Hepatitis surveillance system and a pop-based registry study of infant mortality in the Arctic

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Anders Koch, Senior Researcher, PhD, MPH
Department of Epidemiology Research
Statens Serum Institut
Copenhagen, Denmark
Notification of viral hepatitis in Greenland

- HAV, HBV, HCV reportable by law to the office of the Chief Medical Officer of Greenland (‘Landslægeembedet’)

- Notification of clinical hepatitis from 1952 to present

- Notification of clinical hepatitis by serologic test results from 1989
Testing and reporting of viral hepatitis

- **HBV testing**
  - Pregnant women
  - Children of chronic infected mothers
  - Blood donors
  - Clinical reasons

- **HAV & HCV testing**
  - Clinical reasons

- Laboratory in Nuuk only serologic laboratory in Greenland

- Reporting by local doctors to the Chief Medical Officer after testing
Low completeness of notification system

- Yearly reports from the Chief Medical Officer, but stopped 2003 because of massive underreporting
  - 2007-: Yearly laboratory data from Queen Ingrids Hospital reported to the Chief Medical Officer
    - No clinical data
    - Only HBsAg-positive results – acute or chronic infection?
    - Multiple tests from same person possible

- Data management needed for reliable notification
Register possibilities in Greenland?

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 complete and interwoven collection of statistics touching on almost every aspect of life. The Danish government has compiled nearly 200 databases, some began 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."

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 studies of how medications, infections, nutrition, and even psychological factors affect pregnancy and child health.

Physicians have recruited volunteers among women making their first pregnancy visit. Participants give two blood samples during pregnancy and cord blood when the baby is born. The samples are saved for later use, including possibly for genetic studies. The mothers also answer a detailed questionnaire concerning nutrition; in an 18-month follow-up, they give information on their health and environmental exposures. The public health system is funding the study, 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 citizen has a personal identification number that can be used to track data in centralized health care records, disease registries, and a population registry. Even centralized school records may be used. "It's an epidemiologist's dream," says Mark Klebanoff of the U.S. National Institute of Child Health and Human Development, who says tracking subjects is one of the costliest aspects of long-term U.S. studies.

Norway, which has a system like Denmark's, is launching a mother-child study that will pool data with the Danish group's. Both benefit from streamlined management. It's difficult to get things done with too many decision-makers, says Melbye. "Running such a large study has taught us many things, but the chief lesson is that it is essential to put a very small group of people in charge."

Results are already beginning to trickle out of the Danish study. For example, one group published an article in The Lancet last November that disproved the existing consensus view that a fever early in pregnancy increases the risk for miscarriage. That's just the beginning: Denmark's scientific ethics committee has so far given the green light to more than 70 research protocols based on the mother-child study.

Lone Frank
Lone Frank is a science writer in Copenhagen.
The key to registers in Denmark and Greenland (Danish Kingdom)

- Central person registry number (CPR)

- Unique number assigned at birth, follows the person from cradle to grave

- Uniquely identifies the person in nation-wide registers

- All persons alive by 1967 (Denmark) or 1972 (Greenland)
Important health registers DK and Greenland

- Birth Registry
- Birth Defect Registry
- Cancer Registry
- Childhood vaccinations
- CPR Registry
- Cause of Death Registry
- Microbiological tests results
- National Inpatient Registry
- Pathology Registry
- Reportable infectious diseases
Example of use of registries: Infant mortality study Greenland 1973-1997

• Previous studies estimation of ‘raw’ mortality rates only

• Aim: estimate infant mortality rates in Greenland 1973-1997 and assess significance of maternal origin and birth weight

• Person identifiable information
  – CPR register
  – Birth Registry in Denmark
  – Birth Registry in Greenland

• Infant mortality rates
  – Alaska and Canada

Friborg, Koch, Stenz, Wohlfahrt & Melbye
Infant mortality rates
Arctic areas and Denmark

- Infant mortality rates by year and country
- Infant mortality rates by birth weight


**TABLE 2**—Birthweight Distributions (%) and Mean Birthweights With Standard Deviations: Greenland (1990–1997) and Denmark (1990–1996)

<table>
<thead>
<tr>
<th>Birthweight, g</th>
<th>Greenland(^a) (n=8174), %</th>
<th>Denmark(^a) (n=414,079), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1499</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>1500–2499</td>
<td>3.4</td>
<td>3.2</td>
</tr>
<tr>
<td>2500–2999</td>
<td>12.6</td>
<td>11.7</td>
</tr>
<tr>
<td>3000–3499</td>
<td>32.4</td>
<td>31.8</td>
</tr>
<tr>
<td>3500–3999</td>
<td>32.2</td>
<td>33.4</td>
</tr>
<tr>
<td>4000–4499</td>
<td>14.0</td>
<td>14.6</td>
</tr>
<tr>
<td>≥4500</td>
<td>3.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Birthweight, mean (SD)</td>
<td>3444g (602 g)</td>
<td>3468g (586 g)</td>
</tr>
</tbody>
</table>

\(^a\)Mothers born in Greenland.
\(^b\)Mothers born in Denmark.
Neonatal and postneonatal mortality rates
Greenland and Denmark

- Infant mortality rates by covariates
  - Year of birth
  - Maternal age
  - Gender
  - Birth order
  - Urbanisation

<table>
<thead>
<tr>
<th></th>
<th>Neonatal Mortality Rates</th>
<th>Postneonatal Mortality Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Greenland&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Denmark</td>
</tr>
<tr>
<td></td>
<td>NMR  RR&lt;sup&gt;b&lt;/sup&gt; 95% CI</td>
<td>NMR  RR&lt;sup&gt;b&lt;/sup&gt; 95% CI</td>
</tr>
<tr>
<td>Year of birth</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1973-1977</td>
<td>20.9 1 Ref</td>
<td>7.6 1 Ref</td>
</tr>
<tr>
<td>1978-1982</td>
<td>19.9 1.0 0.7,1.3</td>
<td>5.5 0.7 0.7,0.8</td>
</tr>
<tr>
<td>1983-1987</td>
<td>17.2 0.9 0.6,1.2</td>
<td>5.0 0.7 0.6,0.7</td>
</tr>
<tr>
<td>1988-1992</td>
<td>16.8 0.9 0.6,1.2</td>
<td>4.6 0.6 0.6,0.7</td>
</tr>
<tr>
<td>1993-1997</td>
<td>15.7 0.8 0.6,1.1</td>
<td>4.0 0.5 0.5,0.6</td>
</tr>
<tr>
<td>Maternal age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-19</td>
<td>20.6 1.5 1.1,2.1</td>
<td>8.1 1.4 1.3,1.6</td>
</tr>
<tr>
<td>20-24</td>
<td>18.7 1.2 0.9,1.5</td>
<td>5.8 1.1 1.0,1.2</td>
</tr>
<tr>
<td>25-29</td>
<td>18.6 1 Ref</td>
<td>4.8 1 Ref</td>
</tr>
<tr>
<td>30-34</td>
<td>13.7 0.7 0.5,0.9</td>
<td>5.0 1.1 1.0,1.2</td>
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<tr>
<td>≥ 35</td>
<td>13.5 0.6 0.4,0.9</td>
<td>5.9 1.3 1.2,1.4</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<tr>
<td>Male</td>
<td>19.1 1.0 Ref</td>
<td>6.1 1 Ref</td>
</tr>
<tr>
<td>Female</td>
<td>16.5 0.9 0.7,1.1</td>
<td>4.6 0.8 0.7,0.8</td>
</tr>
<tr>
<td>Birth order</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>16.4 1 Ref</td>
<td>5.7 1 Ref</td>
</tr>
<tr>
<td>2</td>
<td>17.4 1.3 1.0,1.6</td>
<td>4.7 0.8 0.8,0.9</td>
</tr>
<tr>
<td>3</td>
<td>17.8 1.4 1.0,2.0</td>
<td>5.2 0.9 0.9,1.0</td>
</tr>
<tr>
<td>≥ 4</td>
<td>21.8 2.0 1.4,2.9</td>
<td>7.1 1.2 1.1,1.3</td>
</tr>
</tbody>
</table>

Note. NMR = neonatal mortality rate; PMR = postneonatal mortality rate; RR = relative risk; CI = confidence interval; Ref = reference group.

<sup>a</sup>Mother born in Greenland.
<sup>b</sup>Relative risk adjusted for year of birth, maternal age, gender, birth order, and urbanization.
<sup>c</sup>Relative risk adjusted for year of birth, maternal age, gender, and birth order.
Conclusions: Infant mortality study

• Use of nationwide and person identifiable registers has shown that:
  – Postneonatal (1 -12 mo) mortality rates in Greenland have decreased significantly over the past 25 years, while little progress has occurred in lowering neonatal (<1 mo) mortality rates
  – Significant differences exist between DK and Greenland
  – Greenland has the highest infant mortality rate among Arctic countries
Perspectives for hepatitis surveillance in Greenland

• At present hepatitis cases underreported, *but*

• Opportunities for improved surveillance exist
  – Centralised HBV testing in Nuuk
  – CPR numbers allows for identification of tests
  – Morbidity information in Hospital Register

• Greenland – the hepatitis epidemiologists dream?

• Thank you for your attention