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Population-based epidemiological survey of hepatitis B,  
D and C among Inuit migrated to Denmark and in high  
endemic Greenland



Rex KF, Krarup HB, Laurberg P, Andersen S. Population-based comparative epidemiological survey of hepatitis B, D, and C among Inuit migrated to Denmark and in high endemic Greenland. Scand J Gastroenterol 2012 Jan 10. [Epub ahead of print]

Krarup HB, Andersen S, Madsen PH, Okkels H, Hvingel BH, Laurberg P. Benign course of long-standing hepatitis B virus infection among Greenland Inuit? Scand J Gastroenterol 2008;43(3):334-43



I will talk

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most about HBV  
less about HDV and  
least about HCV



# Hepatitis B in Greenland

1973: 2900 cases screened, 7.1 % HBsAg positive

P. Skinhøj Am J Epidemiol 1974

1985: 1893 cases screened in Sisimiut, 11.5 % HBsAg positive

O Rosing Olsen UFL 1989

1997: 503 cases screened, 7.0 % HBsAg positive

B C Langer J Viral Hepat 1997

2007: 8879 cases screened, 7.4 % HBsAg positive

M. Børresen Phd afhandling 2010



# Background

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Greenland is an endemic area of hepatitis B infection (HBsAg > 7%)

Most transmission of hepatitis B virus (HBV) in Greenland takes place before the age of 20 years

Liver cirrhosis and liver cancer (HCC) are less frequent than expected

Until September 2010 HBV vaccination was not part of the national infant immunization programme in Greenland

# Hepatitis B virus infection among Inuit in Greenland

## Study 1:

Participants living in Greenland:

229 men and 205 women with both parents born in Greenland

Age 50 – 69 years

Participation rate 95 %

## Study 2:

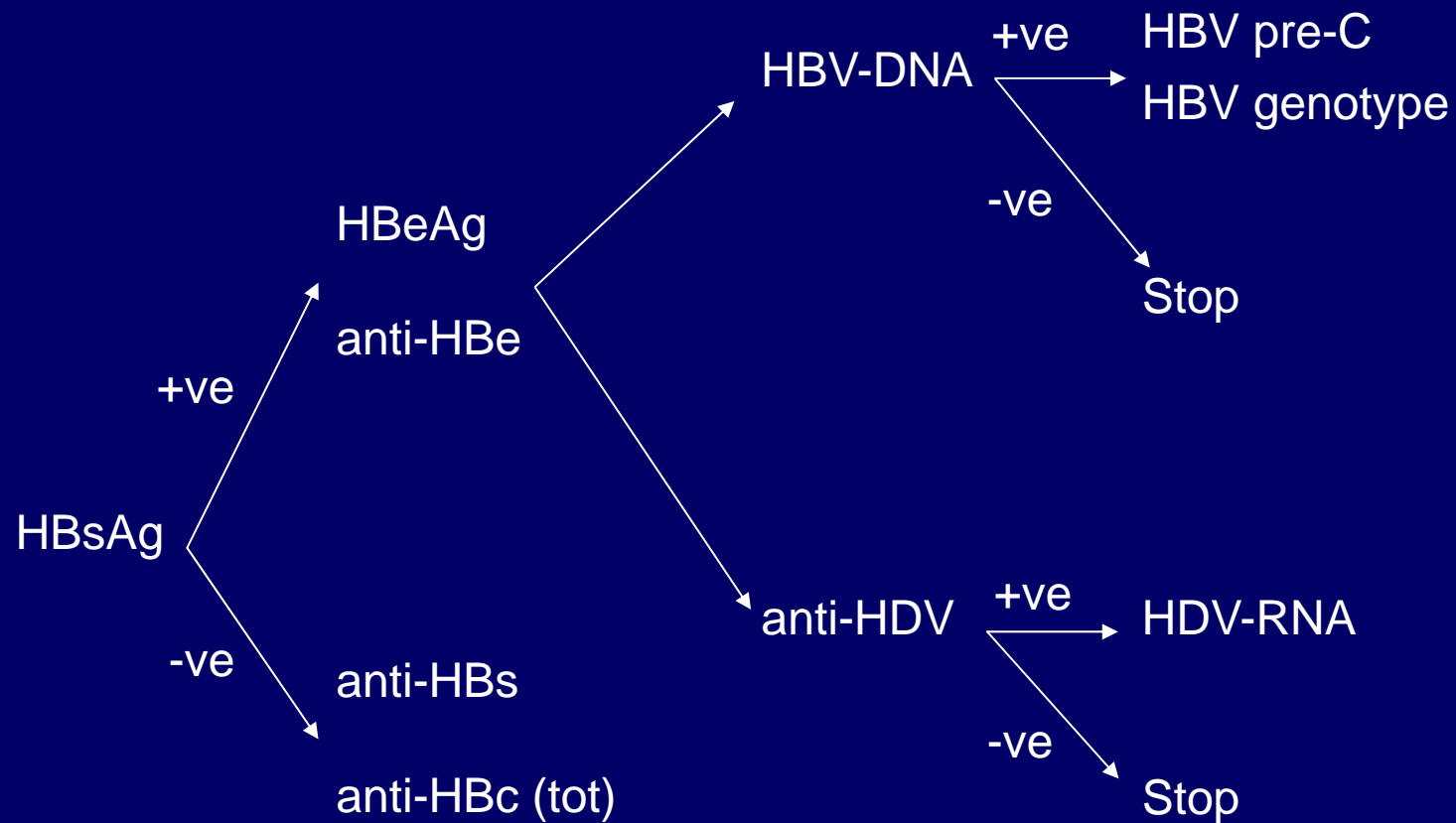
Participants living in Denmark:

33 men and 103 women of which 81% had both parents born in Greenland and 46 % had lived more than half of their life in DK

Age 40 – 69 years

Participation rate 52 %

# Flowchart



# Results Study 1

Median age was 58 years with no gender difference

None had physical signs of liver disease

HBsAg was positive in 20.4%

Fewer were HBsAg positive in Nuuk compared to Tasiilaq and settlements in Eastgreenland (4% vs. 28.9%)

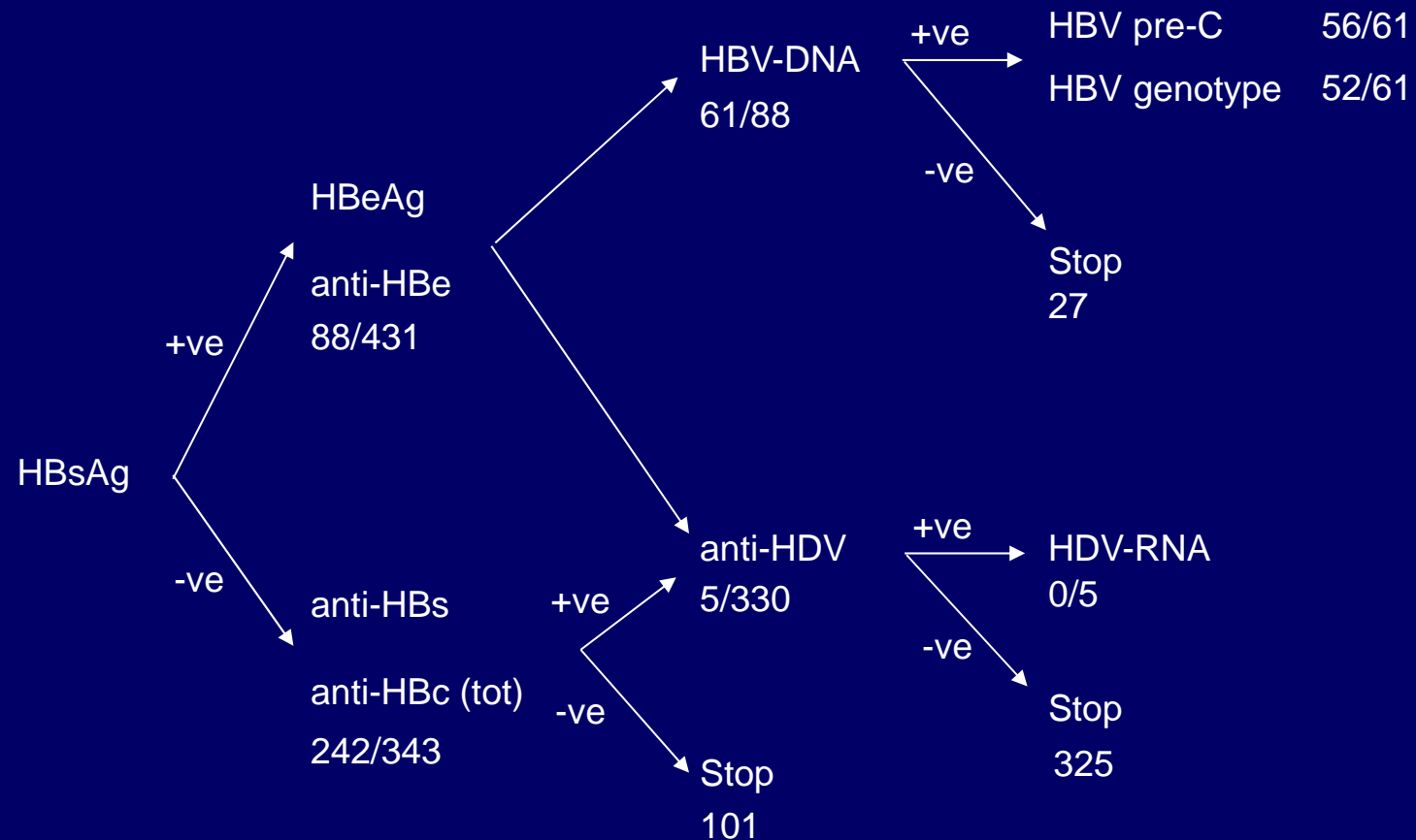
No difference between Eastgreenland town and settlements (28.6% vs. 29.4%)

More men than women were positive (26.4% vs. 13.7%)

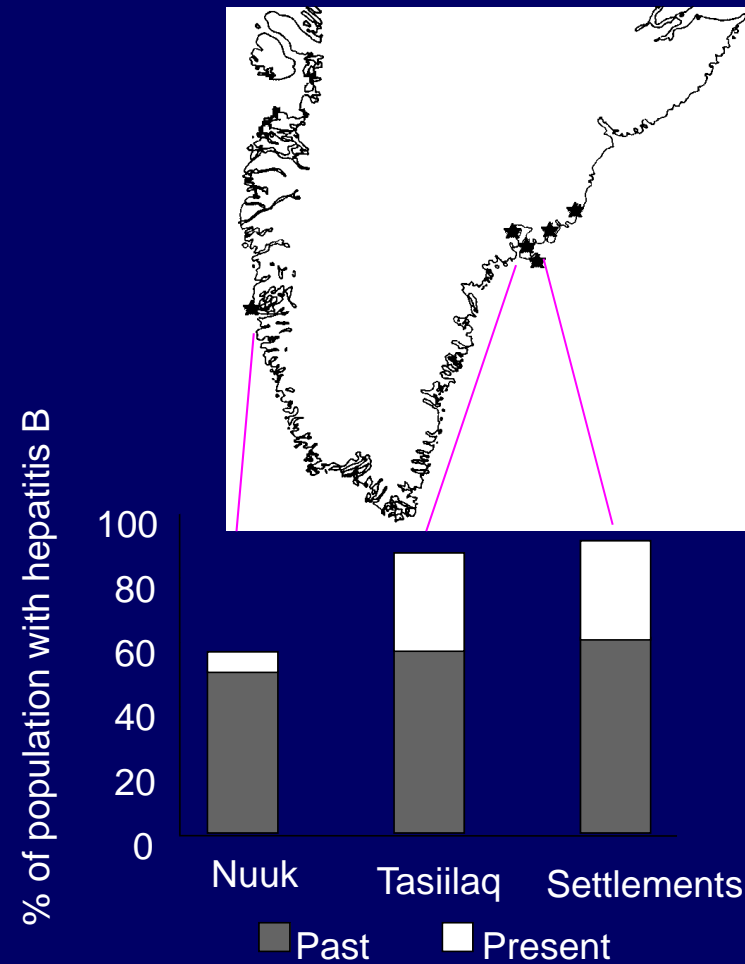
97 % were anti-HBe positive



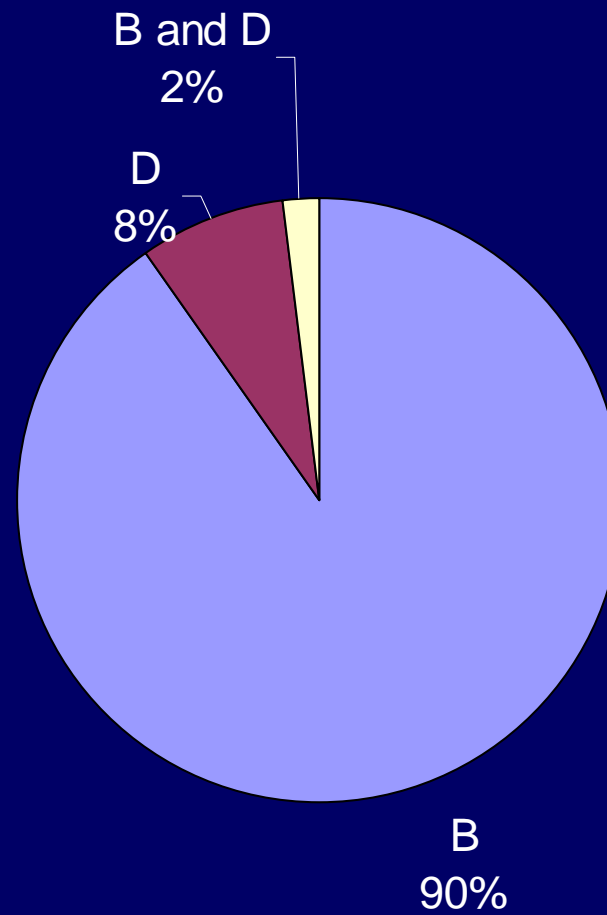
# Flowchart



# Past or present HBV infection among 50 – 70 years old



# Distribution of HBV genotypes



# Results

	1301	1310	1320	1330	1340	1350	1360	1370	1380	1390	1400	1410	1420	1430
B_J	CGACGCGGCTGGAGCGAARCTCATCGGACTGACARTTCTGTCGCTGCTCTCCCGCARGTATACATCGTTTCCATGGCTGCTAGGCTGTGCTGCCAARTGGATCCTGCCGGGGACGCTCCTTTGTTTACGCT													
GL1	.....G.T.C..T.....A.....													
GL2	.....G.....C.T.C..T.....A.....													
GL3	.....G.....C.T.C..T.....A.....													
GL4	.....G.....C.T.C..T.....A.....G.....													
GL5	.....G.....C.T.C..T.....A.....													
Consensus	.....c.....g.t.c..t.....a.....c.....													
B_J	1431	1440	1450	1460	1470	1480	1490	1500	1510	1520	1530	1540	1550	1560
B_J	CCCGTCAGCGCTGAATCCCGCGGACGACCCCTCCCGGGGCGCTTGGGGCTTACCGCCCGCTTCTCCGTCTGCCGTACCGACCCGACCGGGGGCGACCTCTCTTTACGGGACTCCCGCTCTGTGCCT													
GL1	.....G.....A.....T.....													
GL2	.....G.....A.....T.....													
GL3	.....G.....A.....T.....C.....													
GL4	.....G.....A.....T.....T.....													
GL5	.....G.....A.....T.....T.....													
Consensus	.....g.....a.....t.....g.....t.....													
B_J	1561	1570	1580	1590	1600	1610	1620	1630	1640	1650	1660	1670	1680	1690
B_J	TCTCATCTGCCGGCCCGTGTGCACCTTCGCTTACCTCTGCACCTGCCATGGAGACCACCGTGACCGCCACCGGGACCTGCCCAAGGCTTGCATAGAGGACCTCTGGACTTTCAGCARTGTCAACGAC													
GL1	.....C.....T.....A.....													
GL2	.....C.....T.....A.....													
GL3	.....C.....T.....A.....AT.....T.....													
GL4	.....C.....T.....A.....													
GL5	.....C.....T.....A.....T.....													
Consensus	.....c.....t.....a.....ac.....c.....													
B_J	1691	1700	1710	1720	1730	1740	1750	1760	1770	1780	1790	1800	1810	1820
B_J	CGACCTTGAGCCATCTTCARAGACTGTGTGTTTACTGACTGGAGGACTCGGGGAGGAGATCAGGTTAAGGCTTTTGTACTAGGAGGCTGTAGCCATRAATTGGCTCTGTTCCACAGCACCATTGCAC													
GL1	.....A.....AC.....G.....A.....													
GL2	.....A.....AC.....G.....G.....													
GL3	.....A.....AC.....G.....G.....													
GL4	.....A.....AC.....G.....G.....C.....													
GL5	.....A.....AC.....G.....G.....t.....													
Consensus	.....c.....g.....c.....t.....													
B_J	1821	1830	1840	1850	1860	1870	1880	1890	1900	1910	1920	1930	1940	1950
B_J	TTTTTCACCTCTGCCTAATCATCTCTTGTTCATGCTCCTACTGTTCCAGCCCTCCAGCTGTGCCTTGGGTGGCTTTGGGGCATGGACATTGACCCCTTATAAAGATTGGAGCTTCTGTGGAGTTACTCTC													
GL1	.....A.....C.....C.....													
GL2	.....A.....C.....C.....													
GL3	.....A.....A.....C.....C.....													
GL4	.....A.....C.....C.....C.....													
GL5	.....A.....C.....C.....t.....													
Consensus	.....a.....g.....a.....g.....t.....													
B_J	1951	1960	1970	1980	1990	2000	2010	2020	2030	2040	2050	2060	2070	2080
B_J	TTTTTTGCCCTACTGACTTCTTTCCGCTCTGACGAGACCTACTAGATACCCCGCTGCTCTGTATCGGGAGCCCTTAGAATCTCCTGACATTGCTCACCTCACCATACAGCARTCAGGCCAGGCTATTCTA													
GL1	.....G.TT.....T.C.....C.....T.....T.....G.A.....C.....T.S													
GL2	.....G.TT.....T.C.....C.....T.....T.....G.....G.....C.....T.C													
GL3	.....C.....G.TT.....T.C.....C.....T.....T.....G.....G.....C.....T.C													
GL4	.....C.....G.TT.....T.C.....G.....C.....T.....T.....G.....G.....C.....T.C													
GL5	.....T.....G.TT.....T.C.....C.....T.....T.....G.....G.....C.....T.C													
Consensus	.....a.....t.....g.tt.....t.c.a.c.....g.....t.....g.....a.....ac.....a.....t.g													
B_J	2081	2090	2100	2110	2120	2130	2140	2150	2160	2170	2180	2190	2200	2210
B_J	TGCTGGGGGGAATTAACTACTAGCTACCTGGGTGGGTAAATTAATTTACAGATCCAGCATCCAGGGATCTAGTACTCAATTAATGTTACACTACATGCGCCCTAAGATCAGGCATTAATTTGTGGTTTC													
GL1	.....C.....A.....A.....A.....A.....A.....A.....A.....													
GL2	.....C.....G.....C.....C.....A.....A.....A.....A.....A.....A.....													
GL3	.....C.....C.....C.....C.....A.....A.....A.....A.....A.....A.....													
GL4	.....T.....C.....C.....C.....A.....G.....A.....A.....A.....A.....A.....													
GL5	.....T.....C.....C.....C.....A.....G.....A.....A.....A.....A.....A.....													
Consensus	.....t.....c.a.....c.....c.a.....a.....t.....a.....a.....													
B_J	2211	2220	2230	2240	2250	2260	2270	2280	2290	2300	2310	2320	2330	2340
B_J	ACATTTCTGCATTACTTTTGGAGAGCAATTTCTTGAATACTTGGTGTCTTTTGGAGTGTGGATTCCGACTCCTCCTGCCCTACAGACCACCAATGCCCTATCTTATCAATGCTTCCGGAGACTGC													
GL1	.....C.....C.....C.....C.....T.....C.....C.....A.....T.....CA.....A.....A.....													
GL2	.....TC.....C.....C.....C.....T.....C.....C.....A.....T.....CA.....A.....A.....													
GL3	.....TC.....C.....C.....C.....T.....C.....C.....A.....T.....CA.....A.....A.....													
GL4	.....TC.....C.....C.....C.....T.....C.....C.....A.....T.....CA.....A.....A.....													
GL5	.....T.....C.....C.....C.....T.....C.....C.....A.....T.....T.....CA.....A.....A.....													
Consensus	.....ca.....c.....c.....g.....a.c.....t.....c.....a.....t.....a.....cac.....a.....g.													

# Results

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The C- and X-gene and most of the genome of 20 genotype B positive samples could be sequenced

The samples showed > 94 % homology with subtype Bj and < 92 % homology with Ba

The Greenlandic samples were > 97 % mutually homologous

# Results

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Among the 343 HBsAg negative, 242 (56.1%) were anti-HBc and/or anti-HBs positive, 30 were anti-HBs positive only

In adjusted comparisons, a marginal difference was found in Bilirubin, while differences were absent for AST, GGT and BASP

# Results

Of HBsAg positive HBV-DNA was positive in 70 % (median 40,000 copies/mL (10; 90 percentiles: 1,000; 404,000 copies/mL))

Pre-core mutation analysis was feasible in 64 % , all except one had pre-core mutation (G1896A), none had CP mutations

Genotype could be determined in 59 %, of which 90 % had HBV genotype B. 8 % genotype D

Samples sequenced from 20 persons showed HBV subtype Bj (now B6)

## Results Study 2

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5 women and 1 man were HBsAg positive

All were anti-HBe positive and viral load was low, 200 IU/mL being the highest

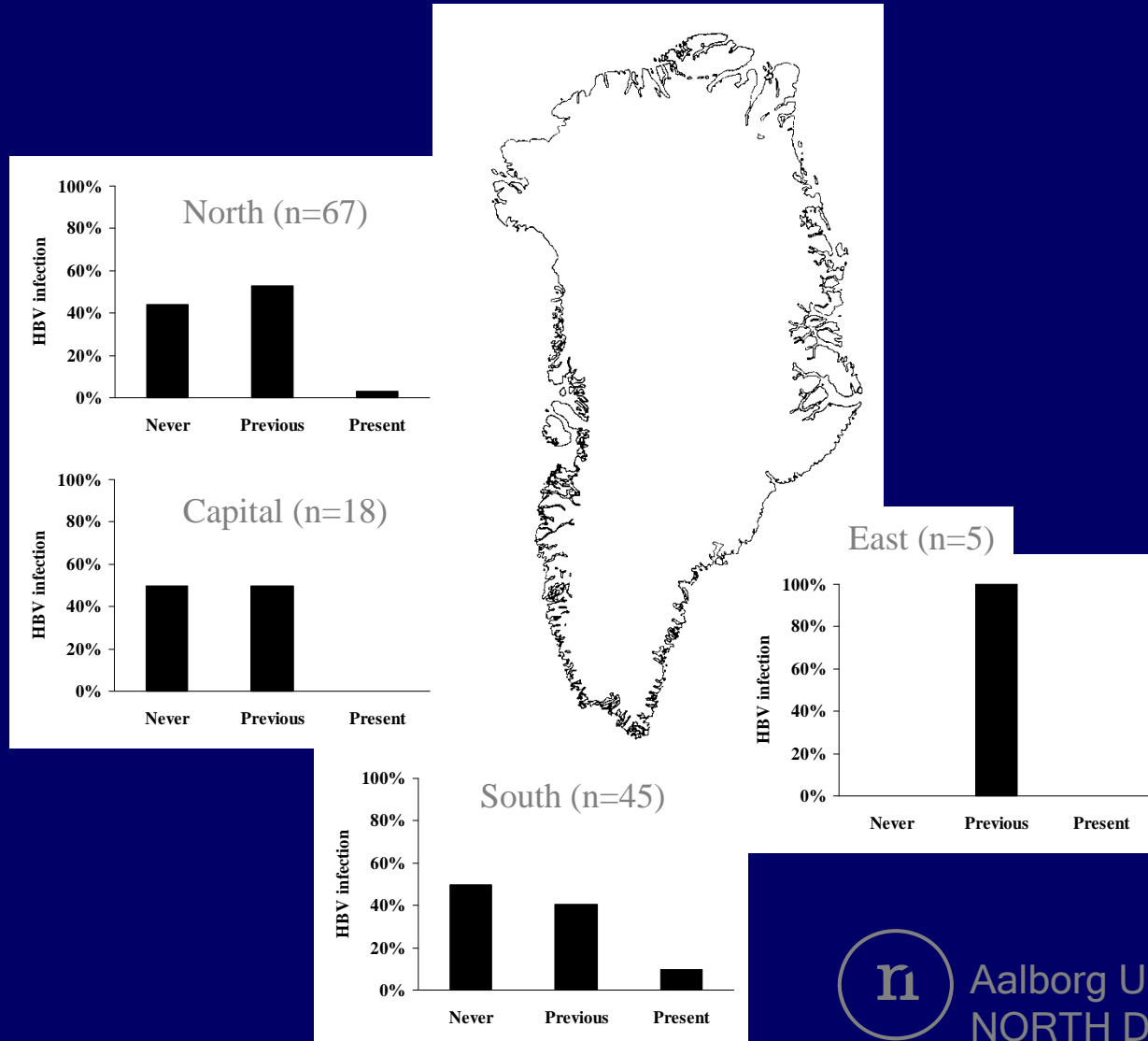
Detection of precore mutation and genotype was not possible in any of these subjects

None of HBsAg positive persons was anti-HDV or anti-HCV positive

One participant had been exposed to both hepatitis B and D virus and one had been exposed to both hepatitis B and C virus



# Markers of HBV among Greenlanders who have migrated to Denmark



# Hepatitis D

- ▶ In all 6 persons were anti-HDV positive
  - ▶ 4 were men and 4 were from Eastgreenland
  - ▶ All had markers of former HBV infection, but only one was HBsAg positive
  - ▶ None was HBV-DNA or HDV-RNA positive
  - ▶ All 6 had elevated GGT, but only one had elevated AST
- ▶ The exposure in both our studies is generally low and lower than reported from certain areas on the west coast of Greenland

B C Langer J Viral Hepat 1997  
M Børresen J Viral Hepatitis 2010
- ▶ Based on our data hepatitis D is rare among Inuit in Greenland and Denmark, but with 7 % HBsAg positive HDV infection can pose a problem



# Hepatitis C

- ▶ Of 434 Inuit in Greenland screened for anti-HCV
  - ▶ 35 (8.1%) were positive with anti-HCV 3.0 (Abbott AxSYM™ System), when tested further
    - ▶ 2 of the 35 were positive with Ortho HCV 3.0 Elisa, while
    - ▶ 0 of 35 were positive using INNO-LIA™ HCV Score as confirmatory test.
    - ▶ HCV-RNA was negative in all 35 samples
- ▶ Of 136 Inuit in Denmark 2 were anti-HCV positive. One was a known IVDU, living in Denmark for 47 of his 50 years
- ▶ **Hepatitis C is rare among Inuit in Greenland and Denmark**



# Conclusion

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More than 75% had markers of present or previous hepatitis B infection

HBV genotype B6 with pre-core mutation was predominating

HBV viral load was generally low

Liver biochemistry did not differ with HBsAg status

None had hepatitis C or D

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**Hepatitis B infection, genotype B, with pre-core mutation, appears to be an indolent disease in Inuit in Greenland**

