Prolonged, exclusive breastfeeding & adiposity, stature & blood pressure: Promotion of Breastfeeding Intervention Trial (PROBIT III)

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Potential child health benefits of breastfeeding

- Increased stature
- Protection against:
  - Obesity
  - CVD risk factors
    - blood pressure, insulin resistance, hyperlipidaemia
- Problems with the evidence base
  - Based on observational studies
  - Residual confounding
  - Selection bias
  - Publication bias
Mean difference in BMI: BF v formula fed (36 studies)

Breast feeding better

Mean difference in BMI (kg/m²)

Breast feeding worse

Fixed-effect: -0.04 (95% CI -0.06, -0.03)

Owen et al, AJCN, 2005;82:1298-307
Mean difference in BMI: effect of adjustment for important confounders

Mean difference in BMI (kg/m²)

Adjustments in 11 studies

Age
Age, maternal smoking
Age, maternal BMI
Age, social class
Age, social class, maternal smoking and BMI

Owen et al, AJCN, 2005;82:1298-307
Mean difference in BMI: effect of adjustment for important confounders

-0.15
-0.1
-0.05
0
0.05

Adjustments in 11 studies

Age
Age, maternal smoking
Age, maternal BMI
Age, social class
Age, social class, maternal smoking and BMI

Owen et al, AJCN, 2005;82:1298-307
Mean difference in BMI: effect of adjustment for important confounders

Adjustments in 11 studies

- Age
- Age, maternal smoking
- Age, maternal BMI
- Age, social class
- Age, social class, maternal smoking and BMI

Owen et al, AJCN, 2005;82:1298-307
Mean difference in BMI: effect of breast feeding duration (6 studies)

After adjustment

Before adjustment

P=0.99

P=0.001

Owen et al, AJCN, 2005;82:1298-307
Mean difference in BMI: effect of breast feeding duration (6 studies)

Adjusted for social class, parental BMI, maternal smoking

After adjustment

Before adjustment

P=0.99

P=0.001

Owen et al, AJCN, 2005;82:1298-307
Solution: RCT with analysis by “intention to treat”

- Best way to minimize multiple biases
- Randomization to breast vs artificial feeding is not feasible / ethical
- The solution is a RCT of an intervention to promote BF exclusivity & duration
- Overlap of BF behaviors requires very large sample size
PROBIT

PROmotion of Breastfeeding Intervention Trial

Follow-up of A Cluster-Randomized Trial in the Republic of Belarus
Trial design

- RCT to promote breastfeeding exclusivity & duration, based on WHO/UNICEF BFHI
- Stratified, cluster randomization of 31 maternity hospitals & one affiliated polyclinic per hospital

- In 1996-7, 17,046 healthy BF newborns ≥37 wks & >2500g enrolled during postpartum stay
Baseline Comparison

Maternal Age & Education (%)

- <20 yr
- 20-34 yr
- >=35 yr
- Incomplete secondary
- Complete secondary
- Partial university
- Complete university

Experimental vs Control
Baseline Comparison

No. of siblings, prev BF, CS, smoking, atopic FH (%)
Degree of Breastfeeding (%)
Long-term follow-up of PROBIT

- Created two *randomized* cohorts differing substantially in exclusivity / duration of BF
- Analysis by intention to treat enables *strong causal inferences* with respect to BF effects on long-term outcomes
- Intervention had significant benefits on:
  - GI infection in infancy (PROBIT I)
  - Atopic eczema in infancy (PROBIT I)
  - IQ at 6.5 years (PROBIT II)
PROBIT III

- Follow-up at 11.5 yrs between Jan 2008 to June 2010
  - Anthropometry
  - CVD risk factors \((BP; \ glucose; \ insulin; \ adiponectin; \ apo \ A1; \ apo \ B; \ IGF-I)\)
- > 13,500 children have been seen (80%)
- 11,674 (68%) have data entered to date
- Interim results are presented today, as still over 2000 records to enter
Comparison By Follow-Up: Probit III

Maternal Age & Education (%)

- <20 yr
- 20-34 yr
- >=35 yr
- Incomplete secondary
- Complete secondary
- Partial university
- Complete university

Followed Up  Not Followed Up
Comparison By Follow-Up: Probit III
Older Sibs, Maternal Smoking, & Gender (%)

Followed Up  Not Followed Up

- 0 older sibs
- 1 older sib
- >=2 older sibs
- Maternal smoking
- Male gender
Interim conclusions – prolonged/exclusive BF at 11.5 yrs:

- Stature: Small positive ass’n with height (leg-length)
- Adiposity: No important reduction in adiposity
- Blood pressure: No important reduction in BP
- In this interim analysis, the 95% CIs indicate that small beneficial or adverse effects cannot be ruled out
- These results are not due to selection bias or confounding, unlike observational studies
- Breastfeeding improves IQ and protects against GI infections and atopic eczema in infancy
Спасибо

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