HEPATITIS B ELIMINATION IN ALASKA

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Goals of My Lecture

- Highlight the Alaska program to demonstrate that elimination of hepatitis B transmission in all infants and children is feasible

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WHO Goals for HBV Elimination

	Indicator	2015 Baseline	2020 Target	2030 Target	Achievable ?
Hepatitis B Vaccination	3 Dose coverage in infancy	84%	90%	90%	Yes
Prevention Perinatal Transmission	Birth Dose Coverage	39%	50%	90%	Likely
Blood Safety	Donations Screened	97%	95%	100%	Yes
Injection Safety	Proportion of Usafe Injections	5%	0%	0%	Yes
Harm Reduction	Syringes and Needle Exchange per PWID*	27	200	200	Likely
Testing Services	% with HBV diagnosed	9%	30%	90%	Will need a Massive Effort and Funding Support
Treatment	% Diagnosed with HBV on Treatment	7%	Not specified	80%	Massive Support Needed

Alaska Experience: The two goals for newborn and infant vaccination are achievable

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Global Elimination of HBV: Steps involved

- Preventing Transmission
  - Universal vaccination including birth dose
    - Will reduce transmission at birth from HBsAg-positive mother with high viral load from 90% to <10%
    - Adding HBIG will further reduce transmission to < 5%
    - Adding antiviral therapy if HBsAg+ mother has >200,000 IU/ml HBV will theoretically completely prevent transmission*
- Detection of all persons with HBV
- Cure of all infected patients

*Brown S, McMahon BJ, Lok ASSF et all Hepatology 2016;63:319-333

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Hepatitis B in Alaska Native People

- Studies in the 1970s found high rates of acute and chronic HBV infection in Alaska Native People western Alaska. This was the only identified US born population with endemic HBV
  - High rates of HCC were found in infected persons including children
- Subsequent studies showed five different HBV genotypes were found in this population: A2, B6, C2, D2,3 and F1
- Transmission was predominately perinatal in NW Alaska where HBV genotype C predominated and horizontal in SW Alaska where the other genotypes were found

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History of Prevention of Perinatal Transmission in Alaska Native People

- 1980: Universal screening of pregnant women instituted at the Alaska Native Medical Center (ANMC) in Anchorage and Bethel Alaska
  - Infants of HBsAg-positive mothers received 3 doses of HBIG starting in the delivery room and at 3 and 6 months
  - Addition of hepatitis B vaccine starting at 3 months in 1981
  - In 1982 1st dose of vaccine given at birth along with HBIG; HB vaccine continued at 1 and 6 months and subsequent doses of HBIG dropped
  - In 1983 Universal statewide HB vaccine instituted starting birth; HBIG at birth also given to HBsAg-positive mothers
  - In 1990 despite HB vaccine and HBIG given right at birth, 2 infants of HBeAg+ mothers acquired HBV and became chronically infected
  - 1991: lamivudine and later TDF was added for mothers who were HBeAg+ in addition to vaccines at birth

Alaska Native Hepatitis B Program

- Universal HBV newborn vaccination starting at birth introduced in 1983
- Screening and catch-up vaccination of children and adults: 1983-1988
  - 53,000 persons screened; ¾ of population, 90% in endemic areas of western Alaska

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Alaska


Barrow
Wainwright
Atqasuk
Nuiqsut
Kaktovik
Point Hope
Anaktuvuk Pass
Kivalina
Kotzebue
Kiana
Ambler
Kobuk
Bettles
Selawik
Fort Yukon
Shishmaref
Deering
Buckland
Hughes
Wales
Huslia
Brevig Mission
Tanana
Fairbanks
White Mountain
Koyuk
Nulato
Ruby
Nenana
North Pole
Eagle
Nome
Elim
Anderson
Shaktoolik
Kaltag
Delta Junction
Gambell
Savoonga
Unalakleet
Stebbins
Saint Michael
Kotlik
McGrath
Nikolai
Anvik
Shageluk
Sheldon Point
Holy Cross
Scammon Bay
Saint Mary's
Hooper Bay
Kalskag
Chuathbaluk
Wasilla
Palmer
Anchorage
Valdez
Kasigluk
Akiak
Whittier
Toksook Bay
Bethel
Kenai
Soldotna
Cordova
Chefornak
Eek
Seward
Nondalton
Quinhagak
Homer
Skagway
Aleknagik
New Stuyahok
Haines
Platinum
Dillingham
Juneau
Egegik
Hoonah
Port Lions
Kodiak
Pelican
Pilot Point
Angoon
Kake
Old Harbor
Saint Paul
Sitka
Petersburg
Port Heiden
Akhiok
Saint George
Port Alexander
Wrangell
Chignik
Coffman Cove
Thorne Bay
Ketchikan
Cold Bay
Sand Point
Craig
Hydaburg
King Cove
Akutan
Unalaska
Atka
State Roads
0
200 KM
200 Miles

Alaska Native Hepatitis B Program continued

- No new cases of acute HBV in AN children since mid 1990's
- No more AN children < age 20 have chronic HBV infection
- Rates of liver cancer in children which were highest reported in world have fallen to zero since mid 1990's

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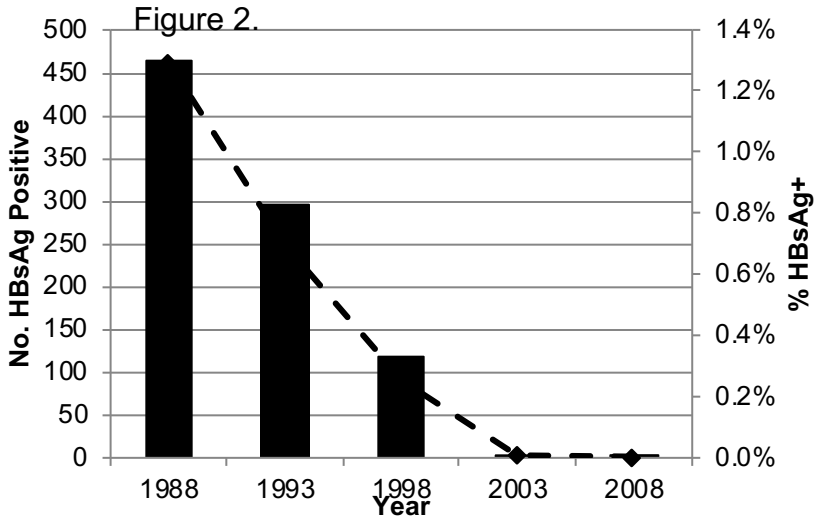
Number of HBsAg-positive Alaska Native Children Under 20 Years of Age: 1988-2008



As of 2013, there are no Alaska Native children known to be HBsAg-positive

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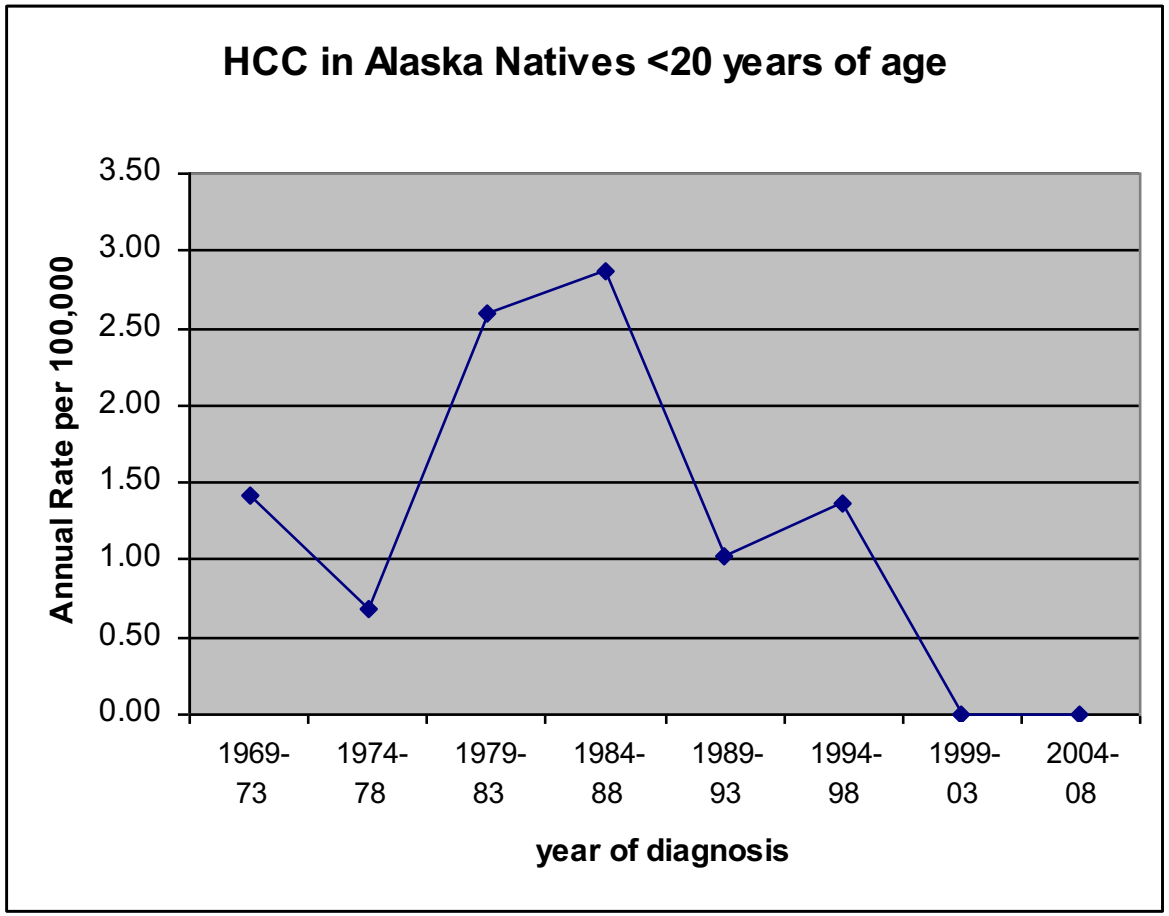

p value for trend = 0.002

Hepatology 2011;54:801-7

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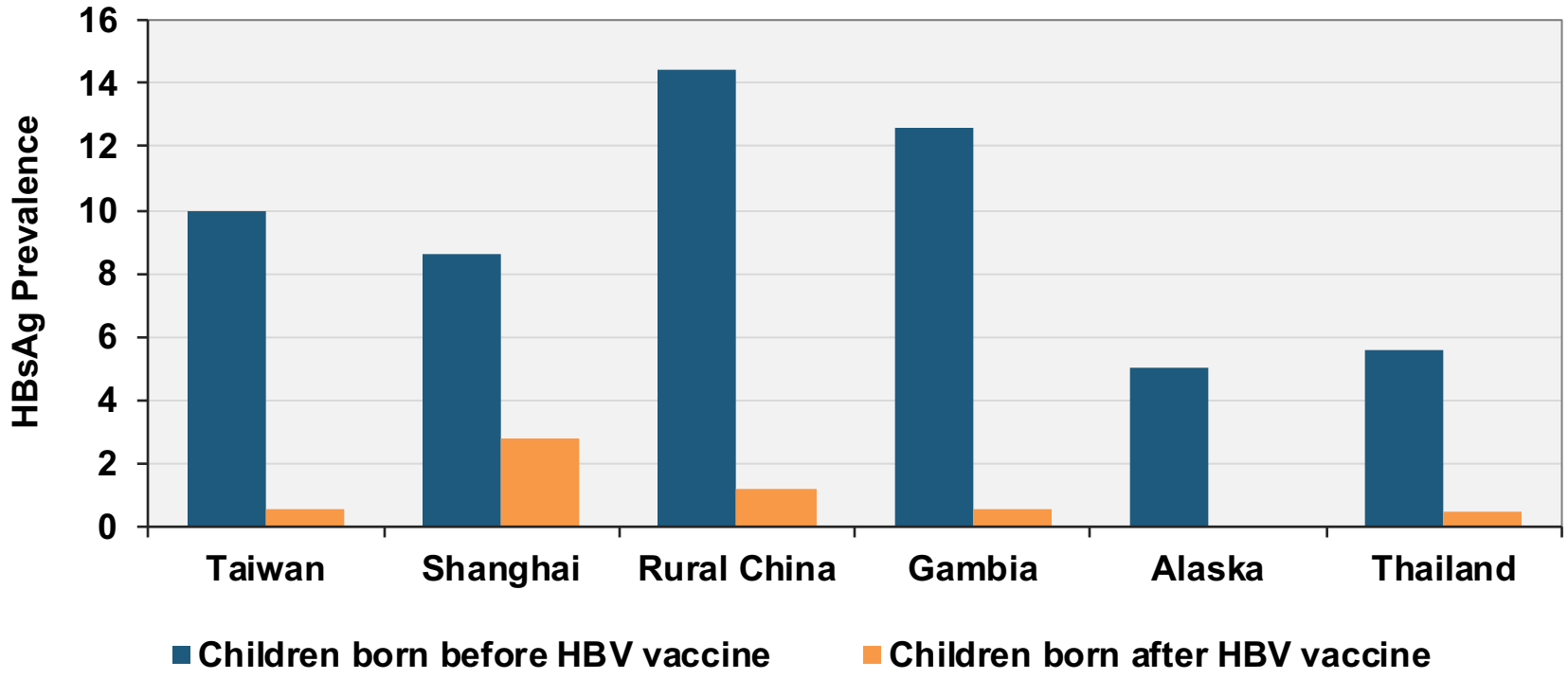
Prevalence of Chronic Hepatitis B Virus Infection Has Markedly Declined Among Children Before and After HBV Vaccine Introduction



Van Damme P, Ward JW, Wiersma S, Shoval D, Zanetti A. Hepatitis B vaccine. In Plotkin SA, Orenstein WA, Offit PA eds. *Vaccines*, 6th Edition. London: Elsevier Health Sciences; 205-234.

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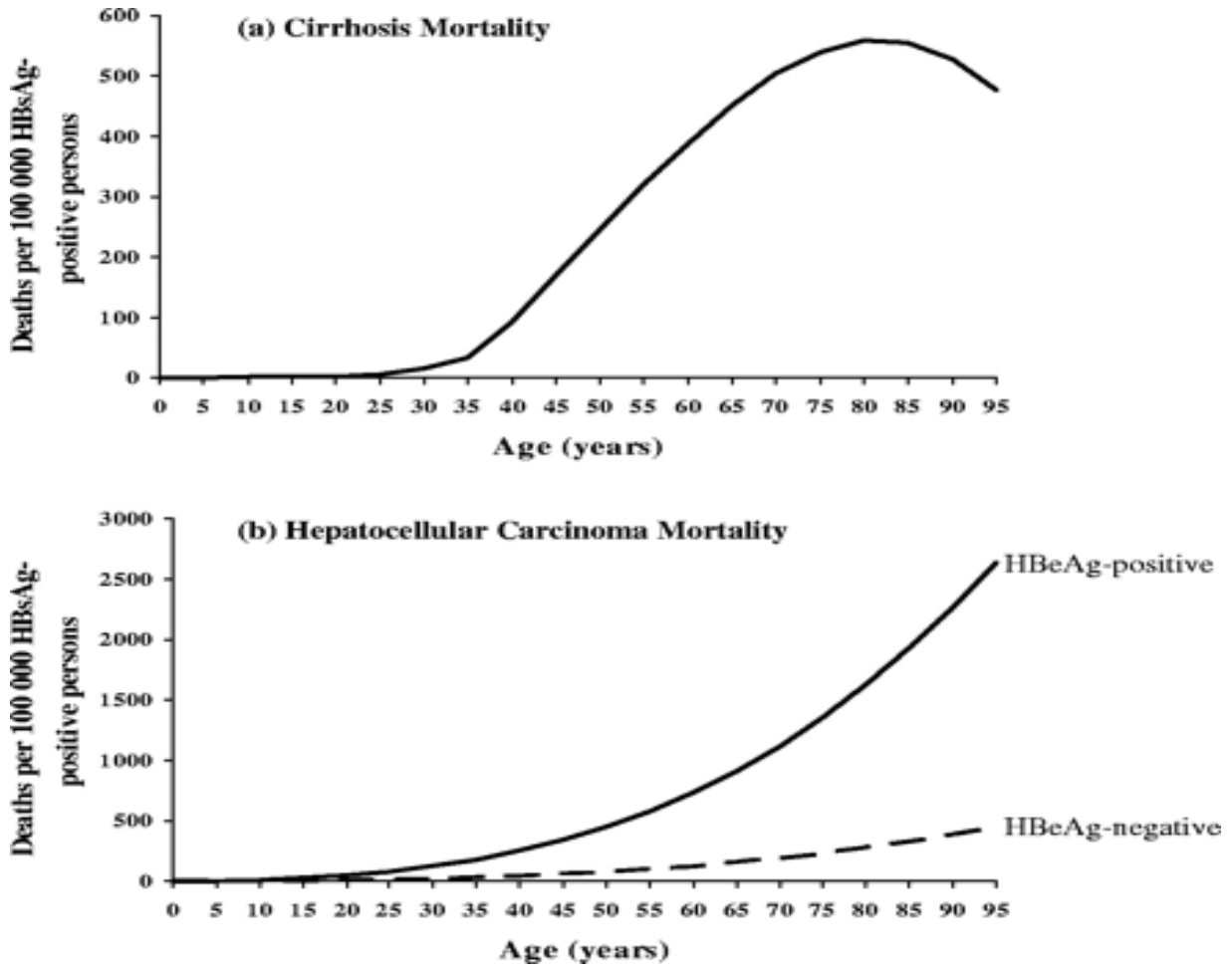
Impact of Reduction of Prevalence of HBV in Children on the Incidence of HCC

- 3-4 decade lag time in overall reduction of HCC incidence in countries once successful vaccination programs in newborns have been introduced
- During this time, any reduction in incidence of HCC will take:
  - Identification of persons with chronic HBV
  - Linking those with chronic HBV to care
  - Identifying candidates meeting guidelines for care
  - Regular surveillance for HCC based on Guidelines recommendations

Mathematical Model: Age-specific hepatitis B-related cirrhosis and HCC mortality



Goldstein Int J Epidemiol 2005;34;1329-39

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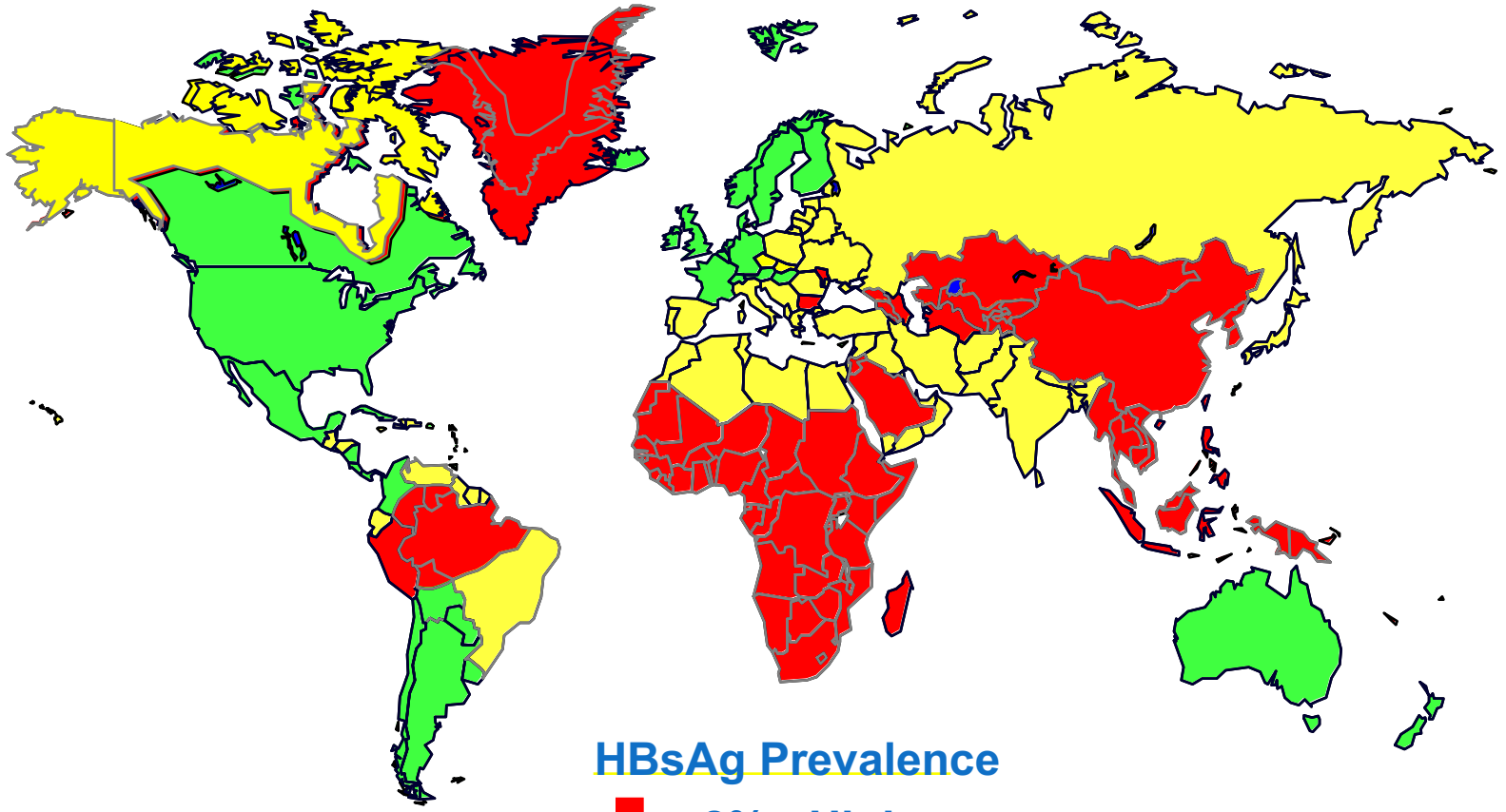
Identifying Persons with HBV in US

- Highest risk is from persons born in countries with prevalence of HBsAg > 2%
- These persons should be screened as per CDC and AASLD guidelines and if positive, linked to care
- HBsAg-positive persons need lifelong monitoring and antiviral therapy if they meet AASLD guideline 2016/guidance 2018

Terrault NA, Bzowej NH, Chang KM et al et al. Hepatology 2016;63:261-83
Terrault NA, Lok ASF, McMahon BJ et al. Hepatology 2018;

Geographic Distribution of Chronic HBV Infection



CDC

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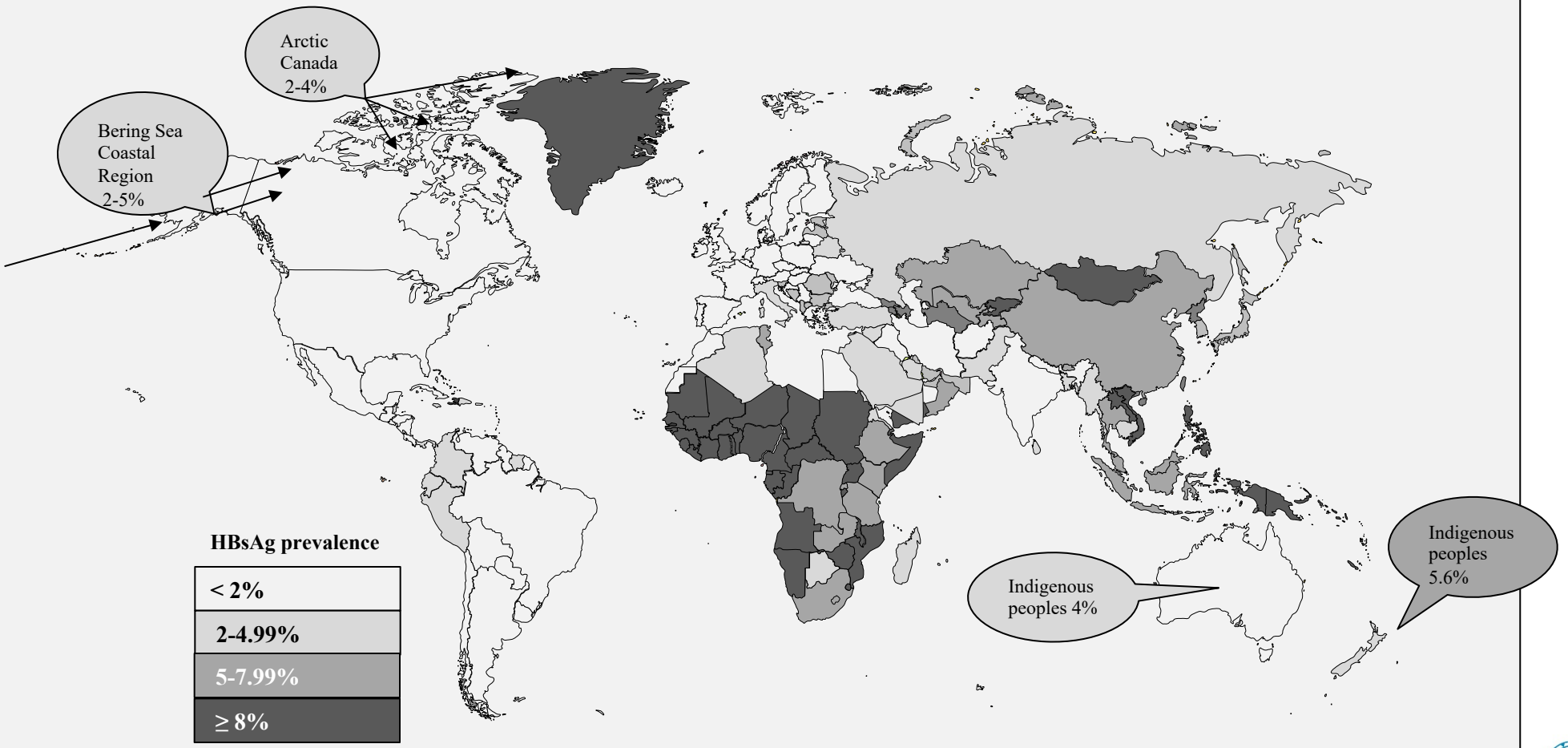
Change in Prevalence of Chronic Hepatitis B Based on Recent Epidemiological Evidence



Map prepared by World Indigenous People's Viral Hepatitis Conference planning committee, 2017

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HCC in Persons under Recommended Age for Surveillance:

- AASLD Guidelines recommend surveillance with 6 month liver US in Asian or black males ≥40 and Asian females ≥50 plus those with family history of HCC, persons with HDV, and those with cirrhosis.
- AASLD guideline says HCC surveillance is cost-effective if incidence of HCC is > 0.2%/year
- Retrospective analysis of prospective 30 year surveillance for HCC 1983-2012 using AFP: 1083 persons followed
  - SEER NIH Cancer Registry also queried during this period
- HCC incidence calculated using Poisson Regression

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Demographics, outcomes, and person-years of follow-up by genotype (Alaska, 1983-2012)

Characteristics	Genotype					
	A	B	C	D	F	Overall
HBV	**154**	**45**	**74**	**650**	**217**	**1142**
Median age entry†	24.5	52.5	24.2	21.2	17.6	25.9
HCC	**5**	**0**	**10**	**6**	**22**	**43**
Median age HCC	59.8	--	59.2	54.2	23.0	44.7
Deaths	**44**	**26**	**27**	**185**	**64**	**346**
Median age death	53.5	77.4	61.9	56.4	39.9	56.4
Total pyrs at risk^	**3884**	**917**	**1813**	**15933**	**5183**	**27729**
Median	29.1	20.6	27.0	29.1	29.8	29.1

†Entry into study is 3/1/1983 or date of first HBsAg positive test.
^Person years at risk is period from entry into study to HCC diagnosis, death, or end of study period on 12/31/2012.

Gounder PP et al. Int J Circ Health 2016 Jan;75(1):31115

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Adjusted odds ratios, HCC (Alaska, 1983-2012)

	Incidence**	HCC aOR††	HCC 95% CI
Age Group (years)*		*p=0.043*	
<40	1.05	1.0	--
40-60	1.43	2.25	(0.99, 5.12)
≥60	3.75	2.81	(0.99, 7.96)
Sex		*p=0.089*	
Female	0.99	1.0	--
Male	1.81	1.83	(0.91, 3.65)
HBV Genotype		*p<0.001*	
B/D	0.38	1.0	--
A	1.29	4.05	(1.21, 13.6)
C	5.52	18.1	(6.29, 52.1)
F	4.24	14.6	(5.74, 36.9)

Gounder PP et al.
Int J Circ Health 2016
Jan;75(1):31115

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†C.I. Confidence Interval. ††aOR = adjusted odds ratio, controlling for age, sex, and HBV genotype. *HCC age represents age at entry into study. **HCC incidence is per 1000 person-years at risk

Incidence of HCC by HBV Genotype in Alaska Native Young Persons

Genotype	Number of Cases	Incidence/1000 persons years
A	2	0.77
B	0	0.0
C	0	0.0
D	2	0.17
F	19	4.31
Total	23	1.01

Genotype F vs all other known: 17.2 (5.7-69.5) p<0.001

Ching LK et al. Liver Int 2016 Oct;36(1): 1507-15.

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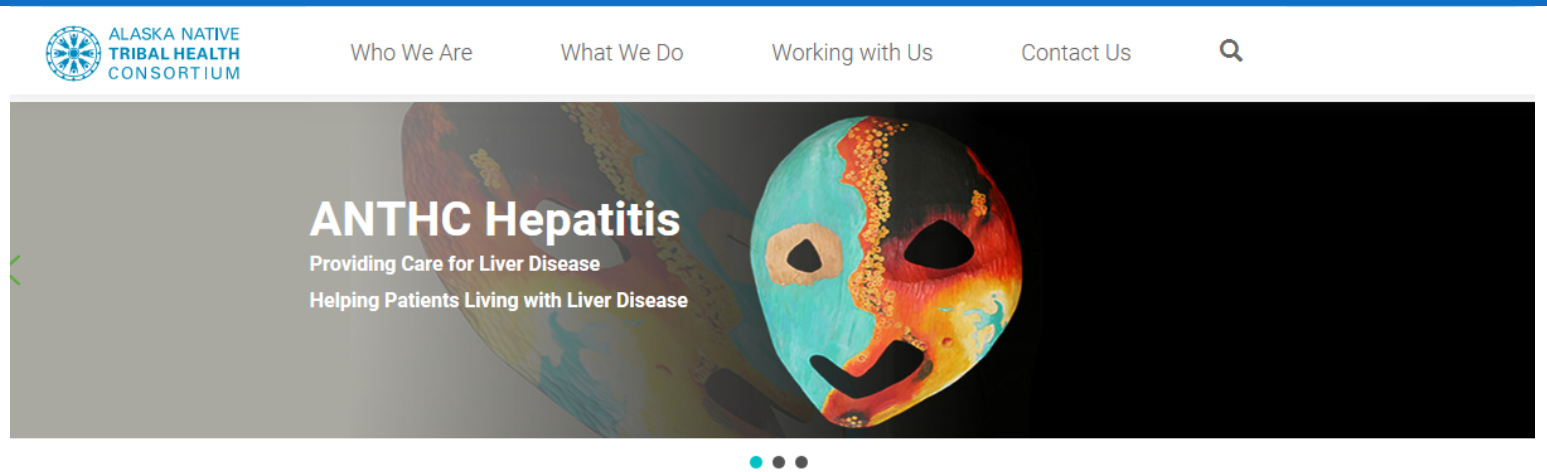
Conclusions

- All pregnant females should be tested for HBsAg and if positive, for HBV DNA
- All newborns, regardless of mothers HBV status should receive hepatitis B vaccine starting at birth plus 2-3 more doses in infancy
- Newborns of HBsAg-positive mothers should receive hepatitis B vaccine and HBIG at birth, in the delivery room/no later than 4 hours after delivery plus 2-3 more doses in infancy
- HBsAg-positive mothers with HBV DNA level >200,000 IU/ml should receive antiviral therapy in the 3rd trimester and for 4-6 weeks post partum
- All persons in the US born in a country endemic for HBV should be screened for HBsAg and if positive, linked to lifelong care and treatment



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Qu'yana!

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