HBsAg Quantification: Should It be Part of The Treatment Algorithm for CHB?

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Outline

- How will HBsAg quantification affect threshold for treatment?
  - Does it influence probability of complications?
  - Does it re-classify patients with chronic HBV infection?
- Is it useful for predicting response/ non-response to treatment?
  - Interferon or nucleos(t)ide analogues
  - HBeAg positive vs. negative

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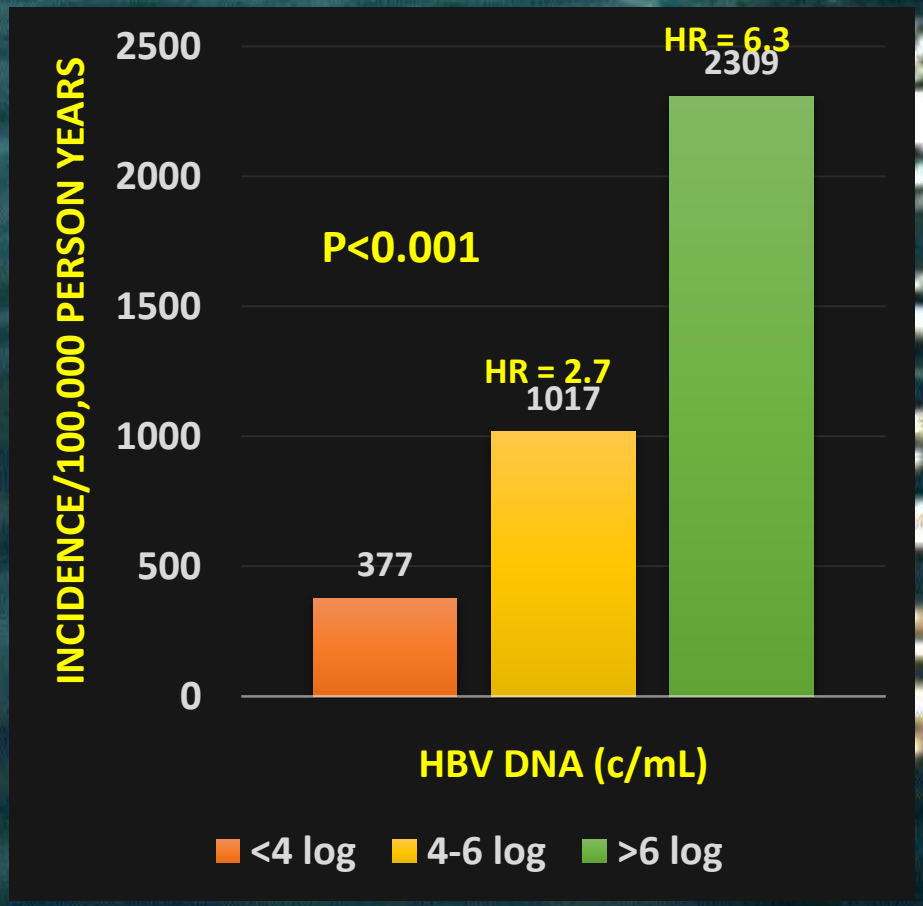
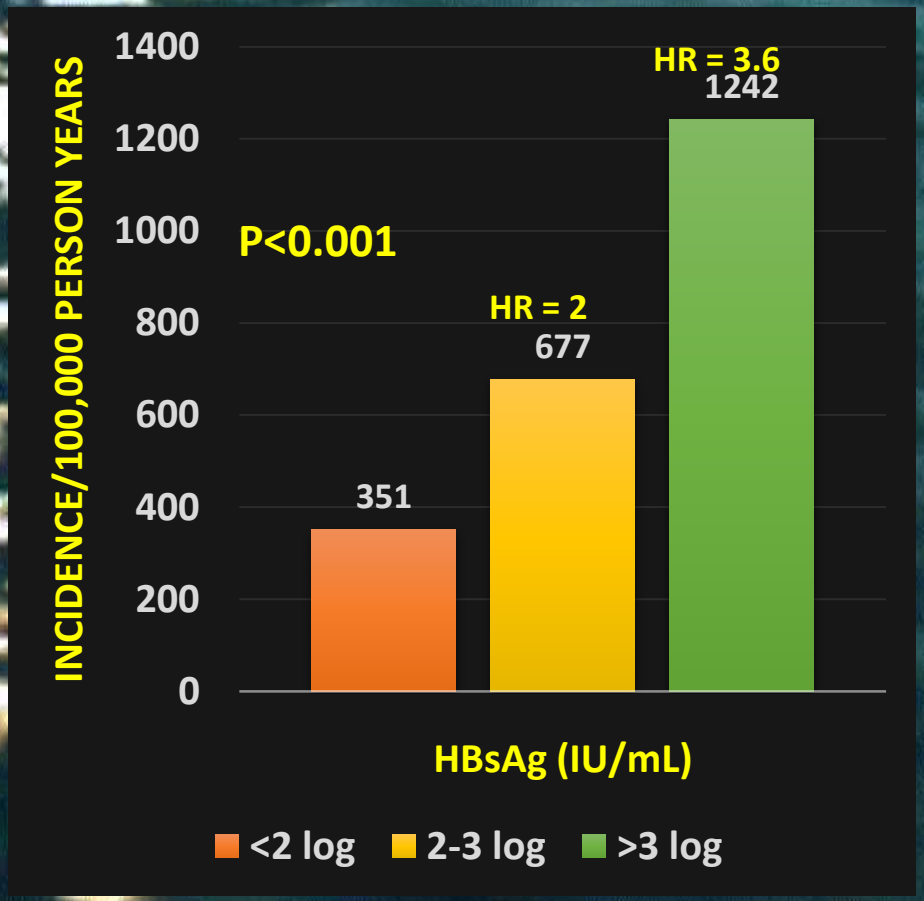
Association of HBV DNA & HBsAg with Cirrhosis – REVEAL-HBV cohort

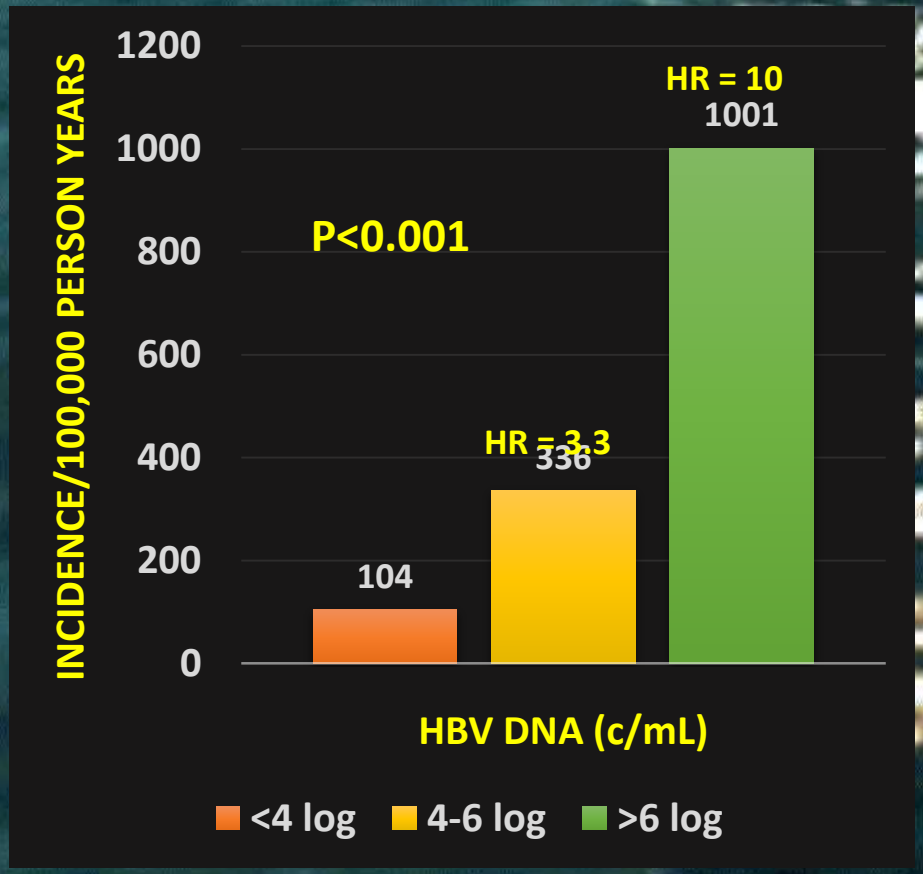


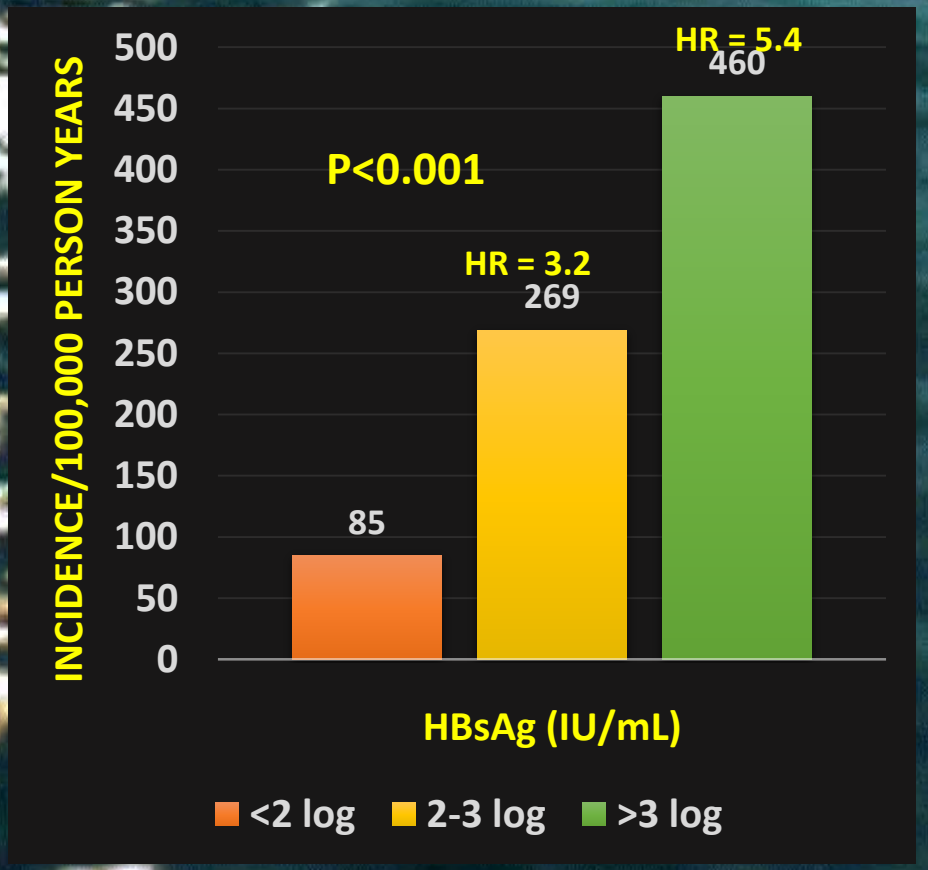


N= 3,342

Lee, et al. Hepatology 2013

Association of HBV DNA & HBsAg with HCC – REVEAL-HBV cohort





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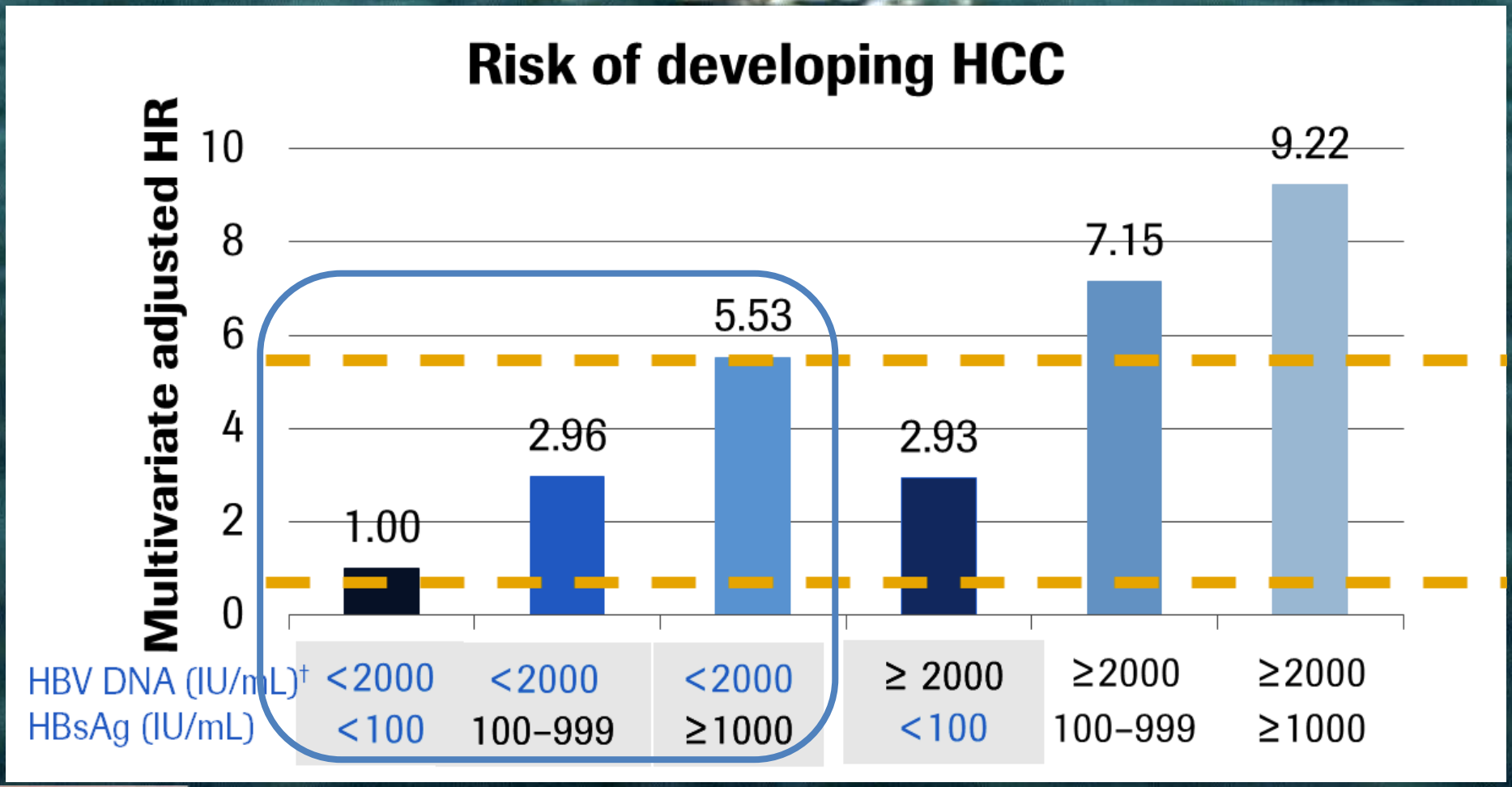
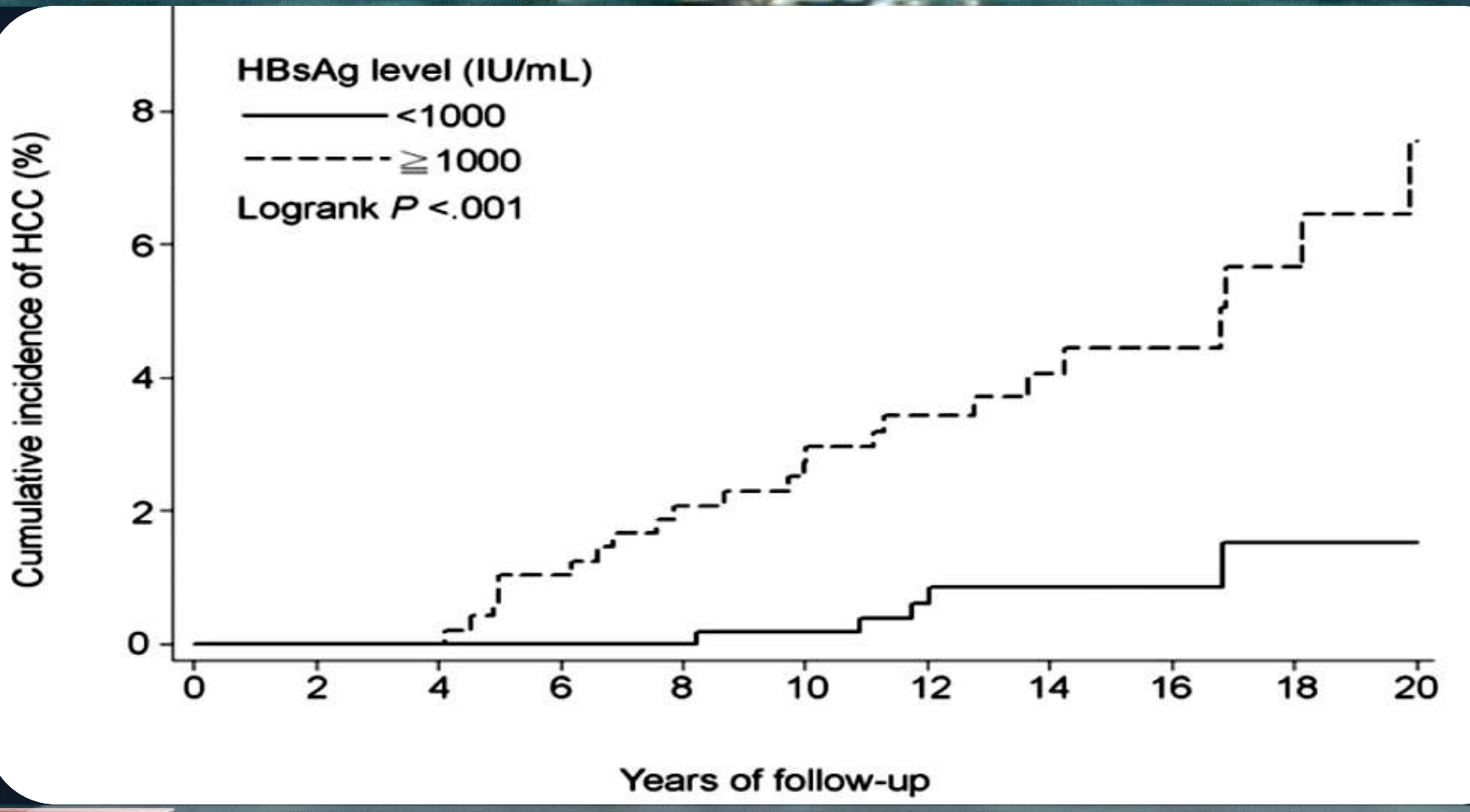
Association of HBV DNA & HBsAg with HCC – REVEAL-HBV cohort



Chen, et al. Hepatology 2011 (abs. 1095)

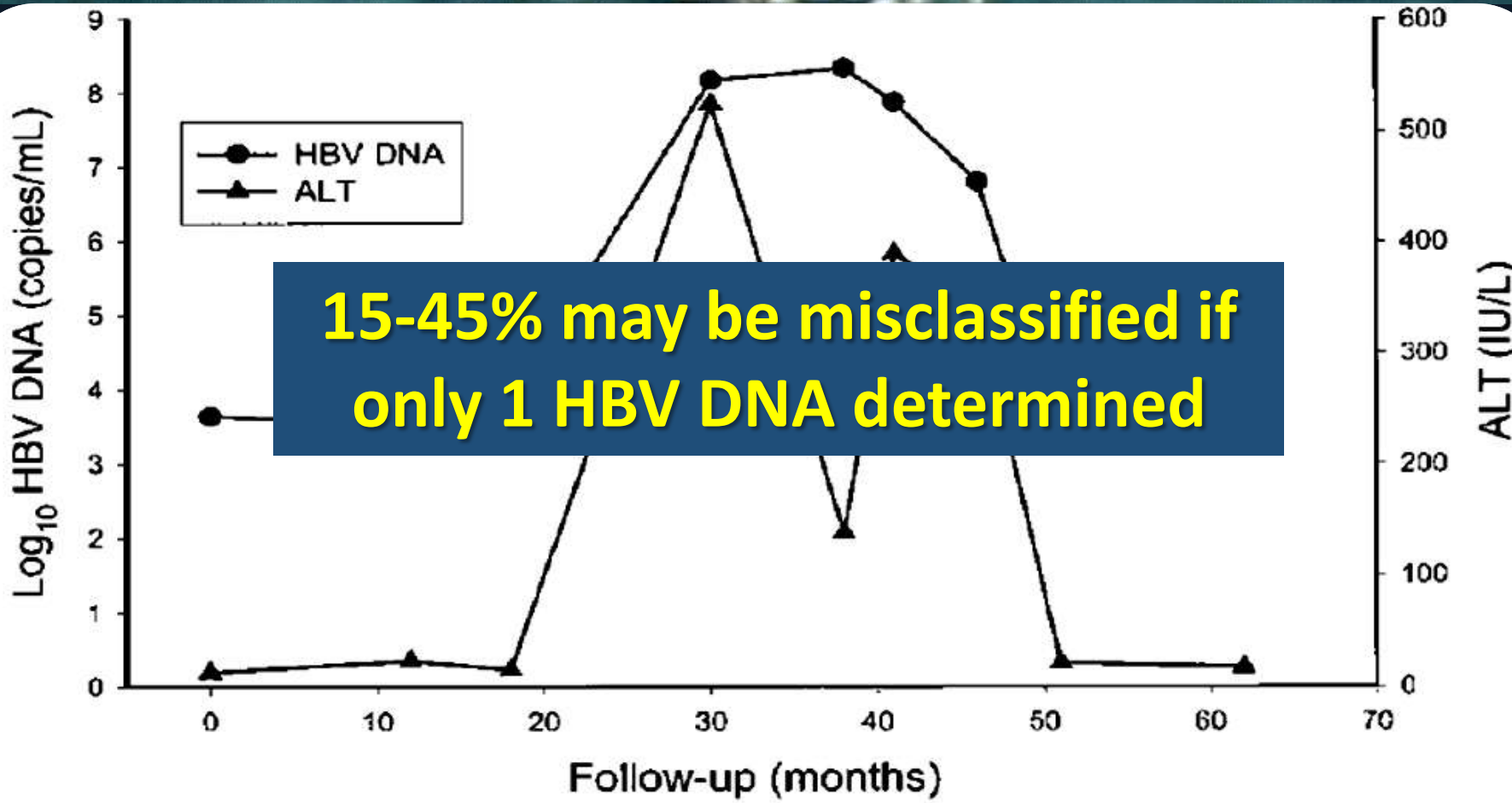
HBsAg ≥1,000 IU/mL = HCC in Patients with HBV DNA <2,000 IU/mL – ERADICATE-B cohort



N= 1,068

Tseng, et al. Gastroenterology 2012

Single HBV DNA Measurement will Misclassify HBeAg-neg CHB



15-45% may be misclassified if only 1 HBV DNA determined

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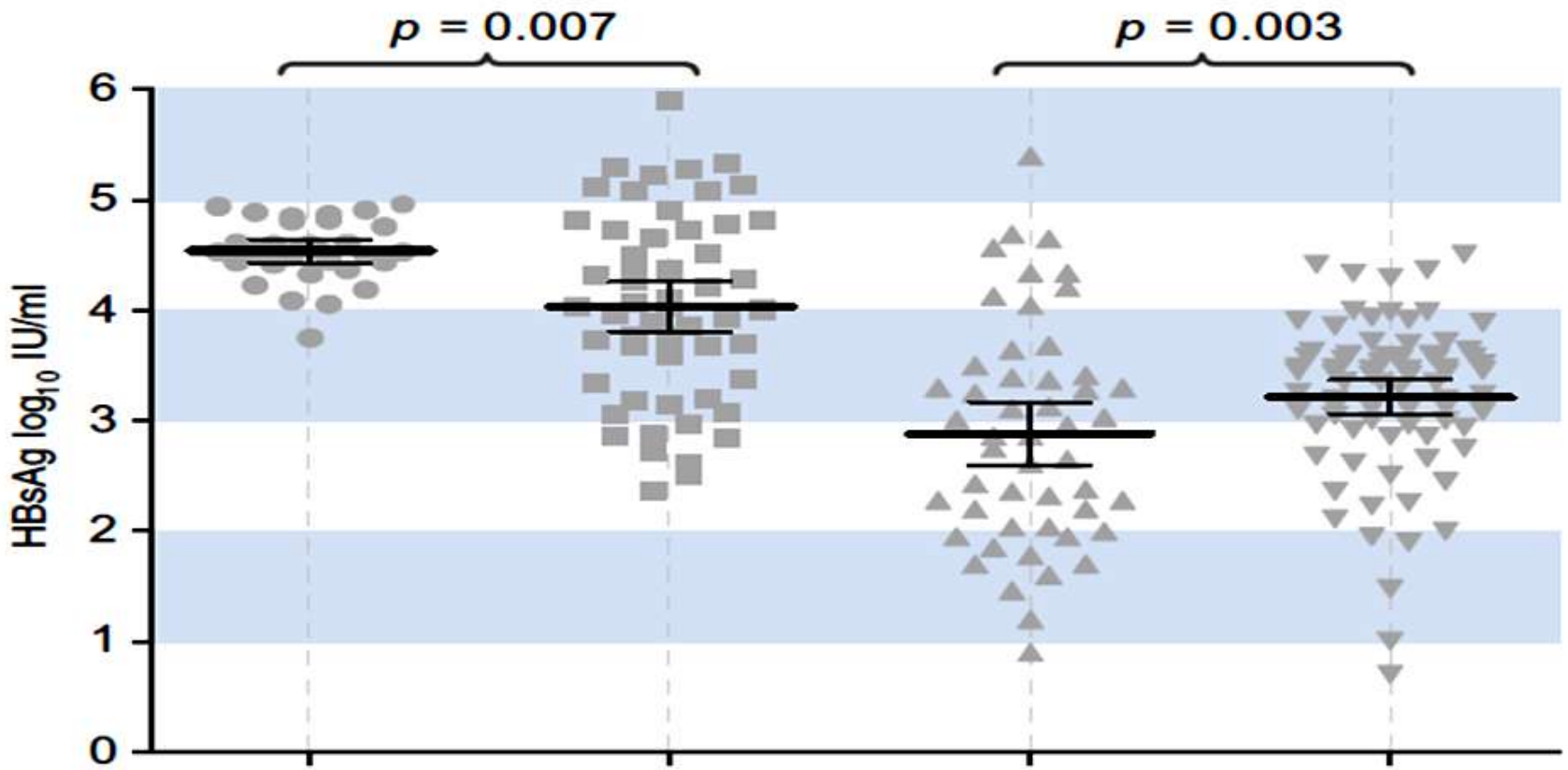
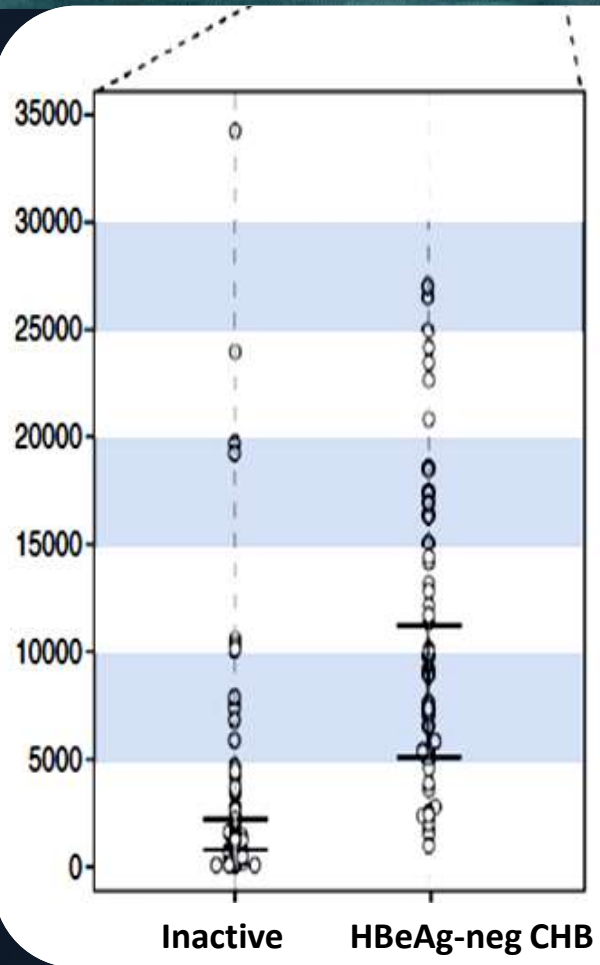
1. Lok, et al. Hepatology 2002; 2. Brunetto , et al. Hepatology 2002; 3. Manesis, et al. Am J Gastroenterol 2003; 4. Brunetto, et al. Gastroenterology 2012

Inactive Carriers Have Lowest HBsAg Levels

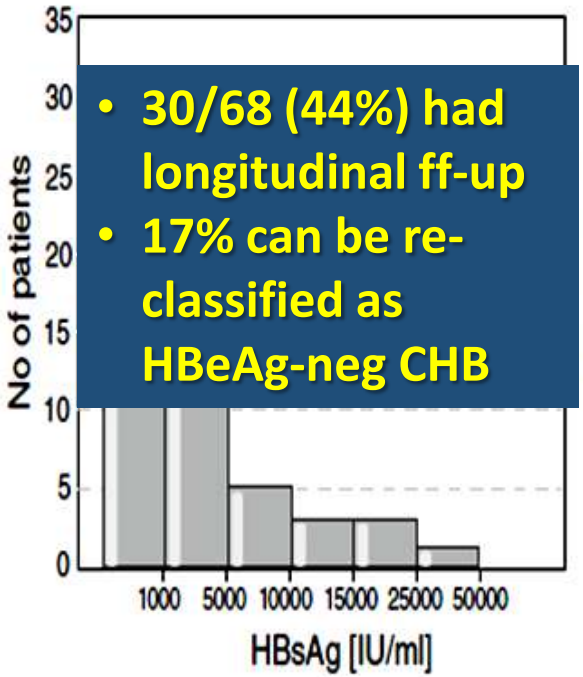


Nguyen, et al. J Hepatol 2010

Lower HBsAg in Inactive Carriers vs. HBeAg-neg CHB

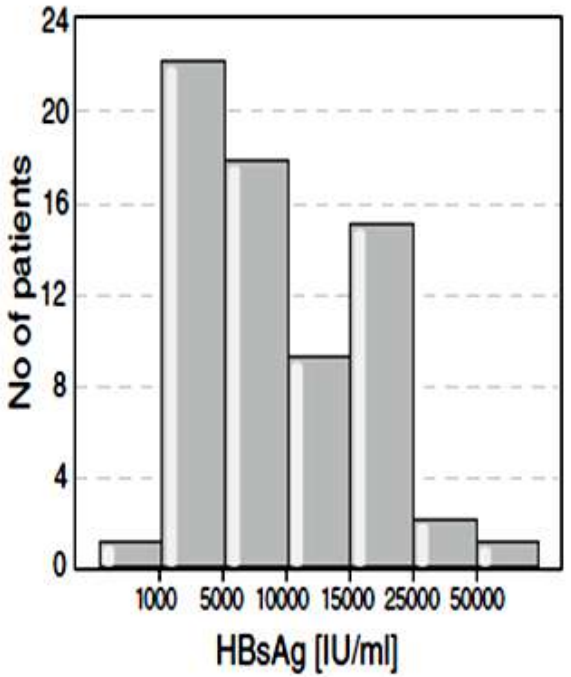


Inactive carrier



- 30/68 (44%) had longitudinal ff-up
- 17% can be re-classified as HBeAg-neg CHB

HBeAg-neg CHB



N= 226

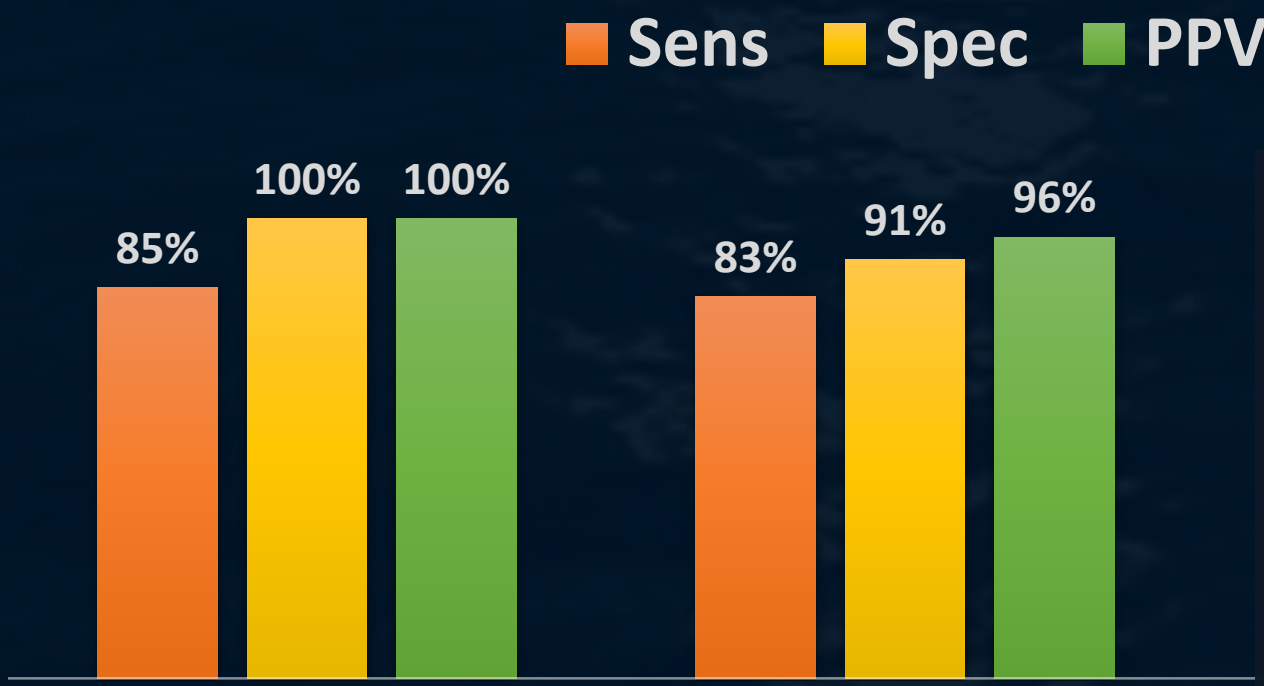
Jaroszewicz, et al. J Hepatol 2010

Baseline HBV DNA or HBsAg as Predictor of Active Disease in HBV-D

- 209 HBeAg-neg patients
- Tests every 1 month for 1 yr. then every 3 months thereafter
- **Inactive carrier** = HBV DNA ≤2,000 IU/ml and normal ALT
- **Active disease** = HBV DNA >2,000 IU/ml ± elevated ALT

Brunetto, et al. Gastroenterology 2010

Baseline HBV DNA or HBsAg as Predictor of Active Disease in HBV-D



Brunetto, et al. Gastroenterology 2010

Persistently or increasing HBsAg (≥1,000) Associated with Increased HCC

Subanalysis of 980/1068 (92%) with repeat serum at year 3

		Patients, n (%)	Adjusted HR[a] (95% CI)	*P* value
Serum HBV DNA level, *IU/mL*				
At baseline	At year 3			
<2000	<2000	842 (85.9)	1.0	
<2000	≥2000	138 (14.1)	2.0 (0.9–4.4)	.104
Serum HBsAg level *IU/mL*				
At baseline	At year 3			
<1000	<1000	493 (50.3)	1.0	
<1000	≥1000	129 (13.2)	14.4 (3.3–62.7)	<.001
≥1000	<1000	33 (3.4)	5.5 (0.5–57.2)	.151
≥1000	≥1000	325 (33.2)	16.6 (4.4–63.6)	<.001

Tseng, et al. Gastroenterology 2012

Will HBsAg quantification affect threshold for treatment?

- Does it influence probability of complications?
  - HBsAg ≥1,000 IU/mL = Increased risk of cirrhosis and HCC in 2 large Taiwanese cohorts (REVEAL-HBV & ERADICATE-B)
  - Studies with serial measurements needed
- Does it re-classify patients with chronic HBV infection?
  - Combined baseline HBsAg and HBV DNA appears to have high accuracy
  - Larger studies with different genotypes needed
- **HBsAg levels complementary but cannot be used as sole marker in treatment decisions**

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Is HBsAg useful for predicting response/ non-response to treatment?

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PEG-IFN in HBeAg+ve: Treatment Failure Prediction Using HBsAg

Study	N	PEG-IFN a2a/a2b	Cut-off	NPV	Tx week	Genotypes
Sonneveld, et al. Hepatology 2010	202	a2b	No decline	97%	12	A & D
Piratvisuth, et al. Hepatology 2011	678	a2a	No decline	71-82%	12	B & C
Lau, et al. J Hepatol 2009	510	a2a	>20,000 IU/mL	84%	12	B & C
Gane, et al. J Hepatol 2011	114	a2a	>20,000 IU/mL	100%	12	B & C
Chan, et al. APT 2010	92	a2a/a2b	>300 IU/mL + <1 log decline	85%	24	B & C

PEG-IFN in HBeAg+ve: Treatment Success Prediction Using HBsAg

Study	N	PEG-IFN a2a/a2b	Cut-off	PPV	Tx week	Genotypes
Sonneveld, et al. Hepatology 2010	202	a2b	<1,500 IU/mL	55%	12	A & D
Lau, et al. J Hepatol 2009	510	a2a	<1,500 IU/mL	51%	12	B & C
Gane, et al. J Hepatol 2011	114	a2a	<1,500 IU/mL	58%	12	B & C
Chan, et al. APT 2010	92	a2a/a2b	<1,500 IU/mL	46%	12	B & C
			<300 IU/mL + >1 log decline	75%	24	

PEG-IFN in HBeAg-ve: Treatment Failure Prediction Using HBsAg

Study	N	PEG-IFN a2a/a2b	Cut-off	NPV	Tx week	Genotypes
Marcellin, et al. Hepatol Int 2010	120	a2a	<10% decline	84%	12	B, C & D
Moucari, et al. Hepatology 2009	48	a2a	<0.5 log decline	90%	12	A, B & D
Rijckborst, et al. Hepatology 2010	102	a2a	No decline + DNA <2 log dec.	100%	12	A & D
Rijckborst, et al. J Hepatol 2012	160	a2a	No decline + DNA <2 log dec.	95%	12	A & D
Peng, et al. APT 2012	61	a2a	No decline + DNA <2 log dec.	75%	12	B & C

PEG-IFN in HBeAg-ve: Treatment Success Prediction Using HBsAg

Study	N	PEG-IFN a2a/a2b	Cut-off	PPV	Tx week	Genotypes
Marcellin, et al. Hepatol Int 2010	120	a2a	>10% decline	47%	12	B, C & D
Moucari, et al. Hepatology 2009	48	a2a	>0.5 log decline	89%	12	A, B & D
Rijckborst, et al. Hepatology 2010	102	a2a	sAg decline + DNA ≥2 log dec.	27%	12	A & D
Rijckborst, et al. J Hepatol 2012	160	a2a	sAg decline + DNA ≥2 log dec.	34%	12	A & D
Peng, et al. APT 2012	61	a2a	sAg decline + DNA ≥2 log dec.	61%	12	B & C

Optimal Prediction Cut-offs Vary Between Genotypes

Genotype	HBsAg wk 48 (IU/mL)	Sustained immune control	PPV/NPV
A (n=13)	<400	75%	PPV = 75%
	≥400	0%	NPV = 100%
B (n=64)	<50	47%	PPV = 47%
	≥50	0%	NPV = 100%
C (n=91)	<75	71%	PPV = 71%
	≥75	20%	NPV = 80%
D (n=31)	<1,000	75%	PPV = 75%
	≥1,000	17%	NPV = 83%

Brunetto, et al. J Hepatol *(in press)*

HBsAg in PEG-IFN Treatment

- HBsAg has moderate PPV for treatment response (HBeAg+ve and –ve). Can be used only to encourage compliance
- ~15% will respond despite poor HBsAg response (HBeAg+ve)
- Combined HBV DNA and HBsAg response (HBeAg-ve) has high NPV but appears to be genotype-related

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Use of HBsAg in NA Treatment

- HBsAg decline is slow (HBeAg+ve > HBeAg-ve) and does not correlate with HBV DNA decline
  - Higher baseline HBsAg and rapid decline associated with HBsAg loss (TDF)
  - HBsAg at end-of-treatment predictive of sustained response in HBeAg-ve (LAM)
- Clinical role is currently limited

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Chan, et al. J Hepatol 2011; Heathcote, et al. Gastroenterology 2010; Chan, et al. Antivi Ther 2011; Papatheodoridis, et al. J Hepatol (in press); Cho, et al. Hepatology 2013 (abs 1005)


Thank You and Welcome to Cebu!
stinations
Cebu
It's more fun in the Philippines!
Sinulog festival, Cebu City