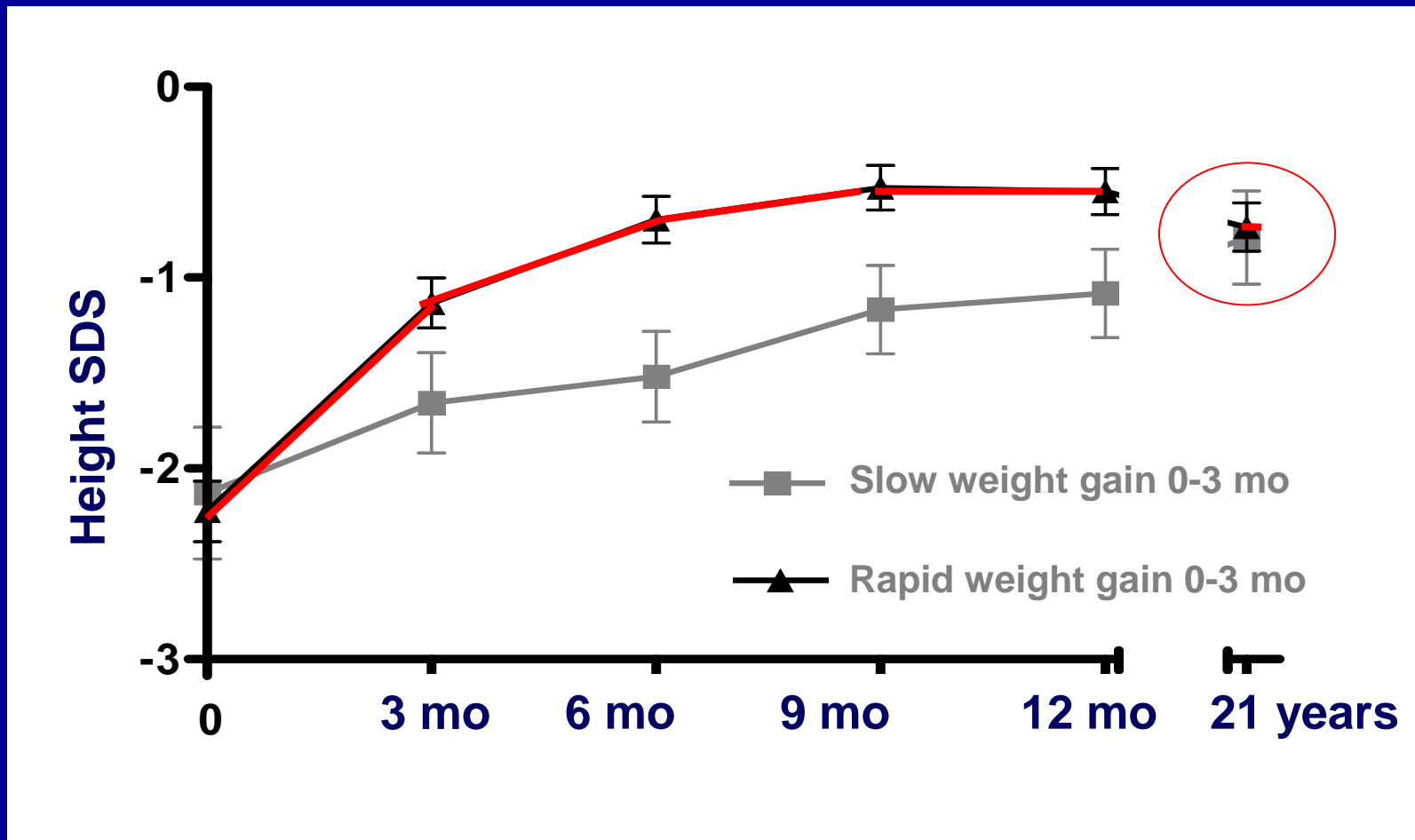
Catch-up defined as gain in height of at least 0.67 SDS in first year



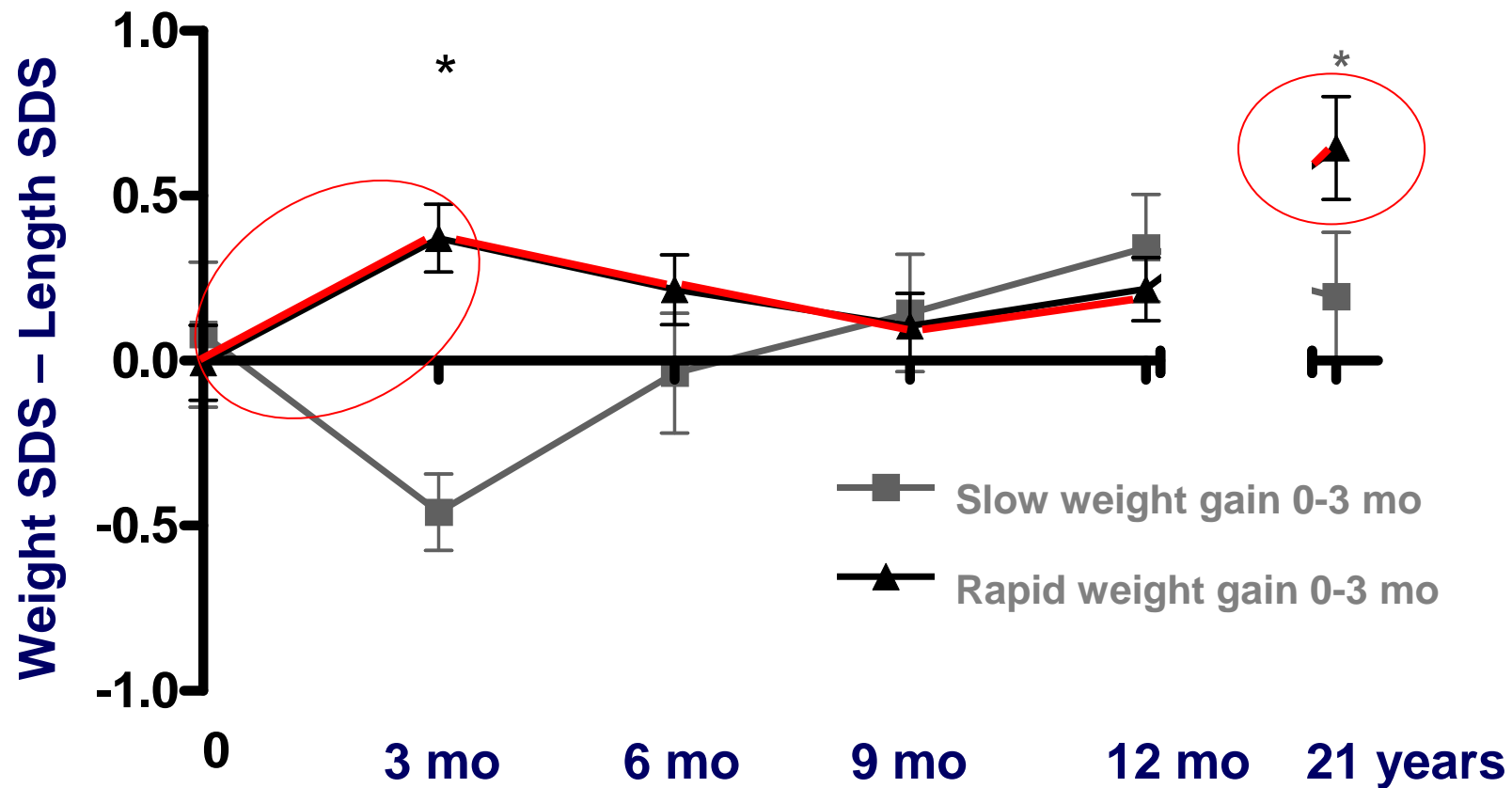
RAPID weight gain in first 3 months



RAPID height gain in first 3 months



RAPID weight gain in first 3 months



CONCLUSION

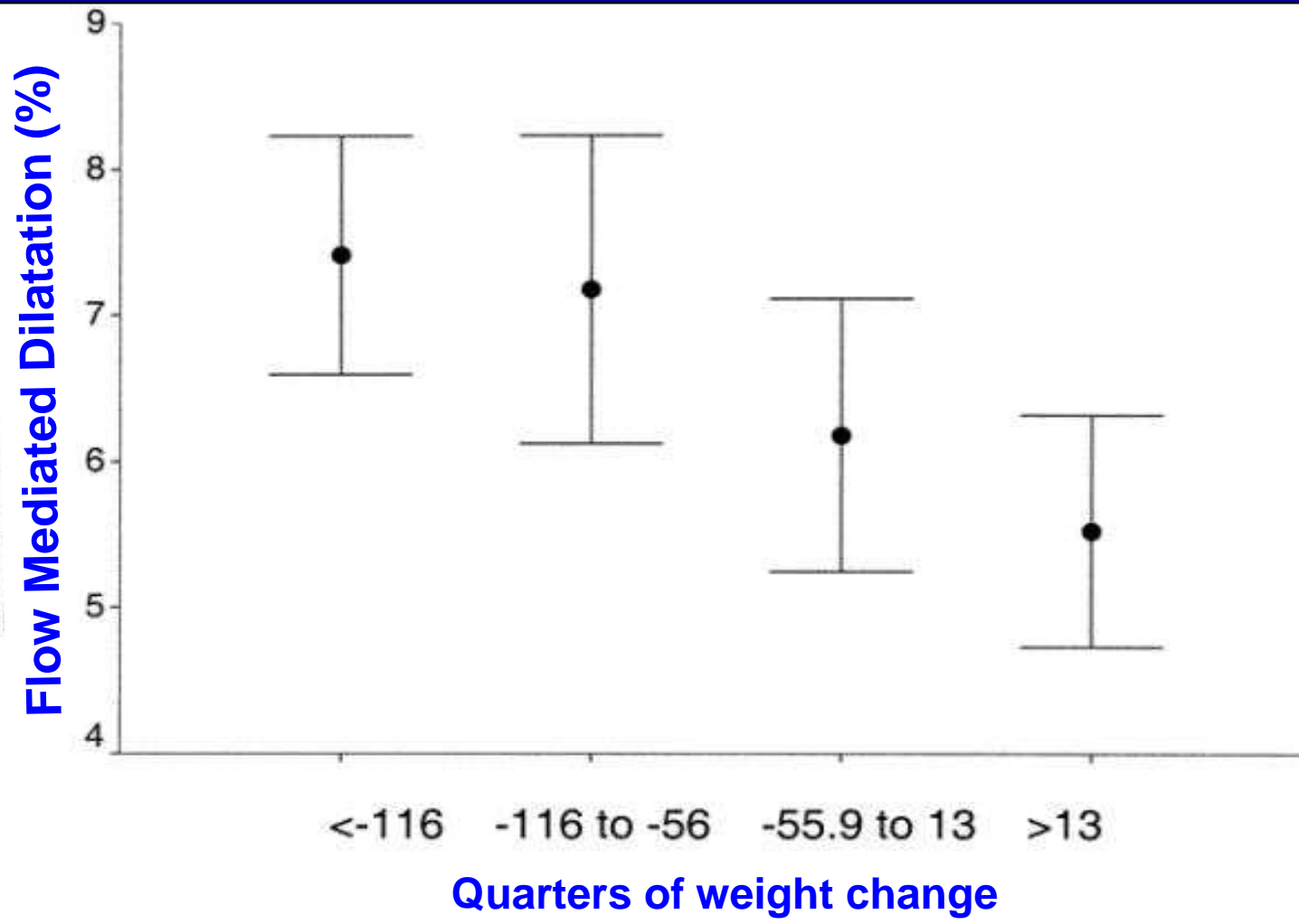


RAPID weight gain in the **first 3 months of life**



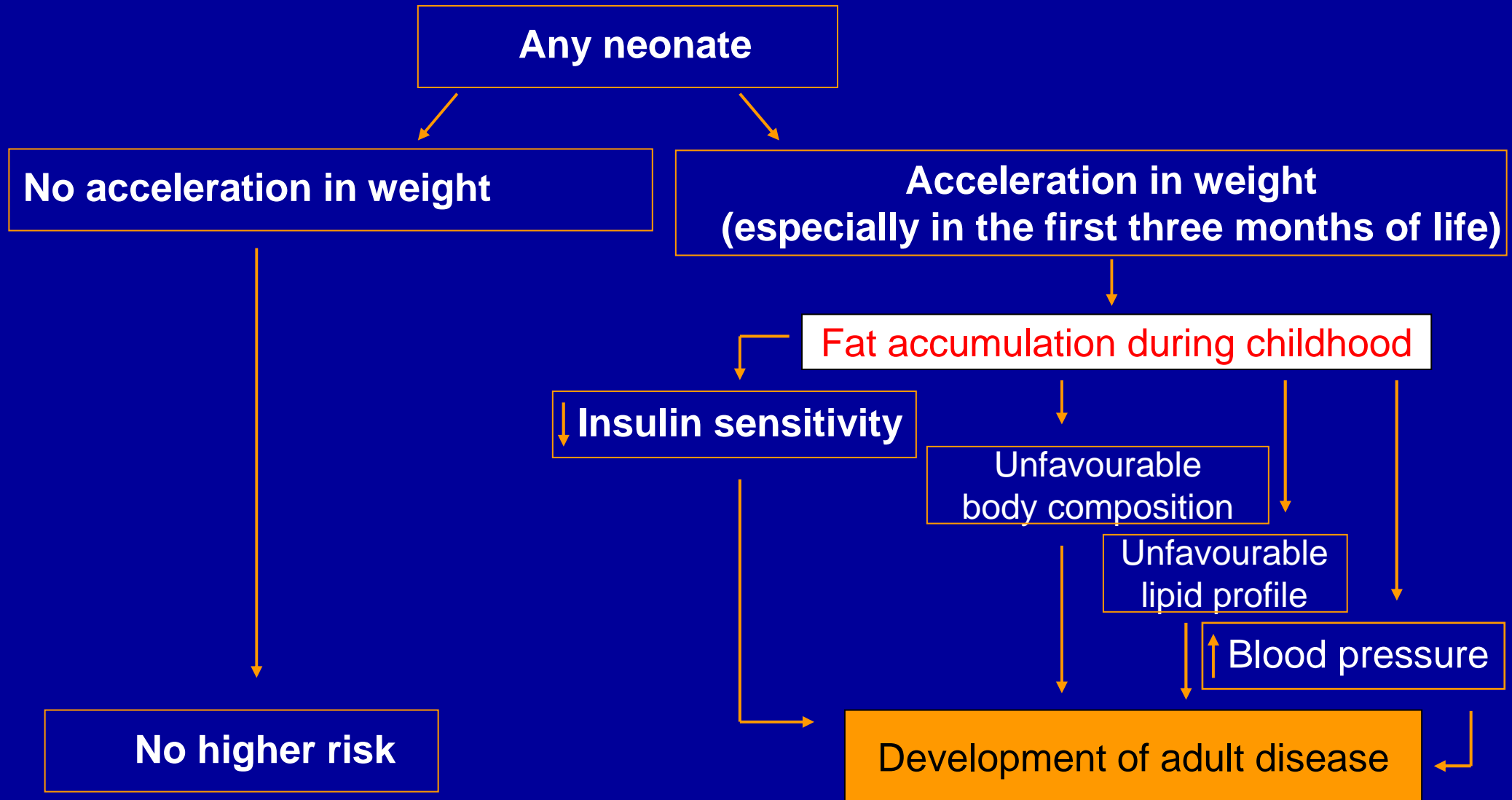
- **Reduced insulin sensitivity**
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- **Increased fat mass %**
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at 21 years

Slower Early Growth - Better Long-Term Cardiovascular Health



277 adolescents
- 13 to 16 years
- 216 preterm
 61 term
- First 2 weeks

New model



Accelerated weight gain in Infancy - be careful ! -

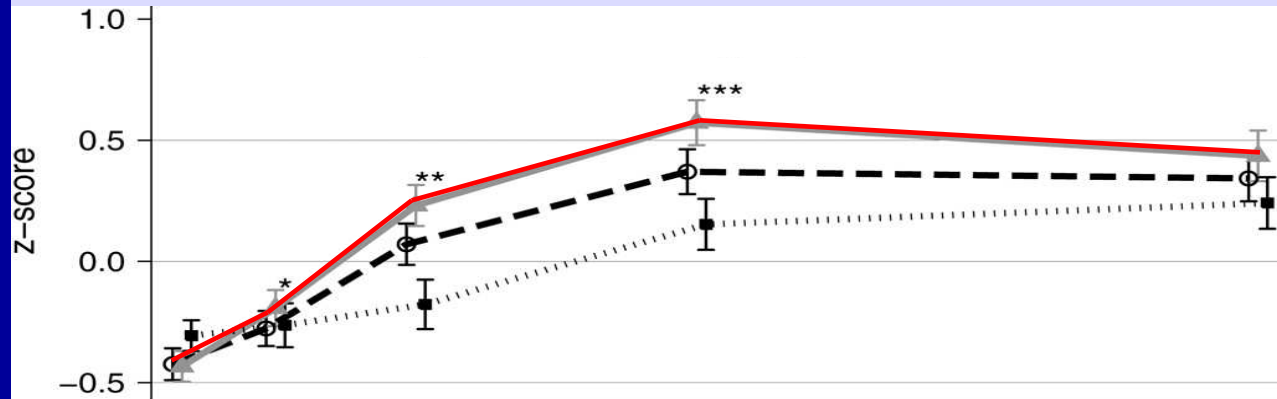


Randomised controlled trial in SGA infants

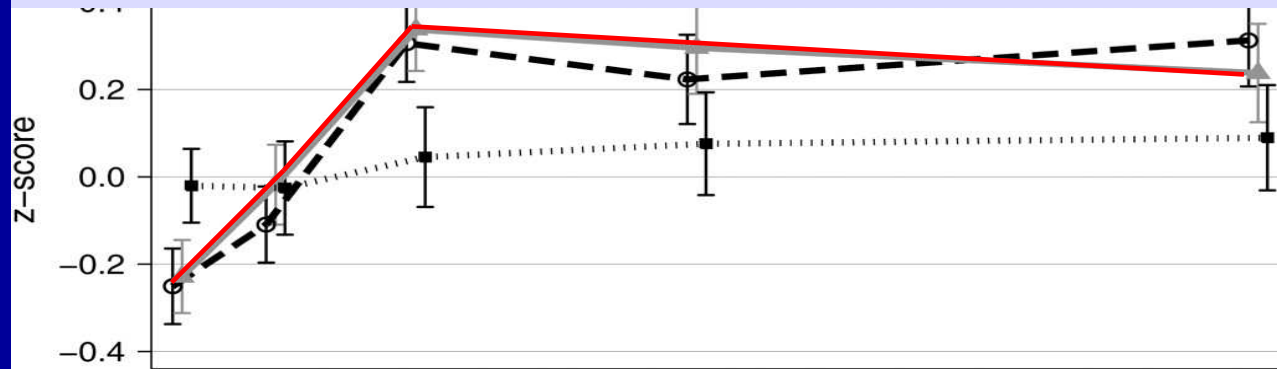
Infants given a **nutrient enriched** formula:

- **No beneficial effect on neurodevelopment & growth**
- **Adverse effect on later blood pressure & adiposity**

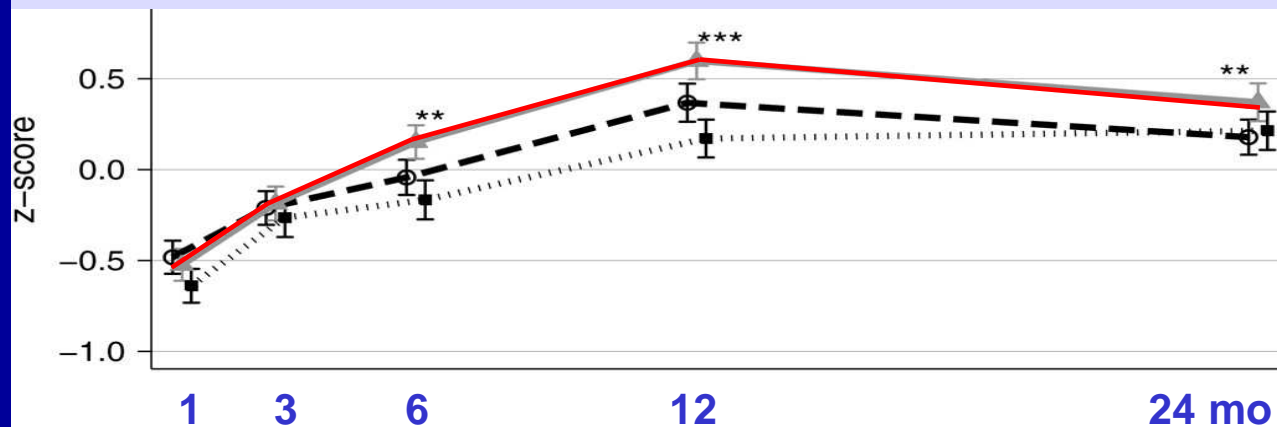
Weight-for-age



Height-for-age



Weight-for-height



- Higher protein (n= 550)
[2.05 g protein/100 ml]

-- Lower protein (n= 540)
[1.25 g protein/100 ml]

.. Breastfeeding (n= 588)
[1.20 g protein/100 ml]

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Conclusions



- Not SGA or prematurity but **postnatal weight (fat) gain during early childhood** is related to determinants of CVD and DMII in early adulthood
- **RAPID** catch-up in weight for height in the first 3 months of life should be prevented – 0-3 months is critical window
- SGA / preterm infants are at **higher risk for receiving nutrient enriched** formula
- **Breastfeeding** is associated with slower catch-up in weight for height and normal neurodevelopment

PhD fellows

Ralph Leunissen

Ruben Willemsen

Sandra de Kort

Gerthe Kerkhof

Research nurses

Joke Dunk

Marian Huibregts



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