Nine months that last a lifetime

Danish National Birth Cohort

Mads Melbye
Copenhagen, Denmark
Overall aim

To identify prenatal and perinatal determinants of importance for reproductive failures and diseases that manifest themselves later in life.
Practical aims

• To recruit 100,000 pregnant women and offspring
• Collect exposure information by means of 4 telephone interviews
• Set up a biobank with 2 blood samples from the mother and 1 from the child
• Get food frequency data and over-the-counter medication from questionnaire
Recruitment

• During 1996-2002 we enrolled 101,042 pregnancies. We have prospectively monitored the outcome of these pregnancies.

• Approximately 30% of all pregnant women in Denmark were recruited through collaboration with GP’s and midwives.

• About half of all GPs were active, about 60% of women invited finally joined.
# Basic data collection in DNBC

<table>
<thead>
<tr>
<th>Method</th>
<th>When</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>blood sample</td>
<td>1st trimester</td>
<td>Blood from the mother taken in connection to first visit to GP</td>
</tr>
<tr>
<td>interview</td>
<td>12 weeks of pregnancy</td>
<td>13 minutes telephone interview</td>
</tr>
<tr>
<td>questionnaire</td>
<td>25 weeks of pregnancy</td>
<td>Questionnaire on dietary habits</td>
</tr>
<tr>
<td>blood sample</td>
<td>2nd trimester</td>
<td>Sample taken in connection to GP visit</td>
</tr>
<tr>
<td>interview</td>
<td>30 weeks of pregnancy</td>
<td>12 minutes telephone interview</td>
</tr>
<tr>
<td>blood sample</td>
<td>Birth or fetal death</td>
<td>Blood from the child taken from the umbilical cord or dead fetus</td>
</tr>
<tr>
<td>interview</td>
<td>Child age 6 months</td>
<td>16 minutes telephone interview</td>
</tr>
<tr>
<td>interview</td>
<td>Child age 18 months</td>
<td>10 minutes telephone interview</td>
</tr>
</tbody>
</table>
Three types of data collected

**Self-reported data on exposures and outcomes.**
Main exposures of interest are: lifestyle factors, diet, social conditions, infections, medications & environmental exposures

**Biological data.**
Blood from mother (pregnancy week 12 and 24), and child (cord blood and PKU card at day 3-5) stored in biobank

**Data from existing registers.**
F.ex. National Patient Registry & the Medical Birth Registry, medical prescriptions, disabilities, and death
The Danish registries are unique

- an investment worth billions of Danish kroner
- follow the individual from birth to grave
- follow diseases through generations
- millions of individuals
- results are robust

CRS-number

Birth characteristics
Diseases
Prescribed medication
Vaccinations
Childcare facilities
School performance
Family, place of living
Education, employment
Biological specimens
One dot for each participating woman...

The many participants’ dots clearly outline the shape of Denmark.

The DNBC truly is a nationwide cohort.
## Later data collections

<table>
<thead>
<tr>
<th>When:</th>
<th>Description:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child age 7 years</td>
<td>Web-based questionnaire and paper version to mother (or father)</td>
</tr>
<tr>
<td>Child age 11</td>
<td>Web-based questionnaire only to both mother (father) and child</td>
</tr>
<tr>
<td>11½ and every 6 months</td>
<td>Onset of puberty, web-based short questionnaire</td>
</tr>
<tr>
<td>Child age 14</td>
<td>FFQ self-administered web-based</td>
</tr>
<tr>
<td>Mother’s Health</td>
<td>Web-based questionnaire to all mothers</td>
</tr>
<tr>
<td>Child age 18 (planned for February 2016)</td>
<td>Web-based questionnaire to all young participants</td>
</tr>
</tbody>
</table>
Data collection waves

Enrolments: 101042
Pre-pregnancy Medication: 87249
Int. 1: 92878
FFQ: 66874
Int. 2: 87794
Int. 3: 70293
Int. 4: 65742
7-year: 57000
52% 47000
63% 40000
52% 13000
55% 40000
Mother’s health: 45%

Ongoing collections
Access to Data

• The DNBC is a national registry, owned by the Ministry of Health.

• DNBC data are available for all researchers (see DNBC@ssi.dk)
  – As long as projects
    • do not harm the DNBC’s reputation
    • are compatible with the overall aim

• Access to biological specimens is restricted

• All applications must be approved by the Management Group and Steering Committee
Governance

Administrative Team (5-6 persons)
- coordinating on-going data collections
- coordination preparations for new data collection waves
- processing research applications for access to data
- handling finances
- cleaning and documentation of data
- preparing datasets for scientists
- withdrawing biological samples from biobank

DNBC Management/founders
- 1st approval of data applications
- Ensure cooperation among research groups
- Securing financing
- Planning new data collections

Steering Committee
- Final approval of applications for data
- Advice and guidance on strategic matters
Interviews 1-4

The four computer-assisted telephone interviews took place in gestational week 12 and 30 as well as when the child was 6 and 18 months old. Each interview lasted approx. 10-15 minutes.

Focus areas in the two pre-natal questionnaires:
- Earlier pregnancies and childbirths, IVF treatment.
- Health in general and during pregnancy as well as medical pregnancy examinations.
- Drug use
- Work environment
- Home environment
- Diet - vitamins - dietary supplements
- Use of alcohol and tobacco
- Sleep
- Exercise
- Estrogen
- Socio-economic variables
- Psycho-social stress

Focus areas in the two post-natal questionnaires:
- Child diet
- Child development
- Child vaccinations
- Follow-up on pre-natal questions

Last revised 22 April 2013
Website

Research results

Participants are primary target group for this communication
Results & Policies

• DNBC widely known as research resource
• Data shared with +50 research groups in Denmark and abroad
• Spin-off: Funding from international sources (European Union, NIH, …) ensure new data collections and research
• 365 peer-reviewed publications (November 2015)
Impact of DNBC

- Contributed to evidence-based information in ante-natal care
- More knowledge about drug safety during pregnancy
- Many aspects of the influence of the diet during pregnancy have been analysed
- Impact of work environment during pregnancy
DNBC publications

Publications/Year

DNBC Applications and Publications 2000 - 2015

Applications for access to DNBC material

Publications based on DNBC data (total 373)
The association of pre-pregnancy alcohol drinking with child neuropsychological functioning.

Predicted vitamin D status during pregnancy in relation to offspring forearm fractures in childhood.

Multi-ancestry genome-wide association study of 21,000 cases and 95,000 controls identifies new risk loci for atopic dermatitis.

Filaggrin genotype and skin diseases independent of atopic dermatitis in childhood.

Occupational exposures and sick leave during pregnancy...
Maternal thyroid disease in the Danish National Birth Cohort: prevalence and risk factors.

Fever and infections in pregnancy and risk of attention deficit/hyperactivity disorder in the offspring.

Preconceptional and prenatal supplementary folic acid and multivitamin intake and autism spectrum disorders.

Perfluoroalkyl acids and time to pregnancy revisited

Maternal use of selective serotonin reuptake inhibitors and risk of miscarriage
Prenatal antidepressant exposure and child behavioural outcomes at 7 years of age.

Developmental Coordination Disorder in Children with a History of Infantile Colic.

Mental disorders in motherhood according to prepregnancy BMI and pregnancy-related weight changes.

Exposure to Road Traffic Noise and Behavioral Problems in 7-Year-Old Children

First trimester coffee and tea intake and risk of gestational diabetes mellitus