Norwegian Mother and Child Cohort Study

Per Magnus, Tokyo, December 15, 2015
The MoBa cohort

Aim: To find causes of disease

• A large population based pregnancy cohort

• A family cohort (mother + father + child)

• Long term follow-up
Collaboration with 50 hospitals

- Hospitals with < 1000 births/year
- Hospitals with >1000 births/year

Inclusion period
1998 - 2008
Norway
~60,000 births/year

 Recruiting pregnant women and their partners midpregnancy
Based on informed consent

- Broad consent
- Can be withdrawn at any point
- Mother consented for herself and the child
- Father separate consent
- Child informed at 15 years
- Child own consent at 18 years
# The MoBa cohort

<table>
<thead>
<tr>
<th></th>
<th>No</th>
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<th>No</th>
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</thead>
<tbody>
<tr>
<td>Mothers</td>
<td>95 000</td>
<td>Pregnancies</td>
<td>113 000</td>
</tr>
<tr>
<td>Fathers</td>
<td>75 500</td>
<td>Twins</td>
<td>1950</td>
</tr>
<tr>
<td>Children</td>
<td>114 500</td>
<td>Triplets</td>
<td>21</td>
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</tbody>
</table>
Data collection

Ultrasound
- 17 W
- 22, 30 W
- Birth
- ½, 1½, 3, 5Y
- 7Y
- 8 Y
- 13, 14Y

Child
- Blood
- Cord blood
- Teeth

Mother
- Blood

Father
- Blood

Teeth

Blood
Planned data collection

Fathers
The fathers answered a questionnaire at recruitment. Presently, a second questionnaire is being sent to all fathers. The main topics are the father’s physical and mental health and the father’s relationship to the child.

13 year
First web-based questionnaire to the children. Main focus on behaviour and mental health.

14 year
Questionnaire to the children regarded diet and nutrition.
Biological samples

MoBa:
Top modern biobank – automated/manual
4.5 million samples stored

- EDTA whole blood and plasma (frozen -80° C)
- DNA extracted from whole blood (frozen -20° C)
- Urine (Mothers only) (frozen -20° C)
- RNA: from cord blood (Tempus-tubes)
Information from blood and urine samples

• genetic information
• environmental toxins
• infections
• dietary factors
• medication, drugs
• various other biomarkers
The Norwegian Mother and Child Cohort Study (MoBa)

- **n = 108 000 pregnancies**

**HARVEST**

- **n = 11 000**

**MoBa-Etox**

- **n = 1000**

**Blood, Plasma, Urin**
HARVEST

- Genome-wide association study for 11 000 trios in MoBa

- Based on an Illumina chip
  - Human Core Exome
    - 265 000 tagSNPs
    - 245 000 exome-focused markers
Biomonitoring: MoBa-Etox
1000 trios

- 930 µL urine
- 1100 µL blood
- 400 µL plasma

**Metals (b)**
- Mercury
- Cadmium
- Lead
- Manganese
- Zinc
- Arsenic
- Thallium
- Cobalt
- Cobber
- Molybdenum
- Selenium
- Jod, Na, K (u)

**Blood sugar (b)**
- HbA1c

**Inflammation (p)**
- CRP

**Hormones (p)**
- TSH
- fT3, fT4
- TPOAb

**Iron status (p)**
- Ferritin
- Transferrin

**Vitamins (p)**
- Vit A (retinol)
- Carotenoids
- 25OHVitD
- Vit E (Tokopheroler)

**Stress marker (u)**
- Cortisol

**Correction factors**
- Cholesterol (p)
- Creatinine (u)
- Albumin (u)
- Uric acid (u)
Links with other registries

- Statistics Norway (education, ethnicity)
- Prescription registry
- Vaccination registry
- National patient registry
- Cancer registry
- Disease specific registers.
- Cause of death registry
Strengths

• The large number of participants

• The father-mother-child trios, with the possibility of studying twins and siblings

• The wealth of information

• The biological specimens

• The combination of genetic and environmental information
Activities

• Active research projects: about 200
• Completed research projects: 125
• 14 projects have additional data collection (sub-cohorts)

• About 400 publications
• 32 PhD projects completed
Research areas

• Infertility
• Diet in pregnancy
• Preeclampsia
• Preterm birth
• Hyperemesis
• Folic acid intake and consequences
• Eating disorders in pregnancy
• Medications in pregnancy
• Physical activity in pregnancy
• Pelvic girdle pain
• Urinary incontinence
• Smoking (maternal and paternal)
• Violence in pregnancy
• Childhood temperament
• Airway disease
• CHD and development
• Effect of early start in nursery
• ADHD
• Autism

Pregnancy

Child health
MoBa–funding

- Governmental direct funding
- National Institute of Public Health
- Project funding
  - National Institutes of Health USA
  - Norwegian Research Council
  - EU Research framework programmes
Some findings

- Folate intake in early pregnancy and neuropsychological development
  - The incidence of autism is reduced (OR = 0.61) for pregnant women who take folate supplements in the first weeks (Surén et al. JAMA 2013:309:570-7)
  - The occurrence of severe language delay is also reduced (OR=0.55) for the same exposure
Some findings

• Intake of paracetamol in pregnancy and child neurodevelopment

  – Infants exposed to long-term paracetamol exposure during pregnancy were at higher risk of adverse developmental outcomes at 3 years – using a sibling controlled design (Brandlistuen et al Int J Epidemiol 2013;42:1702-13)
Some findings

• Use of cell phones by parents was not associated with adverse pregnancy outcomes (Baste et al. Epidemiology 2015;26:613-21)

• Use of anti-depressants during pregnancy was weakly associated with neurodevelopment in children (Handal et al. BJOG 2015;Sept 16)
Norwegian Mother and Child Cohort Study

The Norwegian Mother and Child Cohort Study (MoBa) is a unique study where more than 90,000 pregnant women were recruited between 1999 and 2008. Some of the mothers have more than one child in MoBa and the last child was born in 2009. Over 70,000 fathers have also participated. We will hold contact with these families in the years to come, collecting further data through questionnaires.

2015 research finding
Antidepressant use in pregnancy associated with anxiety symptoms in 3-year-olds
Three-year-old siblings exposed to antidepressants in pregnancy show increased anxiety symptoms compared to their unexposed siblings.
Read more [15.04.2015]

2015 research finding
Link between toddler sleep patterns and behaviour at 5
Toddler who sleep less than 10 hours a night or wake frequently are more likely to have emotional and behavioral problems at the age of five, according to a study from the Norwegian Institute of Public Health.
Read more [15.04.2015]

2015 report
High quality centre-based childcare can prevent developmental difficulties
High quality centre-based childcare appears to prevent the development of language and behavioural difficulties over time, particularly among vulnerable children. The factors that appear to affect children include spaces for learning activities, staff education, relationships with staff, activities offered, time spent in childcare and group size.
Read more [19.02.2015]
Thank you!