National Registries and Biobanks in Denmark

Mads Melbye, MD, DMSc
Statens Serum Institut, Copenhagen, Denmark
When an Entire Country Is a Cohort

Denmark has gathered more data on its citizens than any other country. Now scientists are pushing to make this vast array of statistics even more useful.

For years, any woman who got an abortion had to accept more than the loss of her fetus: For some unknown reason, she also faced an elevated risk for breast cancer. At least that was what several small case-control studies had suggested before Mads Melbye, an epidemiologist at the Statens Serum Institute in Copenhagen, undertook the largest effort ever to explore the link. He and his colleagues obtained records on 400,000 women in Denmark's national Abortion Register, then checked how many of the same women were listed in the Danish Cancer Register. Their foray into the two databases led to a surprising result: As they reported in *The New England Journal of Medicine* in 1997, there appears to be no connection between abortion and breast cancer.

Their success underscores the value of a trove of data the Danish government has accumulated on its citizenry, which today totals about 5 million people. Other Scandinavian countries have created powerful database systems, but Denmark has earned a preeminent reputation for possessing the most comprehensive and interwoven collection of statistics touching on almost every aspect of life. The Danish government has compiled nearly 200 databases, some begun in the 1930s, on everything from medical records to socioeconomic data on jobs and salaries. What makes the databases a plum research tool is the fact that they can all be linked by a 10-digit personal identification number, called the CPR, that follows each Dane from cradle to grave. According to Melbye, "our registers allow for instant, large cohort studies that are impossible in most countries."

Beauty in numbers. These Danish twins stared in a popular TV show at the turn of the 20th century; now it's medical records, part of a database, that are in demand.

But Melbye and other scientists think they can extract even more from this data goldmine. They argue that not enough money is being spent on maintaining and expanding existing databases, and they say that red tape is hampering studies that require correlation of health and demographic data. The problem is that, while they have unfettered access to more than 80 medical databases maintained by the Danish hospitals, their databases over Denmark is tigl mark won't allow its premises dat procedures for acc unwieldy and e: Statistics D to release data concerns. "Th eidence that integ individuals doe sitution," says Last niter Bi to brr datab can b told S entifi W

The Epidemiologist's Dream: Denmark

If the planners of a U.S. study of children's health could work in an ideal world, it might be Denmark. Epidemiologists there finished enrolling a cohort of 100,000 pregnant women into a mother-child research project last September and expect to finish collecting data from the children over the next year. The entire survey—which is large for this country of 70,000 annual births—is to be completed in 2005. It is one of the many projects that fit the dream of the National Institute of Child Health for "an answer specific to the Danish population," as they note. Instead, they use the new cohort to answer questions on nutrition, pregnancy, and other matters among the population.

The next two years will likely be busy for genetic epidemiologists, who face a wealth of genetic, environmental, and historical data from the new cohort. At the same time, they are preparing for a follow-up, the second phase of the Danish Childhood Cohort Study. This study aims to collect data on pregnancy and newborns for a new database.

Science Gold Mine

Health agencies launched a system 40 years ago to identify samples in files that researchers want to access, raising a storm of protest by environmental groups and scientists. The public health system is now trying to resolve the issue, with support from private and public foundations. "Because the Danish population is probably the world's best registered, Denmark is the ideal place for such studies," says epidemiologist Mads Melbye, a steering group member from Statens Serum Institute in Copenhagen. Each cohort can be used to track child registries, and a public health system may be used. "It's an example," he says. "It's a good example of how the U.S. National Institutes of Health can work to protect sensitive data."

Ready subjects. Denmark's 18-month-old twin girls visit their mother in Copenhagen. Each child can be used to track data on the mother's health, and a public health system may be used. "It's an example," he says. "It's a good example of how the U.S. National Institutes of Health can work to protect sensitive data."

Lone Frank is a science writer.
The Danish registries are unique

- an investment worth billions of kroner
- follow the individual from birth to grave
- follow diseases through generations (gene/environment)
- millions of individuals
- results are robust

Birth characteristics
- Diseases
- All microbiological diagnoses
- Prescribed medication
- Vaccinations
- Childcare facility history
- School performance
- Family, place of living
- Education, employment
- Biological specimens

A newborn viking

071215-0001
(CPR-number)
What is it that is so unique?
ALL are included

Avoid the devastating selection bias in research

American case-control studies have a participation rate of 16-20%
Life course epidemiology

Birth

Exposures

Disease

Treatment

Death

Blood specimens
(biomarkers, genetic info, functional aspects)
Research platform on 8.1 million Danes

Delivery
Diseases/pathology
Drug use
Vaccinations
Childcare institutions
Family, address
Education, job

Readmissions
Hospital acquired inf.
Days in hospital
Health care costs
Income
Disability insurance

Lab result*
MR/CT result
X-ray
Blood pressure
Microbiology*
Haematology

DNA
Plasma, serum
Sample tissue
Spinal fluids
Urine
Amniotic fluids
Saliva

CPR number
Consumer Data
Covers 80% of the consumer marked
1. Personalized advice  
2. Track habit changes  
3. Dynamic Warning Features
1. Personalized advice
2. Track habit changes
Danish Cohort of 101,000 pregnant women and offspring

$12 mill.

US cohort:

Everything You Wanted to Know About Children, for $2.7 Billion

Researchers are planning a major study of mothers and children; after 2 years they’ve narrowed the possible objectives of the study down to 70.

Ready subjects. Denmark’s 18-month-long birth cohort survey will collect data from mothers and newborns for a new database.

The Epidemiologist’s Dream: Denmark

If the planners of a U.S. study of children’s health could work in an ideal world, it might be Denmark. Epidemiologists there finished enrolling a cohort of 100,000 pregnant women into a mother-and-child research project last September and expect to finish collecting data from the children over the next year. The entire survey—which is large for this country of 70,000 annual births—is to be completed in 2005 for about $15 million, a tiny fraction of what the cost would be in the United States.

The Danes didn’t design their Better Health for Mother and Child cohort study to answer specific questions or conduct long-term follow-up, as the Americans plan to do (see main text). Instead, they aim to create a database that generations of researchers can mine and use as a starting point for studying how medications, infections, nutrition, and other pregnancy factors influence children’s development and health.

Epidemiologists among the cohort’s 100,000 participants will collect data, including samples for genetic analysis, during routine prenatal visits. Participants can also give blood samples and fill out questionnaires concerning their smoking, alcohol consumption, diet, and other habits.

The public health system is not alone in its pursuit of long-term studies. The U.S. National Institute of Child Health and Human Development, for example, launched a major child development study in 1990. But the Danes won’t have to wait until 2005 to conduct the first survey. The public health system has already begun to trawl for data in the hopes of pulling together information on the country’s 1.5 million children.

One section of the cohort, called the Danish Health and Childhood Project, will follow a single generation from a child’s birth to adulthood. Children up to age 5 will be surveyed every year, and those up to age 18 will be surveyed every 2 years. The project will cost $12 million, compared with $2.7 billion for the U.S. study.

Results from the Danish study are expected to give researchers new insights into the impact of prenatal factors on the child’s health. For example, they may provide information on how obesity in early childhood relates to adult obesity — and how being overweight as a child affects children’s development.

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Lone Frank is a science writer in Copenhagen.

Science, 11 juli 2003
7.9 mill. specimens from 3 mill. Danes

DANISH NATIONAL BIOBANK

Coordinating Centre

22.3 mill. specimens from 5.4 mill. Danes
Danish National Biobank

Store samples
The Danish National Biobank offers fully automated storage at -20°C and -80°C and long-term storage in nitrogen tanks

Read more about storage and calculate the price

Danish Biobank Register
Detailed information about accessible samples in participating Danish biobanks with linkage to register data

Read more about the register and make an online query

Retrieve material
The Danish National Biobank operates under the open access principle to further and strengthen scientific progress

Read more about sample retrieval

The Coordinating Centre
We bridge dry and wet science and offer expertise at every level of project development.
We can also help you with sample

Samples in our freezers:
7,981,657
500,000 new blood specimens/year (cells and plasma)
Total no. of **samples** by sample type
Number of subjects by sample type

- Filter paper: 2,088,702
- Serum: 649,477
- Plasma: 308,528
- Clot: 116,103
- Buffycoat: 225,344
- DNA: 140,001
- RNA: 73,637
- Biopsy: 1,877,378
- Larger specimen: 2,570,322
- Fine needle aspiration: 1,444,621
- Other cytologies: 441,323
- Bone marrow: 299,698
- Autopsy: 119,958
- Brain autopsy: 66,206
- Urine: 6,614
- Spinal fluid: 70,869
- Nasopharyngeal swab: 25,903
- Feces: 1,423
- PBMC: 1,032
- Breast milk: 624
- Amniotic fluid: 31
Three major disease groups
Total no. of samples and no. of blood samples
Gender

Country of birth for patient

Unselect all
- Denmark
- Greenland
- Faroe Islands
- Norway
- Sweden
- Finland
- Iceland
- Other
- Unknown

Country of birth (mother)

Unselect all
- Denmark
- Greenland
- Faroe Islands
- Norway
- Sweden
- Finland
- Iceland
- Other
- Unknown

Country of birth (father)

Unselect all
- Denmark
- Greenland
- Faroe Islands
- Norway
- Sweden
- Finland
- Iceland
- Other
- Unknown

Year of birth

From
1850
To
2014

Age at sample taken (expressed in years)

From
0
To
150

Version: 1.1.17-ed7e4184967fe0fb158703c941141b20dd972d13
Search for diagnosis codes

ICD10

Select codes

ICD10/DC500 (Kraeft i brystvorte el areola mammæ)
ICD10/DC500A (Kraeft i areolæ mammæ)
ICD10/DC500C (Paget's sygdom i mamma)
ICD10/DC501 (Brystkraeft i den centrale del af mammæ)
ICD10/DC502 (Brystkraeft i den øvre mediale kvadrant af mammæ)
ICD10/DC503 (Brystkraeft i den nedre mediale kvadrant af mammæ)
ICD10/DC504 (Brystkraeft i den øvre laterale kvadrant af mammæ)
ICD10/DC505 (Brystkraeft i den nedre laterale kvadrant af mammæ)
ICD10/DC506 (Brystkraeft i processus axillaris mammæ)
ICD10/DC507 (Hypertrophiæ mammae)

Add as primary search criteria
Add as secondary search criteria
Add as omitted search criteria

Delete all
Delete selected
Delete all
Delete selected
Delete all
Delete selected
Select Biobank

- Danish National Biobank
- Copenhagen Hospital Biobank
- Danish Cancer Society Biobank
- Patobanken
- Genetic Biobank of the Faroe
- The Danish Blood Donor Study
- COPSAC
- DD2

Sample types

Blood
- Unselect all
  - Buffycoat
  - Serum
  - Plasma
  - Filter paper
  - Whole blood
  - Clot

Tissue
- Unselect all
  - Biopsy
  - Larger specimen
  - Bone marrow
  - Fine needle aspiration
  - Cervical cytology
  - Other cytologies
  - Autopsy
  - Brain autopsy

Other types
- Unselect all
  - DNA
  - Spinal fluid
  - Amniotic fluid
  - Urine
  - Feces
  - Nasopharyngeal swab
  - Breast milk
  - RNA
  - PBMC

Advanced sample types
- All samples (excluding umbilical cord samples)
- All samples (including umbilical cord samples)
- Only umbilical cord blood samples

Sample taken (expressed in years)
Report definition

Primary variable
Country of birth for patient

Secondary variable
Gender

Counting unit
Number of samples

(Optional) Classify samples into 3 categories:
Sample taken date
- ________ days before the "incident diagnosis" date and earlier
- at the "incident diagnosis" date
- ________ days after the "incident diagnosis" date and later

For more details, use help.

Add report

<table>
<thead>
<tr>
<th>X-value</th>
<th>Y-value</th>
<th>Counting unit</th>
<th>Before interval in days</th>
<th>After interval in days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country of birth for patient</td>
<td>Gender</td>
<td>Number of samples</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Version: 1.1.16-a8db4a5fa1b5af8cb05d3777180f5d08a70ee105c
Legislation – short facts

• Register research: exempted from informed consent
• Biobank materials: Scientific ethics aproval and exempt from informed consent >90% of applications (opt-out register)
  – WGS and exome seq.: informed consent
  – WGA: exempt given in most situations

New model?: e-Boks approach
Denmark - The Leading Country in eHealth Adoption

**In Denmark’s Electronic Health Records Program, a Lesson for the U.S.**

The Frederiksberg University Hospital in Copenhagen looks like any other hospital in the developed world, except for one notable absence: there are no clipboards. Instead, doctors and nurses carry wireless handheld computers to call up the medical records of each patient, including their prescription history and drug allergies. If a doctor prescribes a medication that may cause complications, the computer’s alarm goes off. In the hospital’s department of acute medicine — where patients often arrive unconscious or disoriented — department head Klaus Phanarek’s FDA prevents him from prescribing dangerous medications “on a weekly basis,” he says. “There’s no doubt that it saves lives.”

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**DENMARK IS THE LEADING COUNTRY IN EHEALTH ADOPTION**

Top 10 EU countries by eHealth adoptions of patients and doctors

<table>
<thead>
<tr>
<th>Country</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark</td>
<td>0.87</td>
</tr>
<tr>
<td>Finland</td>
<td>0.84</td>
</tr>
<tr>
<td>Spain</td>
<td>0.72</td>
</tr>
<tr>
<td>Netherlands</td>
<td>0.72</td>
</tr>
<tr>
<td>Sweden</td>
<td>0.68</td>
</tr>
<tr>
<td>Estonia</td>
<td>0.55</td>
</tr>
<tr>
<td>Croatia</td>
<td>0.40</td>
</tr>
<tr>
<td>Portugal</td>
<td>0.39</td>
</tr>
<tr>
<td>Germany</td>
<td>0.37</td>
</tr>
<tr>
<td>France</td>
<td>0.37</td>
</tr>
</tbody>
</table>

*Note: eHealth adoption – doctors transferring prescription electronically, doctors electronically exchanging medical patient data with other healthcare professionals, patients making appointment via website, patients seeking online information about health.*
Who can gain access?

- Scientists in Denmark
- Foreign scientists
- Danish companies
- Foreign companies
The Merck study

Persistent lipid abnormalities in statin-treated patients and predictors of LDL-cholesterol goal achievement in clinical practice in Europe and Canada

- Study in 11 countries
- 2954 clinics
- 22,000 patients
- Costs: ?? mill. kr.

The Danish registries have the same information. Could be done here faster, on a larger population (500,000 statin users) and at lower cost.
Some examples of our studies based on these resources
Acute infection and chronic disease

Do risk factors for schizophrenia operate early in life?

Registry-based cohort study of 1.8 mill. subjects

1. CPR registry
2. Medical Birth Registry
3. Registry of psychiatric disorders

Relative risk of schizophrenia according to month of birth

NEJM 1999
Do women with anal cancer more often than women with other cancers have histories of cervical intraepithelial neoplasia (CIN) or invasive cervical cancer (ICC)?

<table>
<thead>
<tr>
<th>Cancer cases</th>
<th>Cancer controls</th>
<th>Crude odds ratio</th>
<th>Stratified odds ratio (95% CI*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CIN</td>
<td>ICC</td>
</tr>
<tr>
<td>Anus</td>
<td>Colon</td>
<td>7.9</td>
<td>3.7</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
<td>8.7</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Lancet 1991
SEXUALLY TRANSMITTED INFECTION AS A CAUSE OF ANAL CANCER

Other important factors:
- Anal receptive intercourse
- Increasing no. STDs

High-risk HPV in tumor tissue:
- Anal cancer 89%
- Rectal cancer 0%

No. sex partners

NEJM 1997
National Drug Prescription Registry

Pharmacy

1-2 seconds

Central computer (Copenhagen)
What kind of research can be done based on the registry

• Post licensure studies (effectiveness)
• Studies of the long-term use of a particular drug
• New indications for already licensed drugs
• Studies of drug-drug interactions
• Poly-pharmacy: What is the best combination?
A typical official recommendation re. use of a particular drug in pregnancy

"Insufficient safety data for drug X in pregnancy..."
Use of **Macrolides** in mother and child and risk of pyloric stenosis

![Graph showing the association between maternal and infant macrolide use and pyloric stenosis.](image)

**Figure 1. Association Between Maternal and Infant Macrolide Use and Pyloric Stenosis**

The scale of the rate ratio (RR) is a log scale.
Pharmacological studies from our group

Acyclovir, valacyclovir, famciclovir in pregnancy and adv. outcomes (JAMA 2010)
Protom pump inhibitors in pregnancy and risk of adverse outcomes (NEJM 2010)
Angiotensin receptor blockers (ARB) and risk of cancer (Circulation 2011)
Digoxin and risk of breast cancer (J Clin Oncol 2011)
Newer-generation antiepileptic drugs: risk of major birth defects (JAMA 2011)
Antibiotic use and inflammatory bowel diseases in childhood (GUT 2011)
Use of calcium channel blockers and Parkinson's disease (AJE 2012)
Treatment with losartan vs candesartan and mortality among patients with heart failure (JAMA 2012)
Varenicline and Risk of Serious Cardiovascular Events (BMJ 2013)
Use of Azithromycin and Cardiovascular Death (NEJM 2013)
Ondansetron Use in Pregnancy and Risk of Adverse Fetal Outcomes (NEJM 2013)
Fluconazole during Pregnancy and Risk of Major Birth Defects (NEJM 2013)
SSRI Use in Pregnancy and Risk of Autism in Childhood (NEJM 2013)
Metoclopramide in Pregnancy and Cong Malformations/Fetal Death (JAMA 2013)
Association btw Fluorolquinolone Use and Retinal Detachment (JAMA 2013)
Use of macrolides in mother and child and risk of pyloric stenosis (BMJ 2014)
Treatment w/Carvedilol vs. Metropolol Succ. and Mortality (JAMA Int Med 2014)
Use of clarithromycin nd roxithromycin and risk of cardiac death (BMJ 2014)
TNF-alpha antagonists and risk of cancer in infl. bowel disease pt.s (JAMA 2014)
Tumour necrosis factor-α inhibitors, serious infections and IPD (BMJ 2015)
Maternal use of oral contraceptives and risk of birth defects (BMJ 2016)
Oral fluconazole during pregnancy and risk of miscarriage and stillbirth (JAMA 2016)
Pre-pregnancy diabetes and offspring risk of congenital heart disease (Circulation 2016)
Hypertensive Disorders of Pregnancy and Later Risk of Cardiomyopathy (JAMA 2016)
Oral fluoroquinolone use and serious arrhythmia (BMJ 2016)
Personalized medicine
Pharmacogenomics

Patients → Drug → Biobank specimen

Genetic analysis

Example: Statins

Therapeutic response?
No
Yes
Childhood vaccination database

Family doctor → Bill with details

National Health Insurance, National Board of Health

All registrations + Information from other registries

National Vaccination Register 1990-2016

Type, dose, date, cpr-number
Examples on registry based vaccine studies

- MMR vaccination and risk of autism
- Quadrivalent HPV vaccine and adverse outcomes
Febrile seizures after MMR vaccination

**Figure 1.** Adjusted Rate Ratios of Febrile Seizures According to Time Since MMR Vaccination vs Nonvaccinated Children in a Cohort of Children Born in Denmark, 1991-1998

JAMA 2004
Febrile seizures +/- MMR GWAS study

Discovery scans:

I. MMR-related FS vs. Controls 929/4118
II. MMR-related FS vs. MMR-unrelated FS 929/1070
III. MMR-unrelated FS vs. Controls 1070/4118
IV. FS overall vs. Controls 1999/4118

Replication genotyping

6 loci GW significant

- 2 loci specific for MMR-related FS
- 4 loci for FS in general
Variants in *IFI44L* and *CD46* (innate immune system genes) associate with FS as an adverse event of MMR vaccinatio

General FS variants point to altered ion channel function

**SCN1A** and **SCN2A**: well-known epilepsy genes. Novel associations with FS.

**TMEM16C**: OR > 2, MAF~ 3%, affecting neuronal excitability. Novel target for seizure research

**12q21.33**: Mg$^{2+}$ deficiency and FS susceptibility?
Feverish prospect

Sanjay Sisodiya

Febrile seizures can arise in response to factors such as measles, mumps and rubella (MMR) and other pathogens influencing susceptibility to febrile seizures.

It is a frightening experience that a sizeable minority of readers may have had: finding that your child is having a febrile seizure. Anxious parents want to know why it occurs and what it portends. Unlike epilepsy, febrile seizures have been much studied, though answers to these questions have proved elusive. Now, a landmark study, researchers from Denmark report important progress in understanding the genetics of febrile seizures.

Depending on the population, 2–8% of children have febrile seizures. In children who have a history of febrile seizures, nearly 2% will have epilepsy, compared with 0.2% of children without a history of febrile seizures.

A public mission

Enter the Statens Serum Institut in Denmark, a public enterprise under the Danish Ministry of Health. Founded in 1902, the Institut is responsible for research-based health surveillance, rational use of IT in the Danish healthcare system and prevention and control of infectious diseases, biological threats and congenital disorders (http://www.ssi.dk/English.aspx). The study by Feenstra et al. embodies this mission, demonstrating the value of public health initiatives and national registries in addressing very specific questions of importance to individuals and society.

unrelated cases, comparing imputed genotypes with those from 4,118 controls from the same population.
Pyloric stenosis

1. Background
   • Disease in newborns
   • Muscle enlargement:
     • Food cannot pass.
     • Most surgeries in newborns

2. National registries - linkage study

3. Biobank study
   A. Biobank registry
      Identify blood sample on 1,001 pyloric stenosis cases and 2,401 controls
   B. Biobank
      In 2 months: identify samples and extract DNA
   C. Genetic analyses
      Identified 4 important gene variants involved in disease development
   D. Published
      Nature Genetics 2012
      JAMA 2013

National registries info on:
   • Family-linkage info. on all Danes (up to 4 generations)
   • All surgery-confirmed cases in Denmark

JAMA 2010
Low cholesterol levels increase risk of pyloric stenosis

- Chr. 11 association: previously found to decrease levels of total and HDL cholesterol

- Bottle-fed children: Lower cholesterol levels and 5 times increased risk of PS

- We used umbilical cord blood samples from the biobank to measure cholesterol levels (+/-PS)

JAMA 2013
Nature and Nature genetics papers

Cleft lip and palate (NG 2008, NG 2010)
Age at menarche (NG 2009, NG 2010, Nature 2014)
Hodgkin lymphoma (NG 2010)
Follicular lymphoma (NG 2010)
Heritability of complex traits (NG 2011)
Atopic dermatitis (NG 2011, NG 2015)
Pyloric stenosis (NG 2012)
Infant head circumference (NG 2012)
Clonal mosaicism and cancer (NG 2012)
Chronic lymphocytic leukemia (NG 2013, Nat Communication)
Birth weight (NG 2013)
Diffuse large B cell lymphoma (NG 2014)
Hypospadias (NG 2014)
Height (NG 2014)
Febrile seizures and MMR vaccination (NG 2014)
BMI (Nature 2015)
Directional dominance on stature and cognition (Nature 2015)
Body mass index yield new insights for obesity biology (Nature 2015)
Link of adipose and insulin biology to body fat distribution (Nature 2015)
A very large genotyping project
The one million GENLIFE cohort

- Health and population registers
- Laboratory databases
- Genome-wide SNP array data
- Multiple layers of omics data
Mining the Phenome

GWAS:
Target phenotype \rightarrow\text{association P value}\rightarrow\text{chromosomal location}

The phenome-wide association study: with what phenotype(s) is a genetic variant associated?

PheWAS:
Target genotype \rightarrow\text{association P value}\rightarrow\text{diagnosis code}

Requirement for unbiased PheWAS: A large cohort of patients with genotype data and many diagnoses
Loss-of-function mutations

• Surprisingly common; we all have ~150 LoF (partial or complete) mutations across our genome

• Likely to have direct functional impact. But on what phenotype?

• Example: PCSK9 loss-of-function → 40% reduction in plasma levels of LDL cholesterol

• **Translational medicine**: develop drugs that can mimic the effects of an advantageous LoF mutation by **inhibiting a specific pathway**
The one million PheWAS

Phenome

Diagnosis codes
Birth characteristics
Pathology
Surgeries
Medication
Vaccinations

Dental health
Microbiology
Haematology
Blood pressure
… etc.

1,000,000 Danes: GWAS/WGS + imputation

PheWAS scan

PheWAS target, (e.g. loss-of-function mutation)

Functional follow-up → translational medicine
GENLIFE in short

DNA extraction equipment is set up at the central laboratories in the Danish regions and local staff hired to perform the analyses.

All "left over" bloods from the laboratory will be used for DNA extraction. A program will ensure that DNA is only collected once on each person.

DNA and plasma is then transferred to the Danish National Biobank.

A pipeline for array-based genotyping (GWA) is established here that will have a capacity of 400,000 samples/year in 2½ years.

An E-boks letter will be sent to all persons that the DNB receives DNA on. Here information will be given about the project and about the possibility to opt-out.
GENLIFE in short

The genotyping data will continuously be transferred to Computerome.

A bioinformatics section will be established to perform data cleaning, QC, imputation, etc.

- Birth characteristics
- Diseases
- All microbiological diagnoses
- Laboratory analyses results
- Prescribed medication
- Vaccinations
- Childcare facility history
- School performance
- Family, place of living
- Education, employment

A datamanagement section will be handle linkages to other resources, legal issues, etc.
A Modest (Real Estate) Proposal

So Mr. Big Thinker has a way out: the US should dump the National Children’s Study and, instead, buy Denmark. I’m talking the whole country. The advantages should be obvious. The Danes already have a successful 100,000-baby cohort, plus (pay attention here, US) a system of health and death registries that allows complete lifetime follow-up of the cohort at virtually no added expense. Denmark provides everything an epidemiologist could ask for – and the US could stop banging its head against the wall.

Where does the US find the cash... sell Florida.