# LONG-TERM GROWTH OF CHILDREN WITH AUTOANTIBODY-MEDIATED CONGENITAL HEART BLOCK

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# DEFINITIONS

CHB
Congenital heart block
Complete congenital AVB

Diagnosed in utero, at birth or in the neonatal period

Antibody exposure

Fetal exposure to anti-Ro/SSA and/or anti-La/SSB antibodies

# WHY IS LONG-TERM GROWTH AN ISSUE?

CHB are at risk for premature birth and small for gestational age (SGA) Machado et al 1988, Buyon et al 1998, Groves et al 1996, Julkunen et al 1999,

Women with connective tissue disease give birth to children SGA Skomsvoll et al 1998, 1999

# WHY IS LONG-TERM GROWTH AN ISSUE?

## SLE

-Premature birth and IUGR more frequent

Julkunen et al 1995, Aggarwal et al 1999

## Primary Sjögren's syndrome

-Conflicting results

-Premature birth and lower birth weight (BW) Hussein et al, 2011 Skog et al 2016

# GROWTH DEVELOPMENT IN CONGENITAL HEART BLOCK

**AB-exposure?**
- A direct antibody mediated effect on the fetus

**Heart block?**
- Low HR leading to low cardiac output and a hypoperfusion of body tissue

**Maternal disease?**
- Underdevelopment of the placenta and decreased blood flow

# TRANSPLACENTAL STEROID TREATMENT-FETAL INDICATIONS

Fluorinated steroids

Dexamethasone

Betamethasone

Saleeb et al 1999, French 1999, Bloom 2001

# GROWTH DEVELOPMENT IN CONGENITAL HEART BLOCK

Does the occurence of fetal heart block have any additional effect on growth restriction in pregnancies with connective tissue disease?

Outcome and
Heart Block-
Anti-Ro52/S

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32 pregnancies in 30 anti-Ro52 – positive mothers
**At prenatal echo:**
-7 with AVB II-III ( 1 died at GA 36 we)
-8 AVB I
-17 normal conduction

# FETAL EXPOSURE TO ANTI RO52-SSA AUTOANTIBODIES

3/6 Steroid treated

**TABLE 2** Maternal Age, Diagnosis, and Parity From 32 Pregnancies in 30 Women

| Variable | NC | AVB I | AVB II-III | All |
|---|---|---|---|---|
| Maternal age, mean ± 1 SD, y | 31.2 ± 4.9 | 29.9 ± 3.6 | 34.9 ± 4.4[a,c] | 31.7 ± 4.7 |
| Diagnosis, n | | | | |
| SLE | 10 | 4 | 2 | 16 |
| SS | 4 | 3 | 5 | 12 |
| Other | 3 | 1 | 0 | 4 |
| Parity, mean ± 1 SD | 1.6 ± 0.9 | 1.4 ± 0.7 | 2.4 ± 1.0[a,b,c] | 1.7 ± 0.9 |
| First child, n | 10 | 6 | 1 | 17 |
| Second child, n | 5 | 1 | 3 | 9 |
| Third child, n | 1 | 1 | 2 | 4 |
| Fourth child, n | 1 | 0 | 1 | 2 |

[a] P < .05 AVB II-III versus NC.
[b] P < .05 AVB II-III versus AVB I.
[c] P < .05 AVB II-III versus AVB I and NC.

**TABLE 3** Gestational Age and Body Measurements on 31 Newborn Infants

| Variable | NC | AVB I | AVB II-III |
|---|---|---|---|
| Gestational age, mean ± 1 SD, d | 273 ± 15.1 | 277 ± 15.1 | 257 ± 16.2[a,c] |
| Gender, n | | | |
| Girls | 8 | 5 | 3 |
| Boys | 9 | 3 | 4 |
| Weight, mean ± 1 SD, kg | 3.14 ± 0.50 | 3.18 ± 0.55 | 2.59 ± 0.59[a,b,c] |
| Length, mean ± 1 SD, cm | 49.0 ± 2.1 | 49.8 ± 2.8 | 46.2 ± 3.8[a,c] |
| Head circumference, mean ± 1 SD, cm | 34.6 ± 1.4 | 34.2 ± 1.2 | 32.5 ± 2.8[a,c] |
| BMI, mean ± 1 SD, kg/m² | 13.0 ± 1.4 | 12.8 ± 1.4 | 12.0 ± 1.4 |

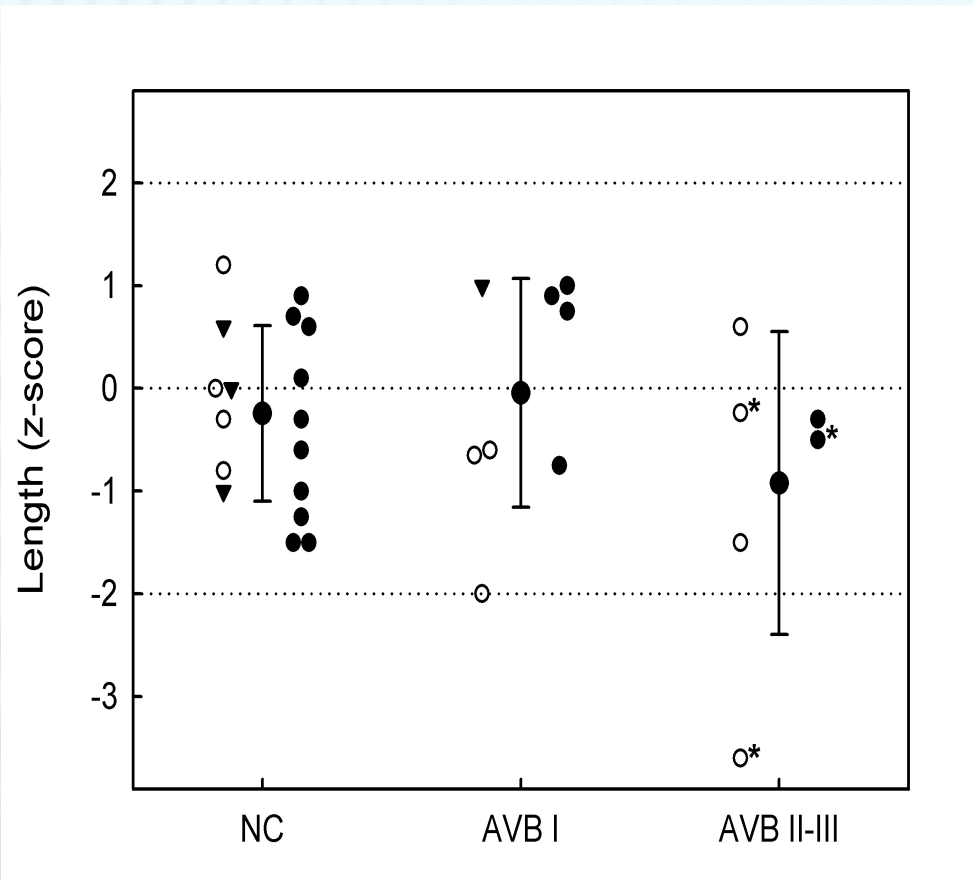Gender also includes 1 case of intrauterine death because of a complete heart block at 36 weeks of gestation.
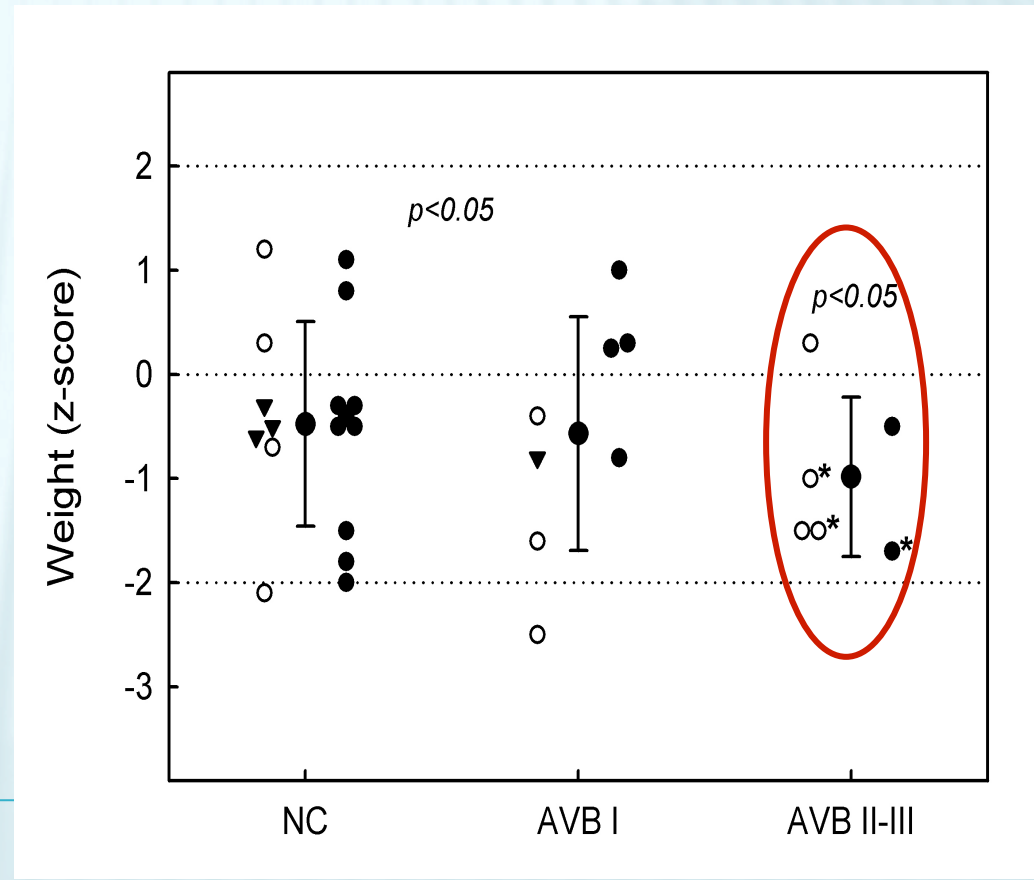[a] P < .05 AVB II-III versus NC.
[b] P < .05 AVB II-III versus AVB I.
[c] P < .05 AVB II-III versus AVB I and NC.

Skog et al Pediatrics 2008

# FETAL EXPOSURE TO ANTI RO52-SSA AUTOANTIBODIES

## LENGTH CORRECTED FOR GA

## WEIGHT CORRECTED FOR GA



Skog et al Pediatrics 2008

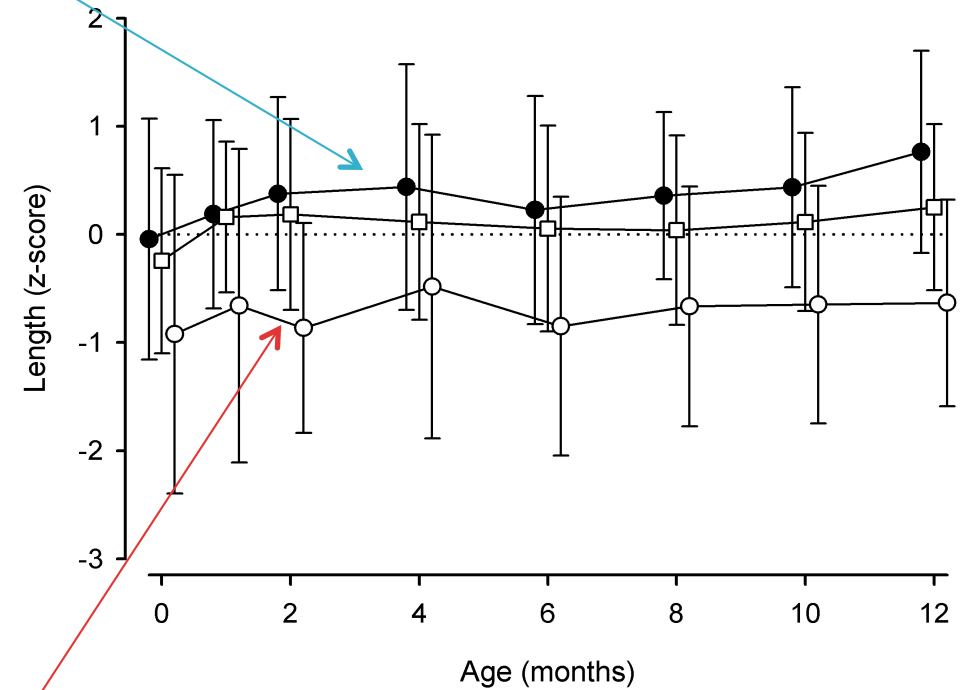# WEIGHT AND LENGTH AT BIRTH UNTIL THE FIRST YEAR OF LIFE



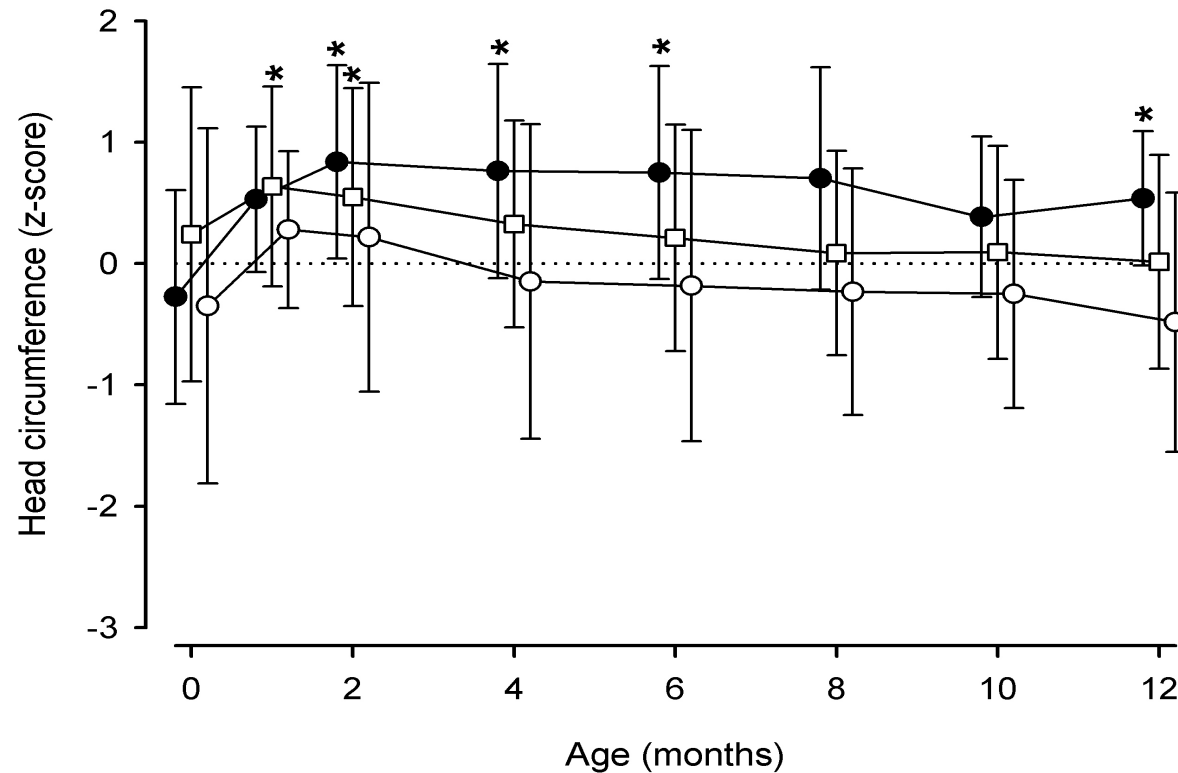Skog et al 2008
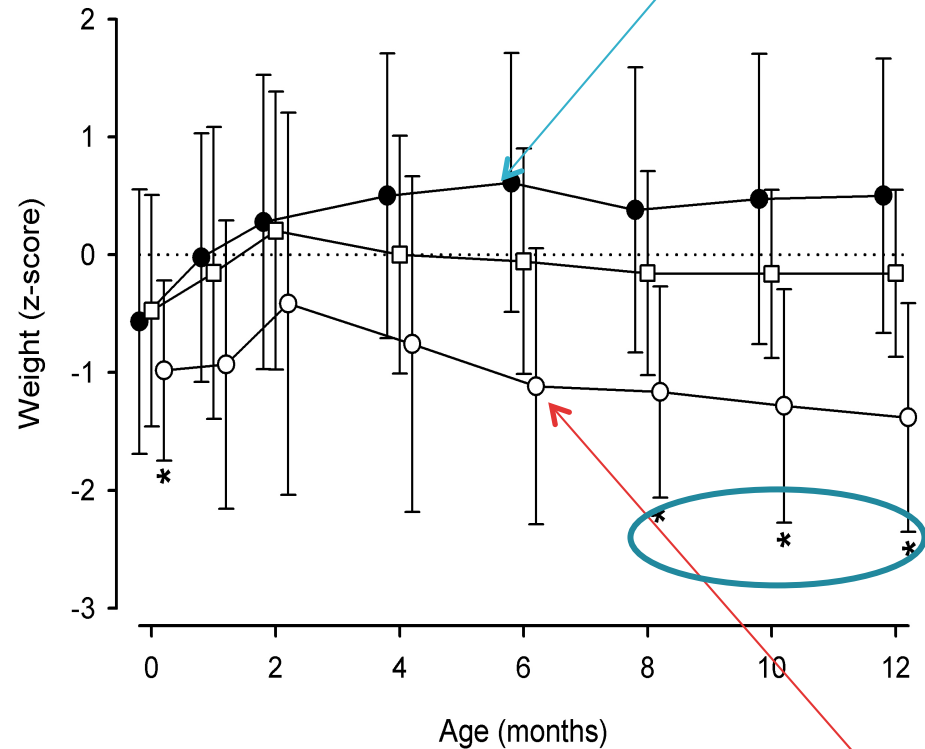
# HEAD CIRCUMFERENCE AT BIRTH UNTIL THE FIRST YEAR OF LIFE



Groups not significantly different
Not deviating from expected z-score (0)

Skog et al 2008

# CONCLUSIONS

AVB II-III
Growth retarded
No catch-up

AVB I/ NC
normal growth

# REMAINING QUESTIONS

Long-term growth?

Catch-up?

PM?

**REGULAR ARTICLE**

# Long-term growth of children with autoantibody-mediated congenital heart block

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3. Unit of Cardiovascular Epidemiology, Department of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

# LONG-TERM GROWTH IN CHB

AIMS

To analyse long-term growth of AB-exposed siblings with and without congenital heart block (CHB) from birth to 18 years of age

-CHB vs non-CHB siblings
-All exposed vs reference standards

# METHODS

+ National cohort of antibody exposed (anti Ro/SSA) siblings with (n=72) and without (n=60) CHB born 1973-2009 was identified and studied retrospectively from birth to 18 yrs

+ Data retrieved from medical records regarding: gestational age, mode of delivery, longitudinal data on weight, height and head circumference (HC) and age at pacemaker implantation

+ Questionnaire sent to the mothers regarding maternal diagnosis and steroid treatment during pregnancy

# METHODS

- 12 time points- 1,3 , 6 ,9 12, 18 months and 2-3, 4-5, 6-8, 9-11, 12-14 and 15-18 yrs of age

- All measurements converted to a standardized z-score (using Swedish standard references))

- Body mass index (BMI) was calculated

# MATERNAL DIAGNOSIS

| | |
|---|---|
| SLE | 34 % |
| Primary SS | 19 % |
| Rheumatoid Arthritis | 6 % |
| Mixed connective tissue disease | 6% |
| No diagnosis/asymptomatic | 35% |

# CHARACTERISTICS OF THE CHILDREN

**Table 1. Characteristics of children included**

| | CHB (n=72) | Siblings without CHB (n=60) | All (n=132) | p-value CHB vs. No CHB |
|---|---|---|---|---|
| **Gender, *n* and %** | | | | |
| Males | 34 (47%) | 26 (43%) | 60 (45%) | |
| Females | 38 (53%) | 34 (57%) | 72 (55%) | |
| **Gestational age** | | | | |
| mean ± 1 SD, weeks | 38.1 ± 2.3 | 38.8 ± 2.3 | 38.4 ± 2.3 | ns |
| median, weeks | 38 | 39 | 39 | |
| Born preterm (GA<37 weeks)*, *n* | 12 | 6 | 18 | ns |
| **Type of delivery, *n* and %** | | | | |
| Vaginal | 28 (39%) | 39 (65%) | 67 (51%) | |
| Elective caesarean section | 30 (42%) | 4 (7%) | 34 (26%) | |
| Emergency caesarean section | 7 (10%) | 4 (7%) | 11 (8%) | |
| Ventouse | 3 (4%) | 8 (13%) | 11 (8%) | |
| No info avaliable | 4 (6%) | 5 (8%) | 9 (7%) | |

# CHARACTERISTICS OF THE CHILDREN

**Table 1. Characteristics of children included**

| | CHB (n=72) | Siblings without CHB (n=60) | All (n=132) | p-value CHB vs. No CHB |
|---|---|---|---|---|
| **Body measurements at birth** | | | | |
| Birth weight, mean ± 1 sd, g | 3024 ± 588.2 | 3380 ± 666.7 | 3184 + 647.0 | p<0.001 |
| Birth length, mean ± 1 sd, cm | 48.9 ± 2.9 | 50.2 ± 3.0 | 49.5 ± 3.0 | p< 0.01 |
| Head circumference at birth, mean ± 1 sd, cm | 33.8 ± 1.8 | 34.4 ± 2.0 | 34.1 ± 1.9 | p<0.05 |
| BMI (mean, sd, kg/m2) | 12.6 ± 1.5 | 13.3 ± 1.8 | 12.9 ± 1.7 | p<0.05 |
| Individuals with low birth weight (< 2500 g), n | 12 | 5 | 17 | ns |
| | | | | |
| **Steroid treatment during pregnancy, *n and %*** | | | | |
| Steroid treatment during pregnancy | 8 (11%) | 2 (3%) | 10 (8%) | |
| Betamethasone | 3 (4%) | 0 (0%) | 3 (2%) | |
| Prednisolone | 5 (7%) | 2 (3%) | 7 (5%) | |
| No steroid treatment during pregnancy | 55 (76%) | 52 (87%) | 107 (81%) | |
| No information avalibale | 9 (13%) | 6 (10%) | 15 (11%) | |
| | | | | |
| **No. of measurements per individual, *mean*** | | | | |
| Weight | 13 | 12 | 12 | |
| Length | 12 | 12 | 12 | |
| Head circumference | 4 | 4 | 4 | |
| | | | | |
| **Pacemaker information** | | | | |
| Individuals with Pacemaker insertion during follow-up (<18 years), n | 61 (85%) | | | |
| Age at pacemaker insertion, mean, years | 3.77 | | | |
| Age at pacemaker insertion, median (range), years | 1.03 (0-16.87) | | | |

\* Data on GA missing for four individuals (1 with CHB and 3 without CHB)

# LONGITUDINAL WEIGHT AND HEIGHT

Progressive catch-up from 2-3 yrs of age
Normal weight around 9-11 yrs of age
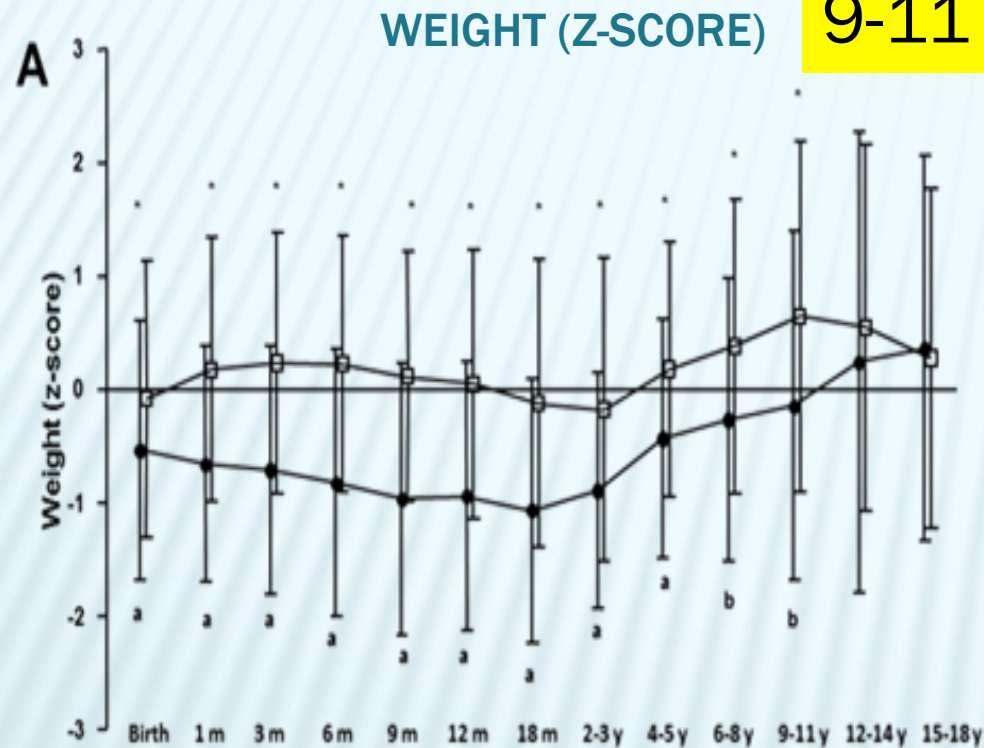


Longitudinal (**A**) weight and (**B**) height from birth to 18 years for children with and without CHB presented as the mean ±1SD. *: p<0.05 CHB vs. No CHB (t-test), [a]: p<0.05 CHB vs. z-score 0, [b]: p<0.05, No CHB vs. z-score 0 (one sample t-test).

# Body Mass Index
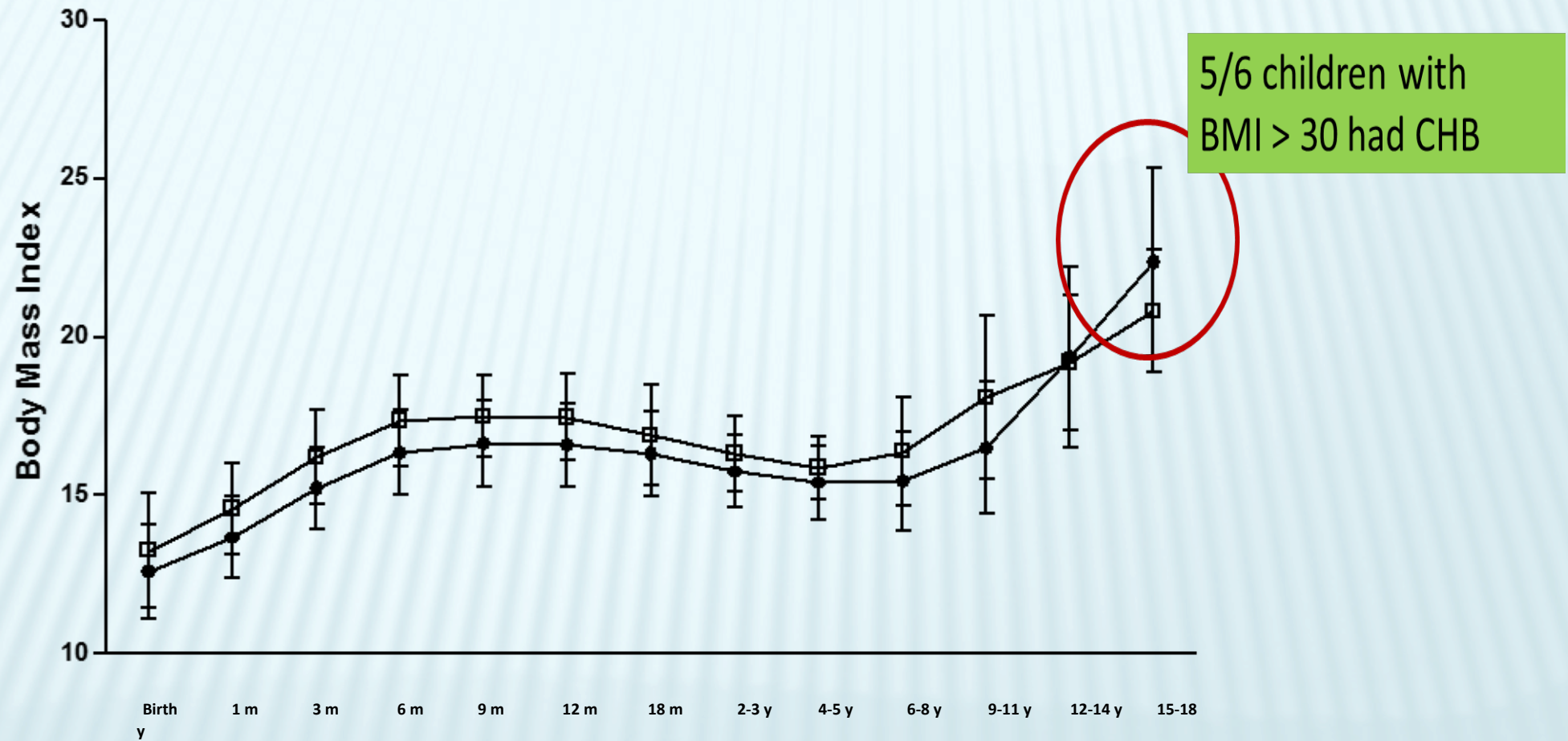


BMI from birth to 18 years for children with and without CHB presented as the mean ±1SD. *: $p<0.05$ CHB vs. No CHB (t-test), [a]: $p<0.05$ CHB vs. z-score 0, [b]: $p<0.05$, No CHB vs. z-score 0 (one sample t-test).

# GROWTH AFTER PACEMAKER INSERTION
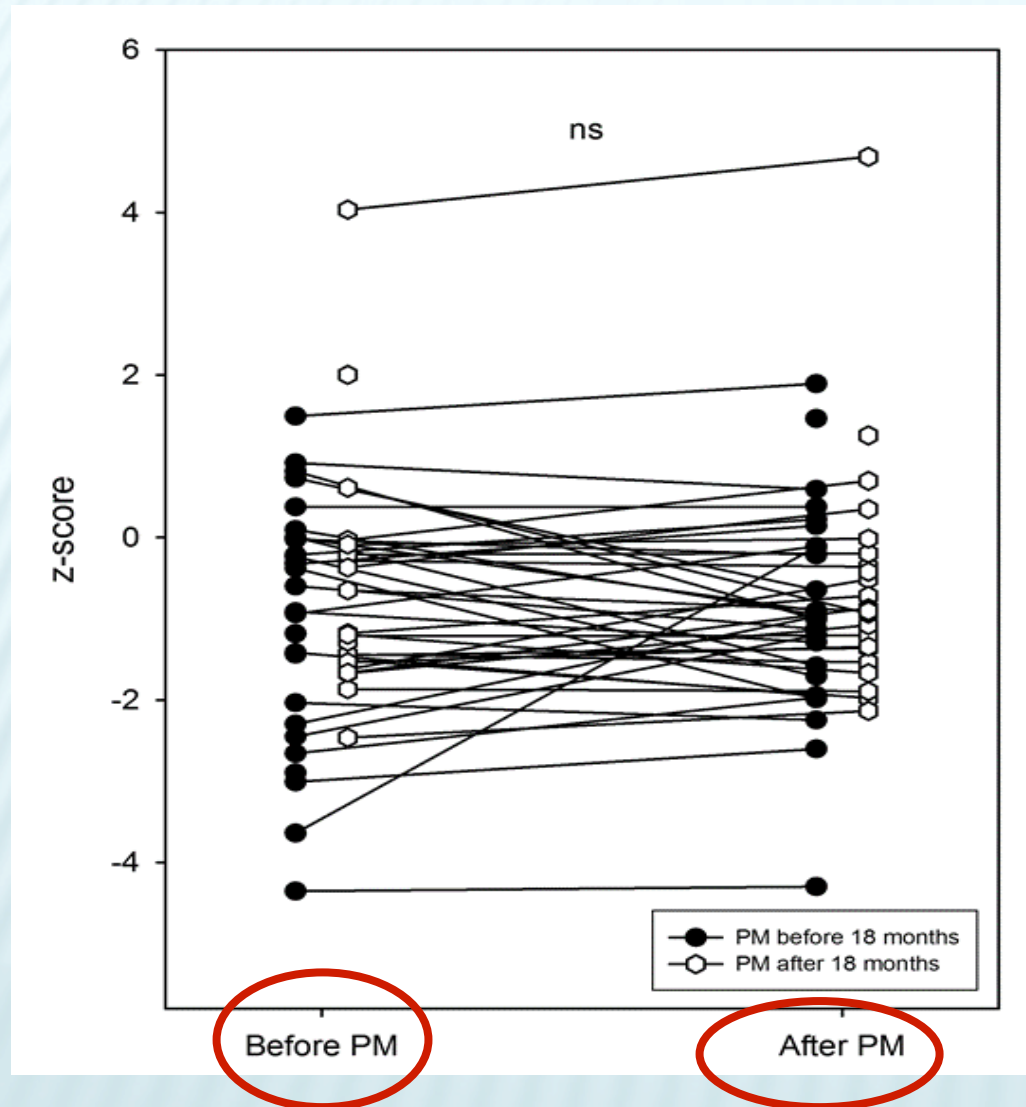


- Comparison before PM implantation vs after implantation (**median 1 year**)

- Separate comparisons patients with PM < 18 months and > 18 months

- No significant differences

# CONCLUSIONS

- CHB children exposed to maternal Ro52-autoantibodies had impaired growth in the first years of life followed by a gradual catch-up

- Non-CHB siblings had normal growth compared to swedish reference standards

- Insertion of a PM did not result in a catch-up in growth in the first year after PM treatment

# CONCLUSIONS

- ✖ Growth restriction was apparantly not an indication for PM treatment in our cohort.

- ✖ To many missing data (HR and heart function) to correlate morbidity before PM to growth

- ✖ Uncertainty about the effect of prenatal steroid treatment on long term growth

TACK!

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|---|---|---|---|
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| X / ☐ | ☐ / X | ☐ / X | ☐ / X |

**SCORE: 1**

# LONGITUDINAL WEIGHT OF CHB WITH AND WITHOUT PACEMAKER



o CHB with PM

• CHB without PM