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

Viral Hepatitis Prevention Board Meeting, Copenhagen 2012

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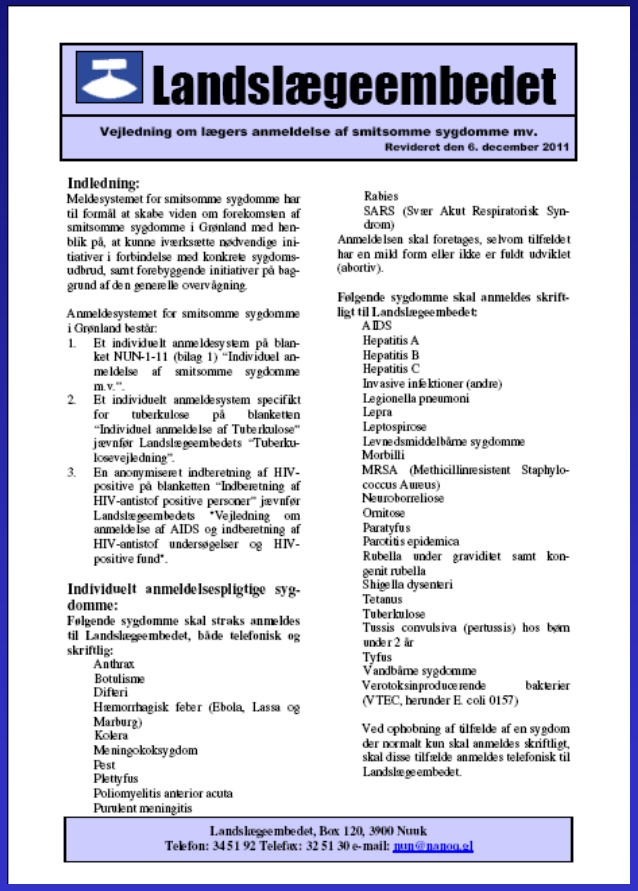
Notification of viral hepatitis in Greenland

- 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



Landslægeembedet

Vejledning om lægers anmeldelse af smitsomme sygdomme mv.
Revideret den 6. december 2011

Indledning:
Meldesystemet for smitsomme sygdomme har til formål at skabe viden om forekomsten af smitsomme sygdomme i Grønland med henblik på, at kunne iværksætte nødvendige initiativer i forbindelse med konkrete sygdomsudbrud, samt forebyggende initiativer på baggrund af den generelle overvågning.

Anmeldesystemet for smitsomme sygdomme i Grønland består:

1. Et individuelt anmeldesystem på blanket NUN-1-11 (bilag 1) "Individuel anmeldelse af smitsomme sygdomme m.v.".
2. Et individuelt anmeldesystem specifikt for tuberkulose på blanketten "Individuel anmeldelse af Tuberkulose" jævnfør Landslægeembedets "Tuberkulosevejledning".
3. En anonymiseret indberetning af HIV-positive på blanketten "Indberetning af HIV-antistof positive personer" jævnfør Landslægeembedets "Vejledning om anmeldelse af AIDS og indberetning af HIV-antistof undersøgelser og HIV-positive fund".

Individuelt anmeldelsespligtige sygdomme:
Følgende sygdomme skal straks anmeldes til Landslægeembedet, både telefonisk og skriftlig:

Anthrax
Botulisme
Difteri
Hæmorrhagisk feber (Ebola, Lassa og Marburg)
Kolera
Meningokoksygdom
Pest
Plettyfus
Poliomyelitis anterior acuta
Purulent meningitis
Rabies
SARS (Svær Akut Respiratorisk Syndrom)

Anmeldelsen skal foretages, selvom tilfældet har en mild form eller ikke er fuldt udviklet (abortiv).

Følgende sygdomme skal anmeldes skriftligt til Landslægeembedet:

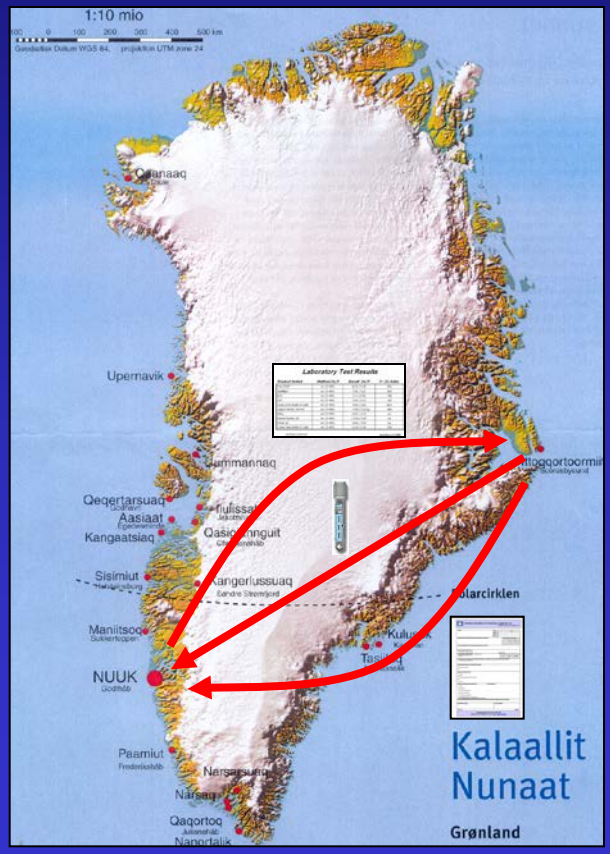
AIDS
Hepatitis A
Hepatitis B
Hepatitis C
Invasive infektioner (andre)
Legionella pneumoni
Lepra
Leptospirose
Levnedsmiddelbåre sygdomme
Morbilli
MRSA (Methicillinresistent Staphylococcus Aureus)
Neuroborreliose
Ornitose
Paratyfus
Parotitis epidemica
Rubella under gravidtet samt kongenit rubella
Shigella dysenteri
Tetanus
Tuberkulose
Tussis convulsiva (pertussis) hos børn under 2 år
Tyfus
Vandbåre sygdomme
Verotoksinproducerende bakterier (VTEC, herunder E. coli 0157)

Ved opdobning af tilfælde af en sygdom der normalt kun skal anmeldes skriftligt, skal disse tilfælde anmeldes telefonisk til Landslægeembedet.

Landslægeembedet, Box 120, 3900 Nuuk
Telefon: 3451 92 Telefax: 32 51 30 e-mail: nun@nanoq.gl

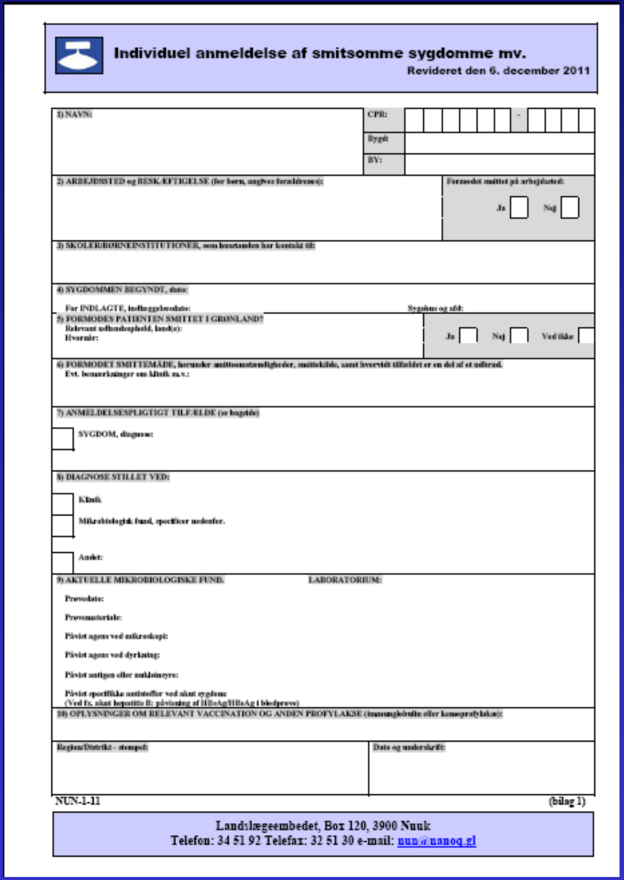
Testing and reporting of viral hepatitis

- 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



Individuel anmeldelse af smitsomme sygdomme mv.
Revideret den 6. december 2011

1) NAVN: | CPR: | Bygd: | BY:

2) ARBEJDSSTED og BESKÆFTIGELSE (for børn, angives forældrenes): | Formodet smittet på arbejdsstedet: Ja ☐ Nej ☐

3) SKOLER/BØRNEINSTITUTIONER, som husstanden har kontakt til:

4) SYGDOMMEN BEGYNDT, dato:
For INDLAGTE, indlæggelsesdato: | Sygehus og afd:

5) FORMODES PATIENTEN SMITTET I GRØNLAND? Ja ☐ Nej ☐ Ved ikke ☐
Relevant udlandsophold, land(e):
Hvornår:

6) FORMODET SMITTEMÅDE, herunder smitteomstændigheder, smittekilde, samt hvorvidt tilfældet er en del af et udbrud.
Evt. bemærkninger om klinik m.v.:

7) ANMELDELSESPLIGTIGT TILFÆLDE (se bagside)
☐ SYGDOM, diagnose:

8) DIAGNOSE STILLET VED:
☐ Klinik
☐ Mikrobiologisk fund, specificer nedenfor.
☐ Andet:

9) AKTUELLE MIKROBIOLOGISKE FUND. | LABORATORIUM:
Prøvedato:
Prøvemateriale:
Påvist agens ved mikroskopi:
Påvist agens ved dyrkning:
Påvist antigen eller nukleinsyre:
Påvist specifikke antistoffer ved akut sygdom:
(Ved fx. akut hepatitis B: påvisning af HBeAg/HBsAg i blodprøve)

10) OPLYSNINGER OM RELEVANT VACCINATION OG ANDEN PROFYLAKSE (immunglobulin eller kemoprofylakse):

Region/Distrikt - stempel: | Dato og underskrift:

NUN-1-11 (bilag 1)

Landslægeembedet, Box 120, 3900 Nuuk
Telefon: 34 51 92 Telefax: 32 51 30 e-mail: nun@nanoq.gl

Register possibilities in Greenland?

EPIDEMIOLOGY

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 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 starred in a variety show at the turn of the 20th century; now it's their medical records, part of a database, that are in demand.

But Melbye and other scientists think they can extract even more from this data gold mine. 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, thei databases overs Denmark is tig mark won't allo its premises dat cedures for acc unwieldy and ex Statistics De to release data concerns. "Th dence that info individuals doe stitution," says Last n ter Bi to bre datab can b told S entifi W can y the U has s twins tive lifest of Sc Kaar tappe whic twins ing more than older, Christe genes about a man longevity by the unmat the Danish Tw The health able for prot smaller studi

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 databank 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.

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

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.

- Science, 2000 & 2003

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

RESEARCH AND PRACTICE

A Population-Based Registry Study of Infant Mortality in the Arctic: Greenland and Denmark, 1973–1997

Jeppe Friborg, MD, Anders Koch, MD, PhD, Flemming Stenz, MD, Jan Wohlfahrt, MSc, and Mads Melbye, MD, DMSc

Infant mortality rates are an important measure of a population's health status. Although infant mortality rates in the Arctic have decreased significantly in recent decades, mortality rates remain high as compared with those among populations in the neighboring regions.[1] This is particularly true in Greenland.[2]

The population in Greenland (56 124 in 2000) is primarily composed of indigenous people of Inuit origin (85%–90%) and represents the largest Arctic Inuit population in the world. Greenland has been a colony of Denmark since 1721, but it acquired home rule within the Danish Kingdom in 1979.

Objectives. We sought to determine precise estimates of infant mortality rates and to describe overall trends in infant mortality in Greenland and Denmark from 1973 to 1997.

Methods. We analyzed data from population-based registries of all live-born infants in Greenland and Denmark to calculate infant mortality rates from 1973 to 1997.

Results. Between the periods of 1973–1977 and 1993–1997, neonatal mortality rates in Greenland declined from 20.9 per 1000 live-born infants to 15.7, and postneonatal mortality rates declined from 20.9 per 1000 to 5.9. Infant mortality rates were significantly higher in Greenland than in Denmark, and the excess mortality was uniformly distributed over all birthweight percentiles. In Greenland, the risk of infant death was significantly lower if the mother was born outside Greenland.

Conclusions. Postneonatal mortality rates in Greenland have decreased significantly during the past 25 years, but little progress has been made in decreasing neonatal mortality rates. Disparities exist among children with different maternal origins. (*Am J Public Health.* 2004;94:452–457)

Friborg, Koch, Stenz, Wohlfahrt & Melbye Am. J. Public Health 2004: 94: 452-57

Infant mortality rates
Arctic areas and Denmark

- Infant mortality rates by year and country

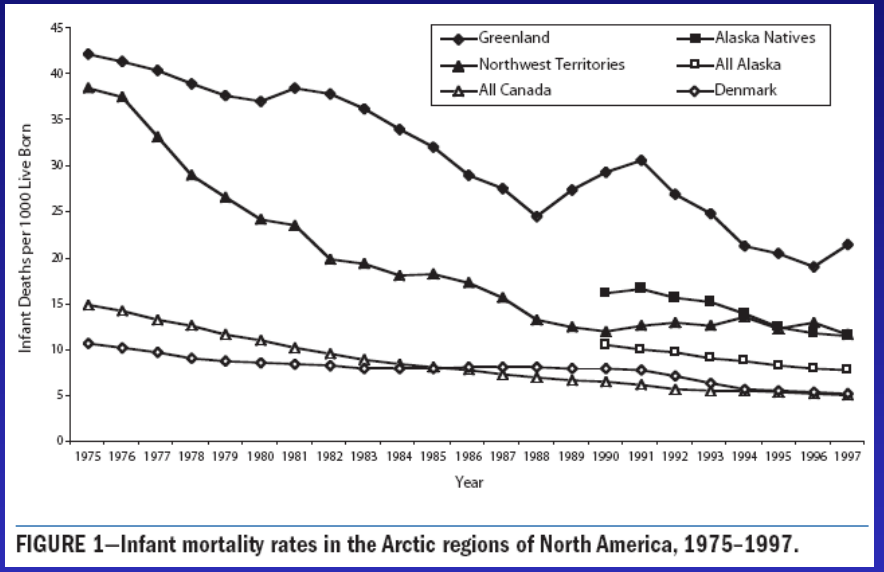


FIGURE 1—Infant mortality rates in the Arctic regions of North America, 1975–1997.

- Infant mortality rates by birth weight

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

Birthweight, g	Greenland[a] (n = 8174), %	Denmark[b] (n = 414 079), %
≤ 1499	1.9	1.9
1500–2499	3.4	3.2
2500–2999	12.6	11.7
3000–3499	32.4	31.8
3500–3999	32.2	33.4
4000–4499	14.0	14.6
≥ 4500	3.5	3.3
Birthweight, mean (SD)	3444g (602 g)	3468 g (596 g)

[a]Mothers born in Greenland.
[b]Mothers born in Denmark.

Neonatal and postneonatal mortality rates Greenland and Denmark

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

TABLE 3—Neonatal and Postneonatal Mortality Rates (Deaths per 1000 Live-Born Infants): Greenland and Denmark, 1973–1997

	Neonatal Mortality Rates						Postneonatal Mortality Rates					
	Greenland[a]			Denmark			Greenland[a]			Denmark		
	NMR	RR[b]	95% CI	NMR	RR[c]	95% CI	PMR	RR[b]	95% CI	PMR	RR[c]	95% CI
Year of birth												
1973–1977	20.9	1	Ref	7.6	1	Ref	20.9	1	Ref	2.7	1	Ref
1978–1982	19.9	1.0	0.7, 1.3	5.5	0.7	0.7, 0.8	17.8	0.9	0.6, 1.2	3.0	1.2	1.1, 1.3
1983–1987	17.2	0.9	0.6, 1.2	5.0	0.7	0.6, 0.7	12.1	0.6	0.4, 0.9	3.2	1.3	1.2, 1.4
1988–1992	16.8	0.9	0.6, 1.2	4.6	0.6	0.6, 0.7	10.3	0.5	0.4, 0.8	2.9	1.2	1.1, 1.3
1993–1997	15.7	0.8	0.6, 1.1	4.0	0.5	0.5, 0.6	5.9	0.3	0.2, 0.5	1.5	0.6	0.6, 0.7
Maternal age, y												
12–19	20.6	1.5	1.1, 2.1	8.1	1.4	1.3, 1.6	14.3	1.9	1.2, 2.9	5.3	3.0	2.7, 3.4
20–24	18.7	1.2	0.9, 1.5	5.8	1.1	1.0, 1.2	12.9	1.4	1.0, 1.9	3.2	1.6	1.5, 1.7
25–29	18.6	1	Ref	4.8	1	Ref	11.9	1	Ref	2.2	1	Ref
30–34	13.7	0.7	0.5, 0.9	5.0	1.1	1.0, 1.2	12.0	0.9	0.6, 1.3	2.2	0.8	0.8, 0.9
≥ 35	13.5	0.6	0.4, 0.9	5.9	1.3	1.2, 1.4	12.3	0.7	0.4, 1.2	2.3	0.8	0.7, 0.9
Gender												
Male	19.1	1.0	Ref	6.1	1	Ref	14.5	1	Ref	2.9	1	Ref
Female	16.5	0.9	0.7, 1.1	4.6	0.8	0.7, 0.8	10.9	0.8	0.6, 1.0	2.2	0.8	0.7, 0.8
Birth order												
1	16.4	1	Ref	5.7	1	Ref	9.9	1	Ref	2.3	1	Ref
2	17.4	1.3	1.0, 1.6	4.7	0.8	0.8, 0.9	11.6	1.5	1.1, 2.2	2.7	1.5	1.4, 1.7
3	17.8	1.4	1.0, 2.0	5.2	0.9	0.9, 1.0	14.5	2.2	1.5, 3.3	2.9	2.0	1.8, 2.2
≥ 4	21.8	2.0	1.4, 2.9	7.1	1.2	1.1, 1.3	18.7	3.0	2.0, 4.6	3.9	2.8	2.5, 3.3

Note. NMR = neonatal mortality rate; PMR = postneonatal mortality rate; RR = relative risk; CI = confidence interval; Ref = reference group.
[a]Mothers born in Greenland.
[b]Relative risk adjusted for year of birth, maternal age, gender, birth order, and urbanization.
[c]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