HBV prevalence estimated by nationwide survey in Cambodia

The sero-epidemiological study on the prevalence of hepatitis B among children and mothers in the Kingdom of Cambodia

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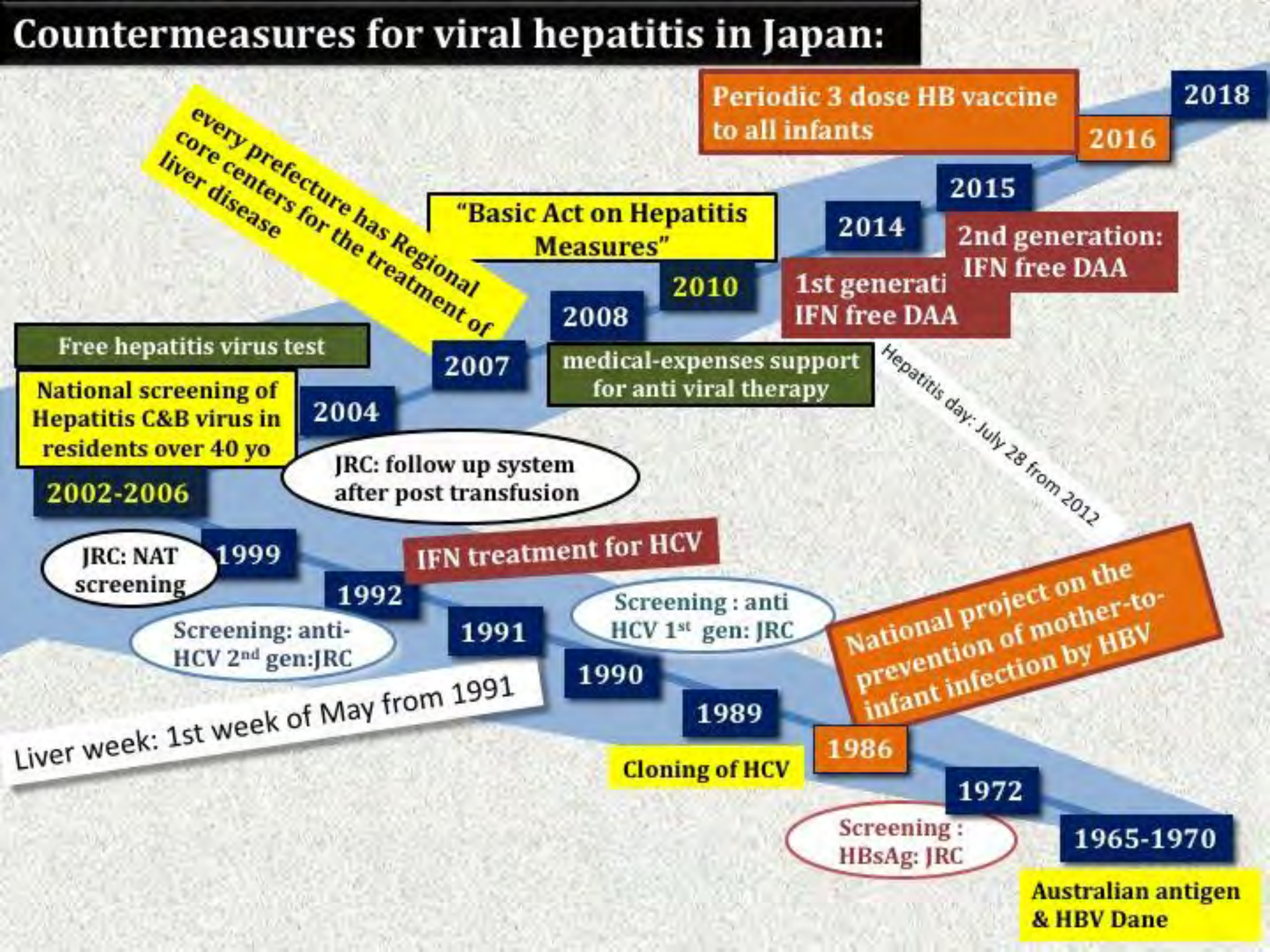
2018. July 25
Hà Nội Vietnam

Countermeasures for viral hepatitis in Japan:



Epidemiological Study in Cambodia so far

2009
2010
2011
2012
2013
2014
2015
2016
2017

Pilot sero-epidemiological study on hepatitis B and C infection among school children and adults in Siem Reap, Cambodia
2010-2014 1th - 8th

Health and dental check-up in Sasar Sdam Elementary School, Siem Reap, Cambodia

Hiroshima Univ.
NGO Hiroshima
Cooperated with MoH

Pilot study on school health check-ups system among school children in elementary school attached to Teacher training school

approved by

- ***Ethic committee for research science, Hiroshima University***
- ***Cambodia National Ethics Committee for Health Research (NECHR)***

Hepatology Research 2015; 45: 480–487 doi: 10.1111/hepr.12367

Short Communication

Seroprevalence, genotypic distribution and potential risk factors of hepatitis B and C virus infections among adults in Siem Reap, Cambodia

Hiroko Yamada,[1] Noboru Goto,[3] M
Keiko Katayama,[1]

[1]Department of Epide
Sciences, [3]Departmen
Hiroshima, [4]Miyakaw
Cambodia

2015
prevalence

PLOS | ONE

RESEARCH ARTICLE

Hepatitis E Virus in Cambodia: Prevalence among the General Population and Complete Genome Sequence of Genotype 4

Hiroko Yam
Sirany Hok[1]
Keiko Kata

1 Department
Health Scienc
General Hosp
College, Phur
School of Soc

* [illegible]

PLOS ONE | DOI:10.1371/jou

2015
Prevalence, incidence,
sequence or HEV

Hepatology Research 2017 doi: 10.1111/hepr.12941

Original Article

A seroepidemiological survey of the effect of hepatitis B vaccine and hepatitis B and C virus infections among elementary school students in Siem Reap province, Cambodia

Mayumi Fujimoto,[1] Channarena Chuon,[1] Shintaro Nagashima,[1] Chikako Yamamoto,[1] Ko Ko,[1] Somana Svay,[2] Sirany Hok,[2] Olline Lim,[2] Masayuki Ohisa,[1] Tomoyuki Akita,[1] Keiko Katayama,[1] Junko Matsuo,[1] Kazuaki Takahashi[3] and Junko Tanaka[1]

[1]Department of Epidemiology Infectious Disease Control and Prevention, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, [2]Department of Medical Sciences, Toshiba General Hospital, Tokyo, Japan and [3]Ministry of Health, Phnom Penh, Cambodia

2017
Incidence, prevalence

published references of HBV prevalence in Cambodia

Author	Year	Study design	Study Subject	Study Area	Sample size	positivity of HBsAg
Soeung et al.,	2009	Cross Sectional	5 years old	Most developed area	598	**3.2**
				Moderate developed area	830	**2.9**
				Least developed area	130	**8.5**
Mao et al.,	2013	Cross Sectional	4-5 years old	PP(Urban)	1196	**0.3**
				Kratie (Rural)	569	**1.4**
★				Steung Treng (Remote)	637	**3.5**
Fujimoto et al.,	2017	Cross Sectional	Elementary School student 7-	Siem Reap	248	**2.0**
Ol et al.,	2009	Cross Sectional	Voluntary Blood Donor	Battambang (Remote)	600	**6.5**
★				Pailin (Urban)	600	**8.8**
Yamada et al.,	2015	Cross Sectional	18- 89 years old	Siem Reap	483	**4.6**
Samati et al,	2003	Cross Sectional	General population	Sdau Village, Kratie	164	**9.1**

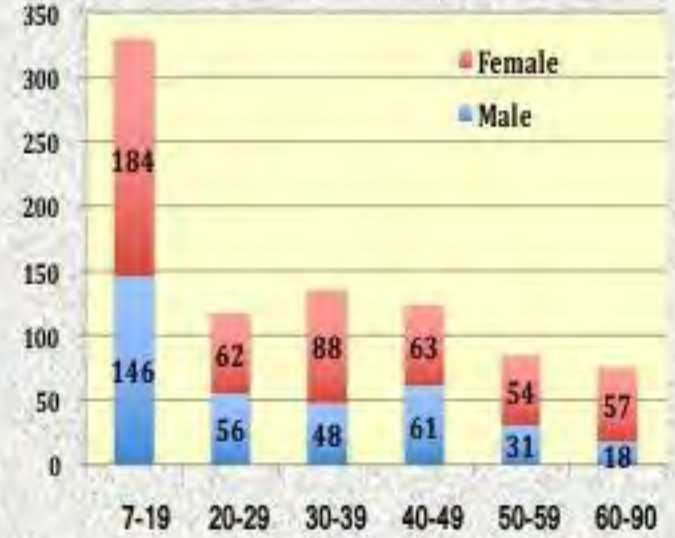
Subject of the sero-prelvalence study of HBV and HCV infection in Kingdom of Cambodia

Siem Reap province 2010-2014 N=868

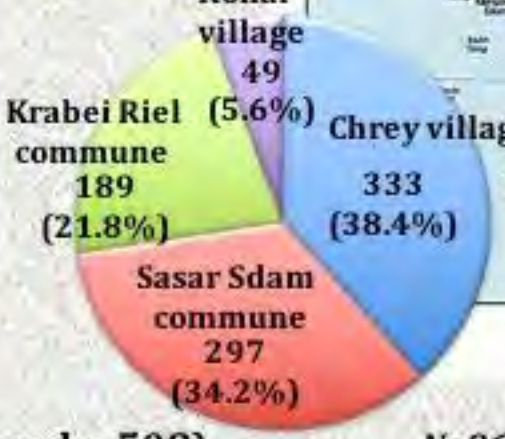
Survey period ➢ 2010.2～2014.8 (8 times)

Subjects N=868

- The general population in Siem Reap province:
- Chrey village, Krabei Riel commune, Rohal village, Sasar Sdam commune



【Location】



N=868

【Occupation】

N=868

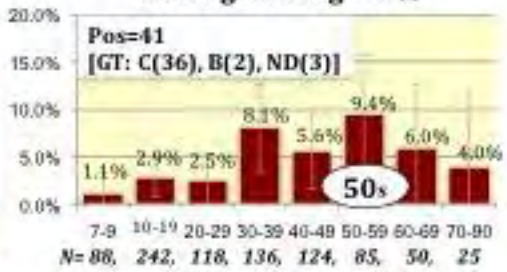
Subjects: 868 people (Male: 360, Female: 508)
Ages: 7-90 years old (as of 2014)
mean: 30.5±18.8, median: 29 years old

Yamada H, Tanaka J et al: Hepatol Res. 2015;45(4):480-7.

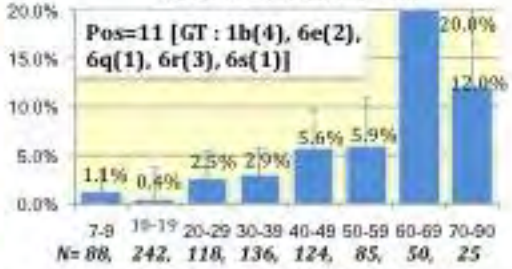
Prevalence of HBV and HCV among residents based on Sero-epidemiological study in Kingdom of Cambodia

Siem Reap province 2010-2014 N=868

Average HBsAg 4.7%

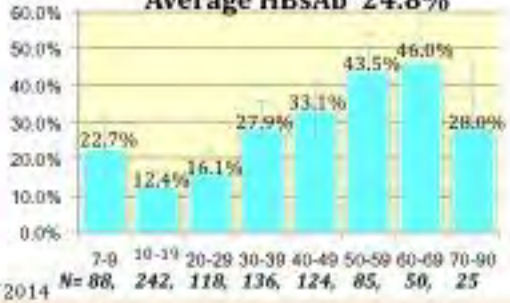


Average anti-HCV 3.9%
but.. HCV RNA 1.3%



Average HBcAb 28.3%

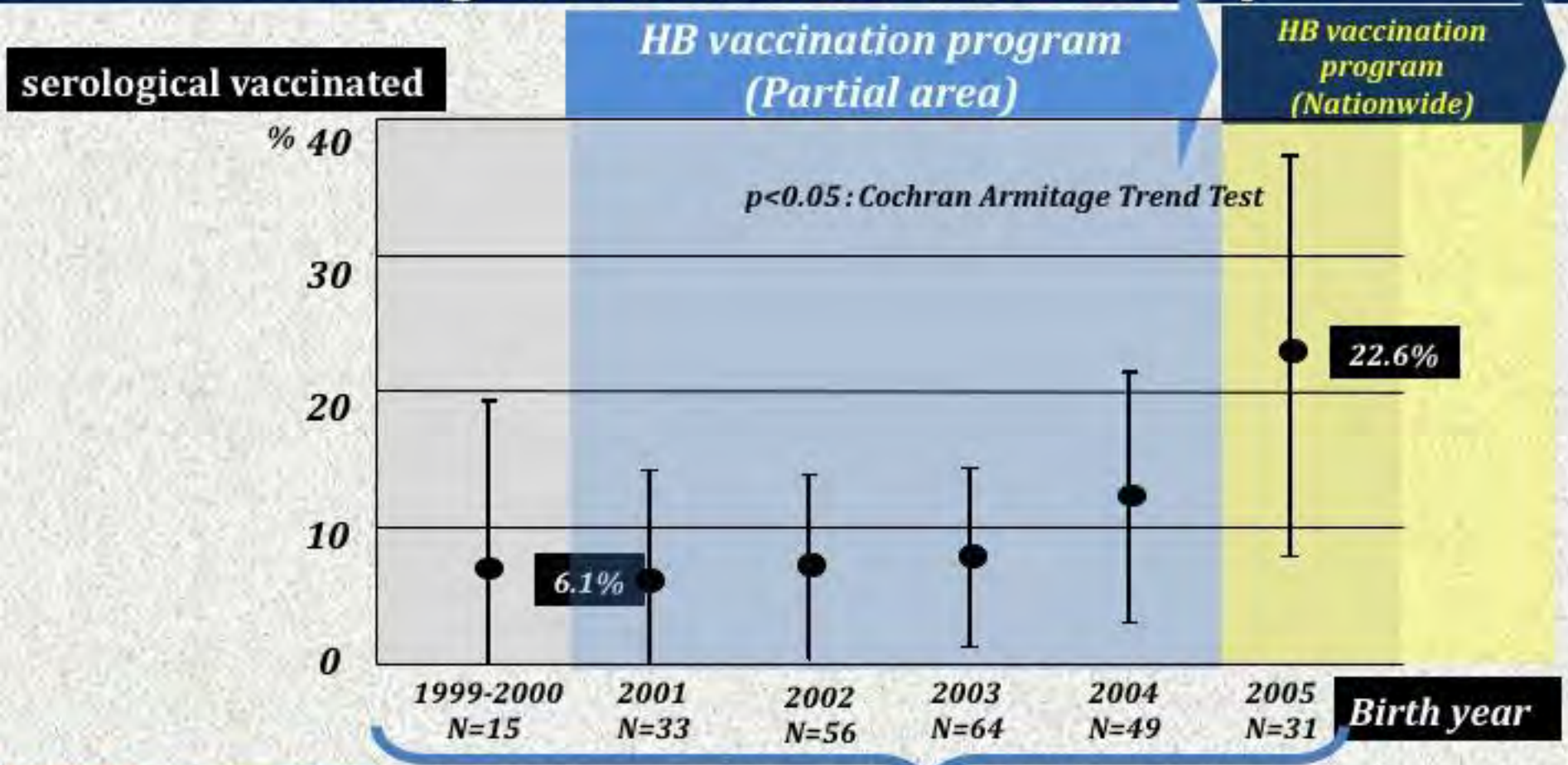
Average HBsAb 24.8%



Age as of 2014

- Yamada H, Takahashi K, Lim O, Svay S, Chuon C, Hok S, Do SH, ... Tanaka J. Hepatitis E Virus in Cambodia: *PLoS One. 10(8):e0136903, 2015*
- Yamada H, Fujimoto M, Svay S, Lim O,,.. Tanaka J. Seroprevalence, genotypic distribution and potential risk factors of hepatitis B and C virus infections among adults in Siem Reap, Cambodia. *Hepatol Res.* 45(4):480-7.2015

"Serological vaccinated rate" classified by birth year among 248 school children in Siem Reap



HBsAg	anti-HBc	anti-HBs	Status
Positive	Positive	Positive	HBV Carrier
		Negative	
	Negative	Positive	
		Negative	
Negative	Positive	Positive	Previous infection
		Negative	
	Negative	Positive	Serological Vaccinated
		Negative	Not infected

average 10.1%

Fujimoto M, Tanaka J et al:
Hepatol Res. 2017. doi: 10.1111

Analyzed by Hiroshima Univ.

The sero-epidemiological study on the prevalence of hepatitis B among children and mothers in the Kingdom of Cambodia

HIROSHIMA UNIVERSITY

University of Health Sciences

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

2018. July 25
Hà Nội Vietnam

"The sero-epidemiological study on the prevalence of hepatitis B among children and mothers in the Kingdom of Cambodia"

Principle investigator:

•**Junko Tanaka, PhD, Professor**, Department of Epidemiology Infectious Disease Control and Prevention, Institute of Biomedical and Health Sciences, Hiroshima University, Japan; Director, Project Research Center for epidemiology and prevention of viral hepatitis and hepatocellular carcinoma, Hiroshima University; and Assistant Director, the Research Center for Hepatitis and Immunology, National Center for Global Health and Medicine, Japan

Co-Principle Investigators

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•**Annemarie Wasley, ScD, Technical Officer,** U.S. Centers for Diseases Control and Prevention, Atlanta, Georgia

•**Md. Shafiqul Hossain, MBBS, MPH, Technical Officer**, Expanded Programme on Immunization, World Health Organization Country Office, Cambodia

•**Mao Bunsoth, MD,** University of Health Sciences, Phnom Penh, Cambodia

- **Ork Vichit, Manager,** National Immunization Program (NIP), Ministry of Health, Cambodia
- **Hok Sirany, MD**, Focal Point for Viral Hepatitis, Department of Preventive Medicine, Ministry of Health, Cambodia

Sampling Method

Multistage stratified random sampling

- **Seventy communes** were randomly selected among three strata: Phnom Penh; urban non Phnom Penh; and rural.
- **Four villages** were selected among each communes. (Totally 70*4 villages)
- **Nine children and their mothers** were selected in each village (Totally 70*4*9 = 2,520 pairs of child and his/her mother)

Sample size: 2,520 children & their mother (Totally 5,040)

$n = (Z_{1-\alpha/2})^2 * [p\,(1-p) / d^2] * \text{Deff} * (1/R)$

With

p: assumed prevalence of HBsAg = 1.41%
d: absolute precision = 0.5%
confidence level = 95%, $Z_{1-\alpha/2} = 1.96$
Deff: design effect =1.15
R: response rate = 97.5%

Analyzed by Hiroshima Univ.

Method

【*Study design*】 Nation-wide

A cross sectional sampling strategy with random selection

【*Subject*】

1) **children aged 5 - 7 years of age** who were born since implementation of widespread infant immunization

2) **children's mothers**, most of whom were born befo introduction of hepatitis B va starting in 2001.

HemaSpot

【Investigations】

1)Questionnaire: 40 questio C)

2) **Rapid test and DBS**

3) (A subset of subjects) **Venipun e**

【*ethical considerations*】

The survey will be conducted in accordance wi 10 and Cambodia's ethical idelines on research involving human subjects. The study mitted to the ethics co nittee for epidemiological research at Hiroshima University is in compliance to th Ethical Guidelines for Medical and Health Research Involvi Su ts ub by the Ministry of Health and Welfare in Japan and the Cambo ion thics nittee fo Health Research (NECHR) for approval.

Analyzed by Hiroshima Univ.

Nationwide Survey　2017.3.6～4.6

Laboratory testing

【***Definitions of study subjects HBV status***】

- Chronic HBV infection: participants with a positive HBsAg test
- Not currently infected with HBV: participants with a negative HBsAg test

【***Laboratory testing***】

The following point-of-care HBV marker will be tested in the field:

- **Rapid HBsAg testing** will be tested with Abbott Determine test strip using 50 microliters of blood (1 drop); Dainabot Co. Ltd, Tokyo, Japan

The following HBV and HCV markers will be tested in Hiroshima University, Japan for all samples using DBS and venipuncture-derived serum samples:

- **HBsAg** will be tested by CLEIA with Lumipulse II; Fujirebio, Tokyo Japan.
- **Anti-HBs** will be tested by CLEIA with Lumipulse II; Fujirebio, Tokyo Japan.
- **Anti-HBc** will be tested by CLEIA with Lumipulse II; Fujirebio, Tokyo Japan.
- **Anti-HCV** will be tested by CLEIA with Lumipulse II Ortho HCV; Ortho Clinical Diagnostics, Tokyo, Japan.
  - In HBsAg or anti-HCV positive cases, **HBV DNA** or **HCV RNA** will be also tested by real-time PCR, respectively.

Result of today's presentation

1. **HBsAg positivity of Children and their mothers**

   tested by Rapid HBsAg testing, Dainabot Co. Ltd, Tokyo, Japan

2. **HB vaccination coverage** by questionnaire

3. **HBsAg positivity of Children** by **HB vaccination coverage**

4. **"serologically vaccinated rate" by DBS**

5. **The risk analysis of HBsAg positivity of Children**

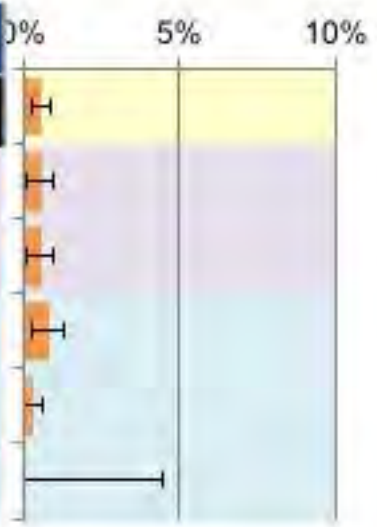
Analyzed by Hiroshima Univ.

1. HBsAg positivity of Children and their mothers

tested by Rapid HBsAg testing, Dainabot Co. Ltd, Tokyo, Japan (rapid test)

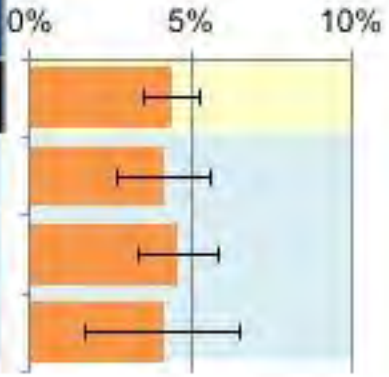
Children (N=2,520)

	N	Positives	HBsAg positivity	(95%CI)	
Total	2520	14	0.56%	(0.27%-	0.85%)
Male	1275	7	0.55%	(0.14%-	0.95%)
Female	1245	7	0.56%	(0.15%-	0.98%)
5 years old	1237	10	0.81%	(0.31%-	1.31%)
6 years old	1200	4	0.33%	(0.01%-	0.66%)
7 years old	83	0	0.00%	(0.00%-	4.44%)



Mothers (N=2,026)

	N	Positivse	HBsAg positivity	(95%CI)	
Total	2026	89	4.39%	(3.50%-	5.29%)
under29	698	29	4.15%	(2.67%-	5.64%)
30-39	1063	49	4.61%	(3.35%-	5.87%)
over40	265	11	4.15%	(1.75%-	6.55%)



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2. HB vaccination coverage

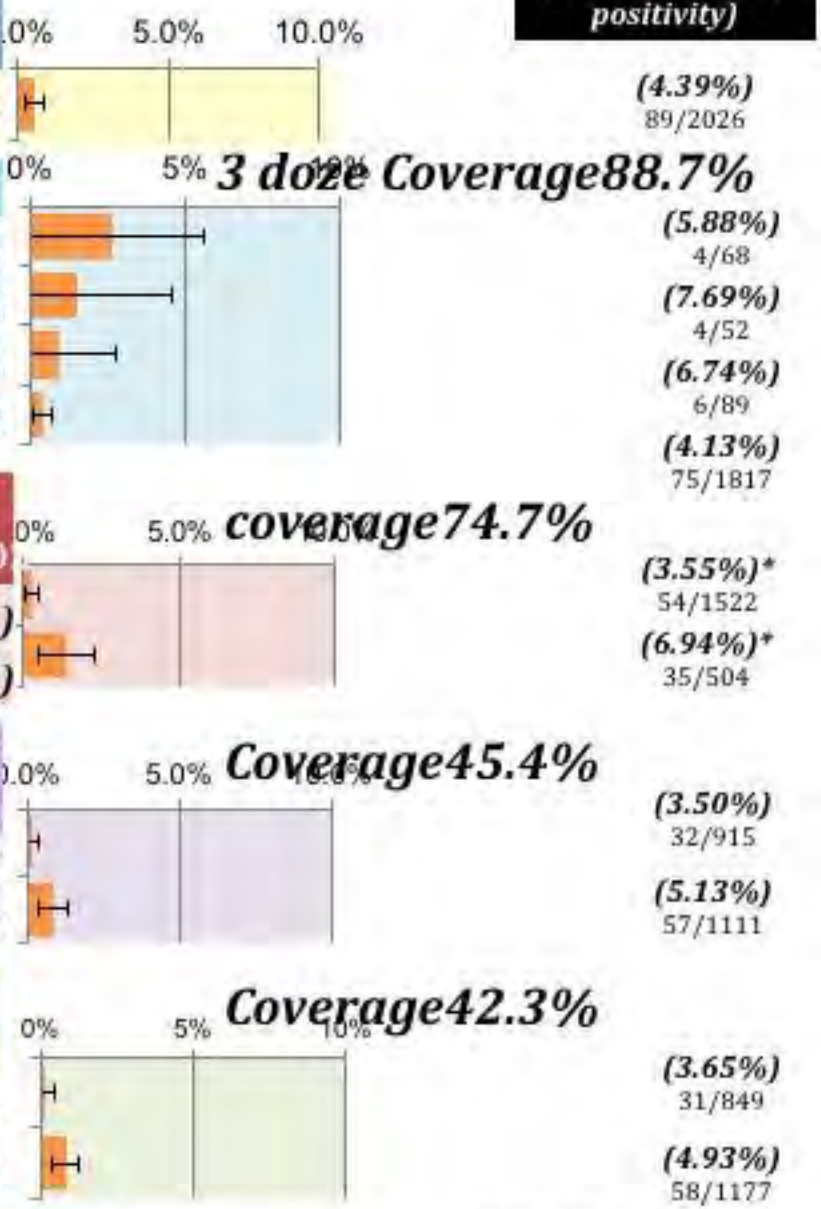
either birth dose or 3-dose pentavalent vaccine by questionnaire Q12,13,14

Birth dose coverage 78%

		Birth dose ≤7days						Birth dose ≤24h					
		Dosed	N	Coverage	95%CI		P-value	Dosed	N	Coverage	95%CI		P-value
Total		1882	2520	74.7%	73.0%	76.4%		1145	2520	45.4%	43.5%	47.4%	
Place where child was Born	Public hospital	420	512	82.0%	78.7%	85.4%	<0.0001	223	512	43.6%	39.3%	47.8%	<0.0001
	Health center	1065	1271	83.8%	81.8%	85.8%		747	1271	58.8%	56.1%	61.5%	
	At home	208	486	42.8%	38.4%	47.2%		87	486	17.9%	14.5%	21.3%	
	Other	189	248	76.2%	70.9%	81.5%		88	248	35.5%	29.5%	41.4%	
	Don't know	0	3	0.0%	0.0%	100.0%		0	3	0.0%	0.0%	100.0%	
The place of receiving most vaccines for child	Public hospital	65	73	89.0%	81.9%	96.2%	<0.0001	30	73	41.1%	29.8%	52.4%	<0.0001
	Health center	1518	1864	81.4%	79.7%	83.2%		915	1864	49.1%	46.8%	51.4%	
	Private clinic	8	8	100.0%	53.9%	100.0%		4	8	50.0%	15.4%	84.6%	
	Other place	286	520	55.0%	50.7%	59.3%		194	520	37.3%	33.2%	41.5%	
	Don't know	2	20	10.0%	0.0%	23.1%		0	20	0.0%	0.0%	18.4%	
	Never received vac.	3	35	8.6%	0.0%	17.8%		2	35	5.7%	0.0%	13.4%	
Age of mother	under 29 yrs	534	699	76.4%	73.2%	79.5%	0.1373	321	699	45.9%	42.2%	49.6%	NS
	30- 39 yrs	802	1063	75.4%	72.9%	78.0%		477	1063	44.9%	41.9%	47.9%	
	over 40 yrs	187	266	70.3%	64.8%	75.8%		117	266	44.0%	38.0%	50.0%	
Mother's Educational background	No/Primary	1045	1468	71.2%	68.9%	73.5%	<0.0001	645	1468	43.9%	41.4%	46.5%	NS
	JHS	367	438	83.8%	80.3%	87.2%		215	438	49.1%	44.4%	53.8%	
	HS/College/Univ	111	122	91.0%	85.9%	96.1%		55	122	45.1%	36.3%	53.9%	
Mother's HBsAg	Negative	1468	1937	75.8%	73.9%	77.7%	0.0013	883	1937	45.6%	43.4%	47.8%	NS
	Positive	54	89	60.7%	50.5%	70.8%		32	89	36.0%	26.0%	45.9%	

3. HBsAg positivity of Children categorized by their vaccination status

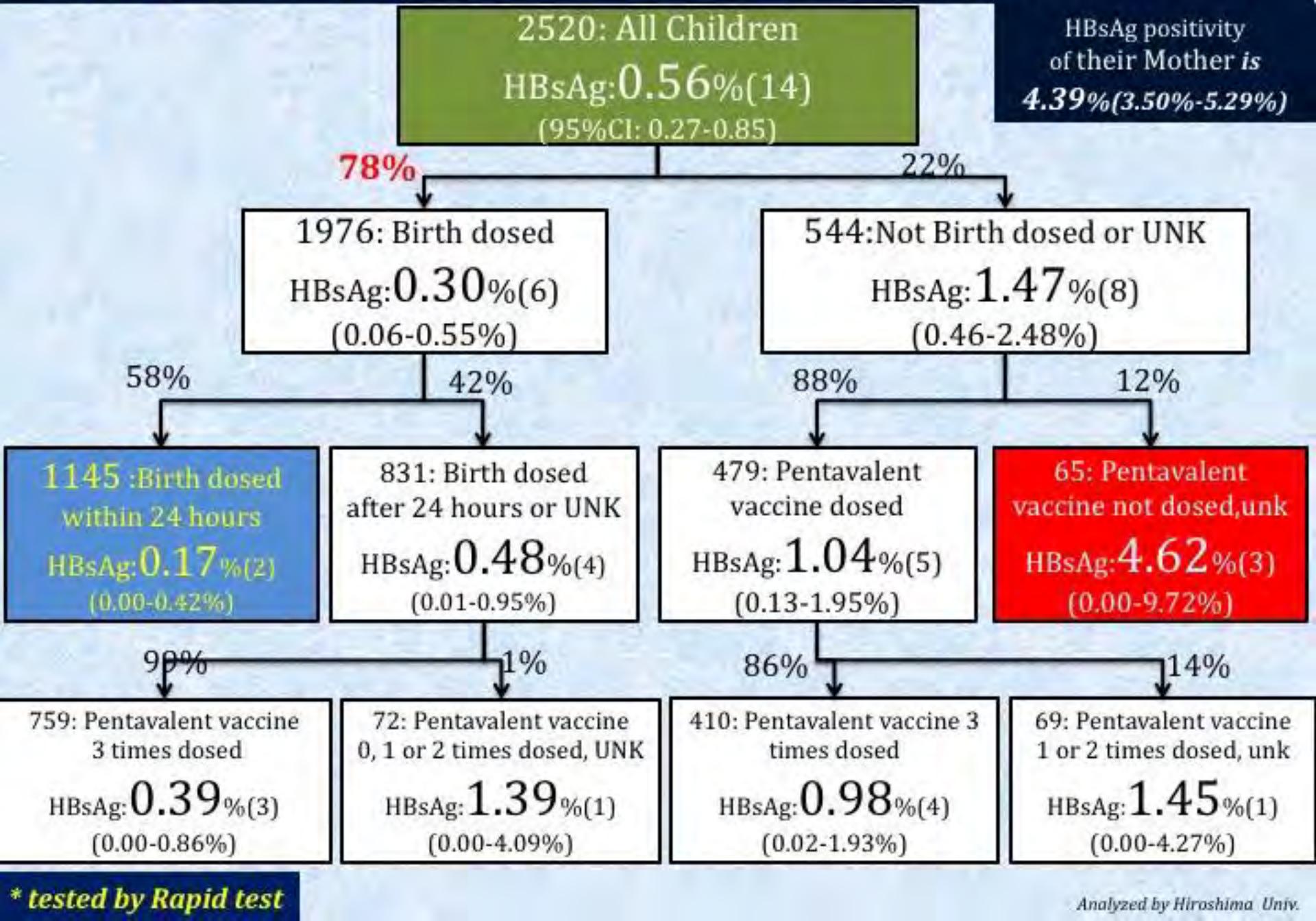
	N	Positivity of Child's HBsAg (95%CI)		(Mother's HBsAg positivity)
Total	**2520**	**14**	**0.6% (0.3%-0.8%)**	(4.39%) 89/2026
Child has received pentavalent vaccine P=0.010				3 doze Coverage88.7%
0 dose	114	3	2.6% (0.0% - 5.6%)	(5.88%) 4/68
1 dose	64	1	1.6% (0.0% - 4.6%)	(7.69%) 4/52
2 doses	107	1	0.9% (0.0% - 2.8%)	(6.74%) 6/89
3+ doses	2,235	9	0.4% (0.1% - 0.7%)	(4.13%) 75/1817
Child has received birth dose within 7 days P=0.00				coverage74.7%
Yes	1882	5	0.3% (0.0% - 0.5%)	(3.55%)* 54/1522
No	638	9	1.4% (0.5% - 2.3%)	(6.94%)* 35/504
Child has received birth dose within 24h P=0.038				Coverage45.4%
Yes	1145	2	0.2% (0.0% - 0.5%)	(3.50%) 32/915
No	1375	12	0.9% (0.4% - 1.4%)	(5.13%) 57/1111
Child has received birth dose within 24 hours & 3 doses of pentavalent vaccine NS				Coverage42.3%
Received	1066	2	0.2% (0.0% - 0.5%)	(3.65%) 31/849
Not Received	1454	12	0.8% (0.4% - 1.3%)	(4.93%) 58/1177



*Significant difference of mother's positivity among questionnaire categories

Analyzed by Hiroshima Univ.

HBsAg positivity of 2520 children classified by HB vaccine status



**** tested by Rapid test***

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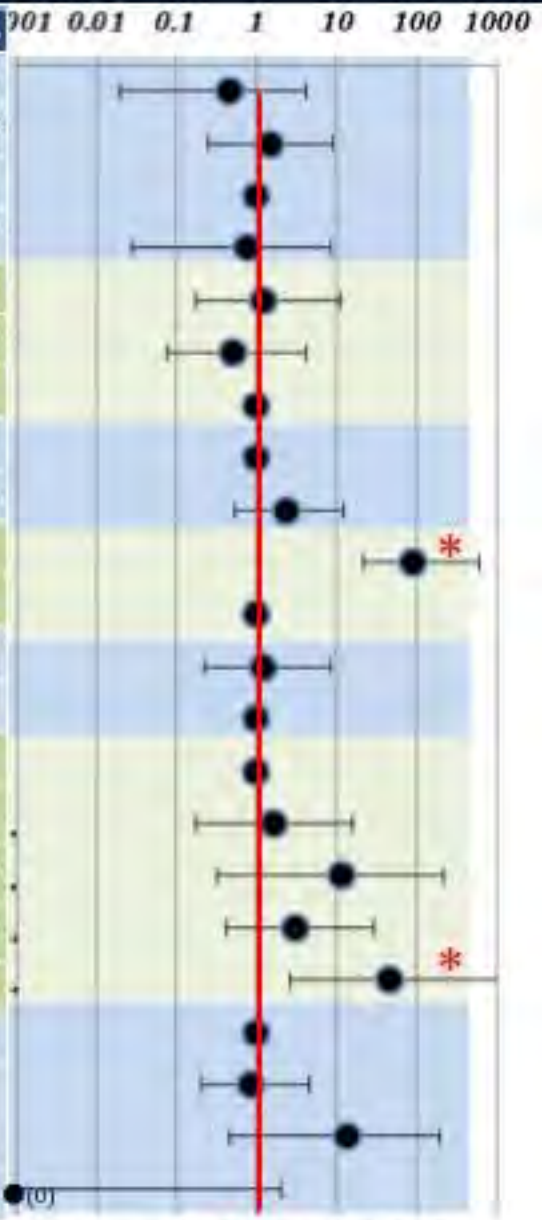
4. Multivariate- risk analysis of HBsAg positivity of Children *tested by Rapid test* <Logistic regression analysis>

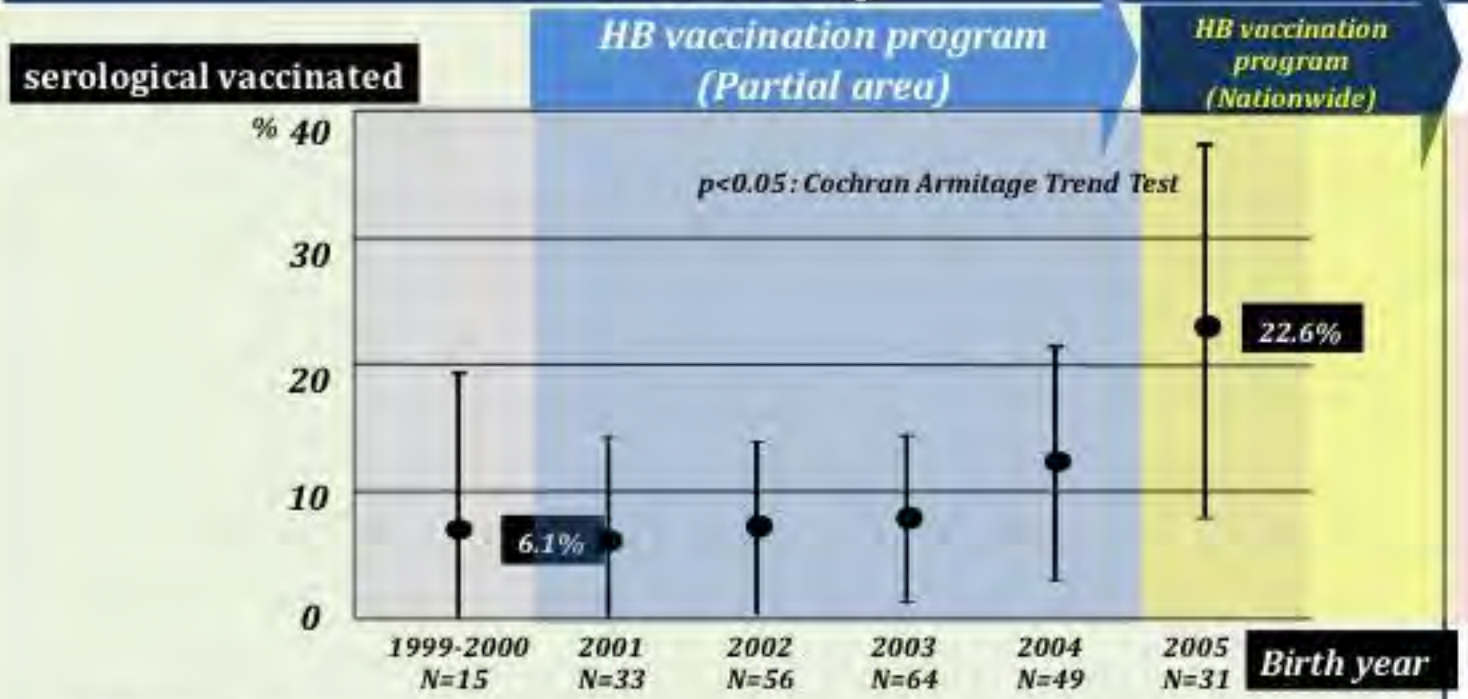
Factor		AOR	(95%CI)	p-value
Place where child was born	Public hospital	0.5	0.0-4.2	0.5474
	Health center	1.5	0.3-9.2	0.6427
	Home	1.0		
	Other	0.8	0.0-8.6	0.8497
Age of mother	under 29 yrs	1.2	0.2-11.1	0.8302
	30 - 39 yrs	0.5	0.1-4.3	0.4948
	over 40 yrs	1.0		
Total number of children in household	under 2	1.0		
	over 3	2.5	0.5-12.5	0.2508
Mother's HBsAg	Positive	91.2	21.3-588.8	<.0001
	Negative	1.0		
Mother has her child's immunization card	Yes/Seen at HC	1.2	0.2-8.8	0.8254
	No/unknown	1.0		
HB vaccine status of child	Birth dose<24h	1.0		
	Birth dose>24h & Penta. 3 times	1.7	0.2-16.0	0.631
	Birth dose>24h & Penta. 0-2 times	11.6	0.3-218.9	0.1139
	Birth dose none & Penta. 1-3 times	3.2	0.4-29.9	0.2648
	Birth dose none & Penta. none	46.5	2.7-104.9	0.0116
House roof	Tile	1.0		
	Metal/Aluminium	0.9	0.2-4.6	0.866
	Cement/Bricks	13.5	0.5-198.8	0.067
	Other	0.0	0.0-2.1	0.987



R^2=0.43, p<0.0001, N=2,000

"Serological vaccinated rate" among 248 school children in Siem Reap

Nationwide Cambodia 2017



Fujimoto M, Tanaka J et al: Hepatol Res. 2017. doi: 10.1111

HBsAg	anti-HBc	anti-HBs	Status
Positive	Positive	Positive	HBV Carrier
		Negative	
	Negative	Positive	
		Negative	
Negative	Positive	Positive	Previous infection
		Negative	
	Negative	Positive	Serological Vaccinated
		Negative	Not infected

SiemReap	Whole Cambodia
average 10.1%	average 29.8%

from the result of DBS sample

Analyzed by Hiroshima Univ.

Summary

1. **HBsAg Positivity of 2520 Children is 0.56% (95%CI: 0.27-0.85%)**
2. **That of their mothers is 4.39% (3.50-5.29%)**
3. **Coverage of birth dose HB vaccine is 78% and HBsAg positivity among them is 0.3%.**
4. **22% of children did not receive any birth dose HB vaccine and their positivity is 1.47%.**
5. **Coverage of birth dose HB vaccine within 24 hours is 45.5% and HBsAg positivity among them is 0.17%.**
6. **Controvertially, HBsAg positivity among children who never received any type of HB vaccine is 4.62%**
7. **The HB vaccine program is well practiced. However, it is desirable to further raise BD <24 hours vaccine coverage or to recommend to give birth dose vaccine at a hospital.**

Continue to next step.....

- ***Screening of pregnant*** ***to prevent vertical infection***
- ***Coverage of vaccine*** ***to prevent horizontal***

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- Dr. Ko Ko

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CDC
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Cambodia

NIP
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MoH
- Dr. Somana Svay
- Dr. Olline Lim
- Dr. Sirany Hok

UHS
- Prof. Saphonn Vonthanak
- Dr. Mao Bunsoth

◆Epidemiological Research Group on viral hepatitis, **Granted by MHLW**, Japan (PI: Junko Tanaka)