

Nov. 22, 2019

SCGO 18th Symposium on Maternal and Newborn Health

# Current status and future perspectives on cervical cancer prevention in Japan and in the world

Etsuko Miyagi, MD, Ph.D.

Chief Professor, Department of Obstetrics and Gynecology,  
Yokohama City University School of Medicine, Japan



**Disclosure**

**I have nothing to declare according to the instruction of COI in The Japan Society of Obstetrics and Gynecology.**

# Yokohama City University School of Medicine

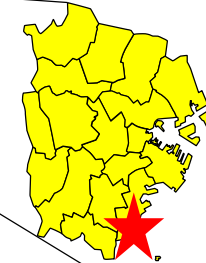
**Japan**



**Kanagawa  
Prefecture**



**Capital, Yokohama  
City (3,700,000  
population)**





**Do you think Japan is  
one of the **real** developed countries?**



**After The Great East Earthquake on March 11, 2011, Fukushima nuclear plant disaster occurred, and the areas are not livable even now.**



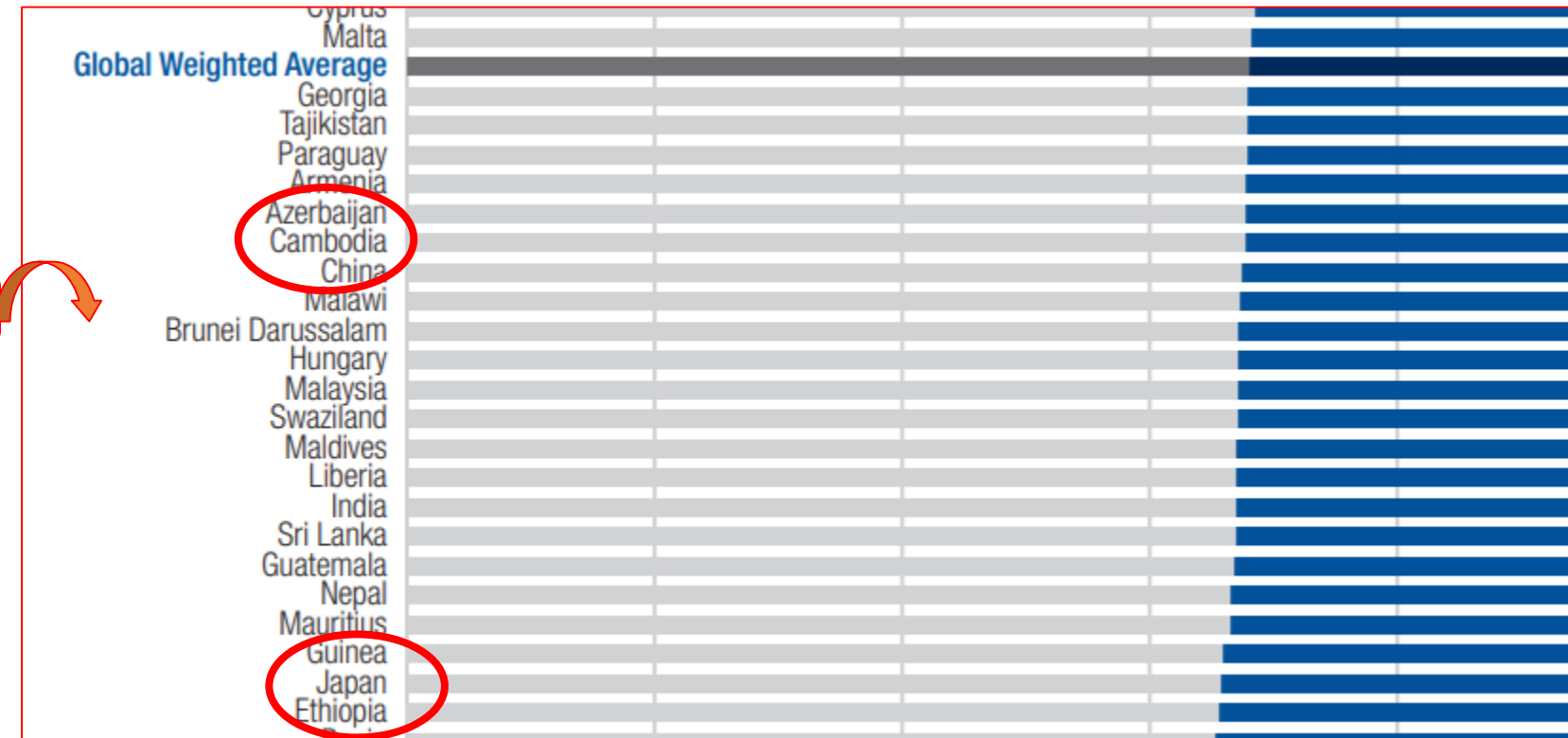
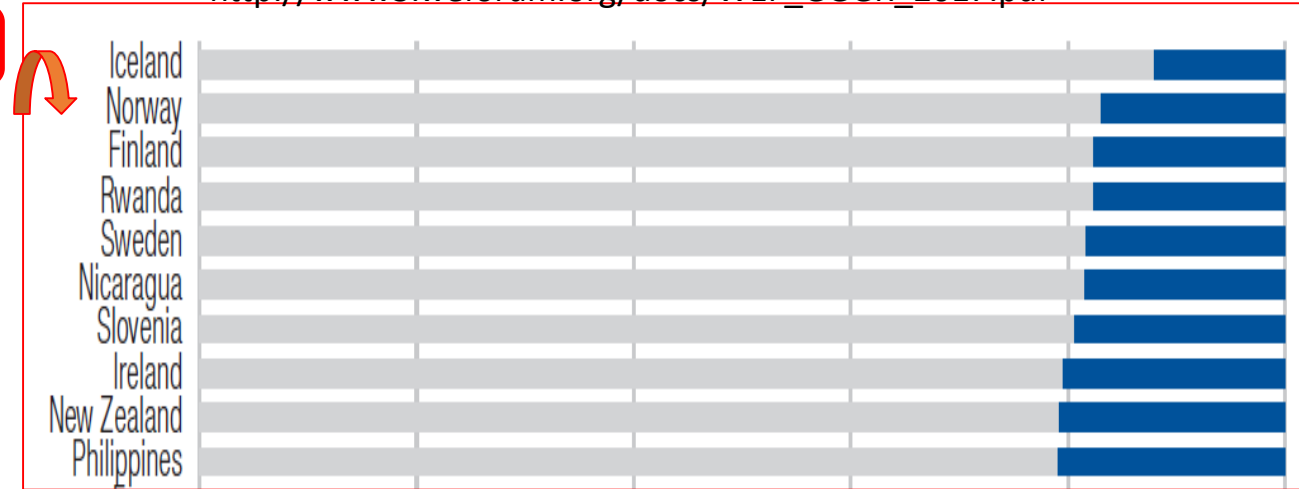
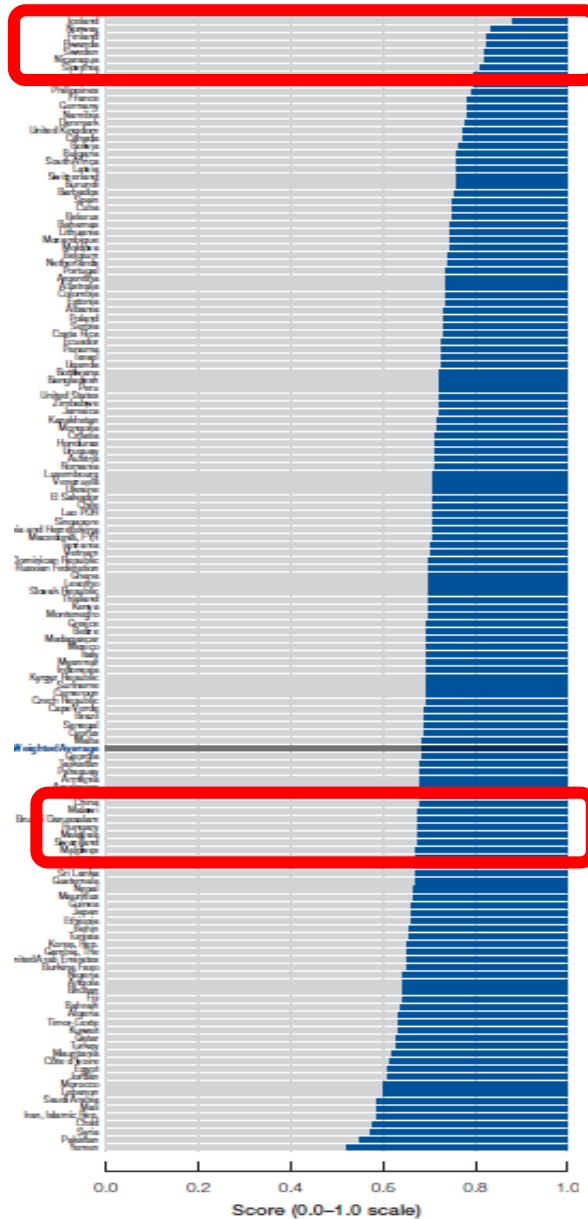
**After the heavy rain caused by the 19<sup>th</sup> big typhoon on Oct. 13, 2019, the 1<sup>st</sup> class rivers flooded over the fields, and more than 80 people died.**

**Thus, Japan has very fragile infrastructures against natural disasters.**



# Global Gender Gap by Country in 2017

[http://www3.weforum.org/docs/WEF\\_GGGR\\_2017.pdf](http://www3.weforum.org/docs/WEF_GGGR_2017.pdf)



## Gender Gap Index Score Ranking in East Asia and the Pacific, 2017

EAST ASIA AND THE PACIFIC		
Country	Overall rank	Overall score
New Zealand	9	0.791
Philippines	10	0.790
Australia	35	0.731
Mongolia	53	0.713
Lao PDR	64	0.703
Singapore	65	0.702
Vietnam	69	0.698
Thailand	75	0.694
Myanmar*	83	0.691
Indonesia	84	0.691
Cambodia	99	0.676
China	100	0.674
Brunei Darussalam	102	0.671
Malaysia	104	0.670
Japan	114	0.657
Korea, Rep.	118	0.650
Fiji*	125	0.638
Timor-Leste	128	0.628

[http://www3.weforum.org/docs/WEF\\_GGGR\\_2017.pdf](http://www3.weforum.org/docs/WEF_GGGR_2017.pdf)

## the japan times NEWS

**XX Medical University discriminated against female applicants by lowering entrance exam scores**

The practice likely began around 2010 and was apparently aimed at avoiding a shortage of doctors at affiliated hospitals. The medical college believed female doctors often resign or take long leave after getting married or giving birth, leading to a shortfall of medical doctors.

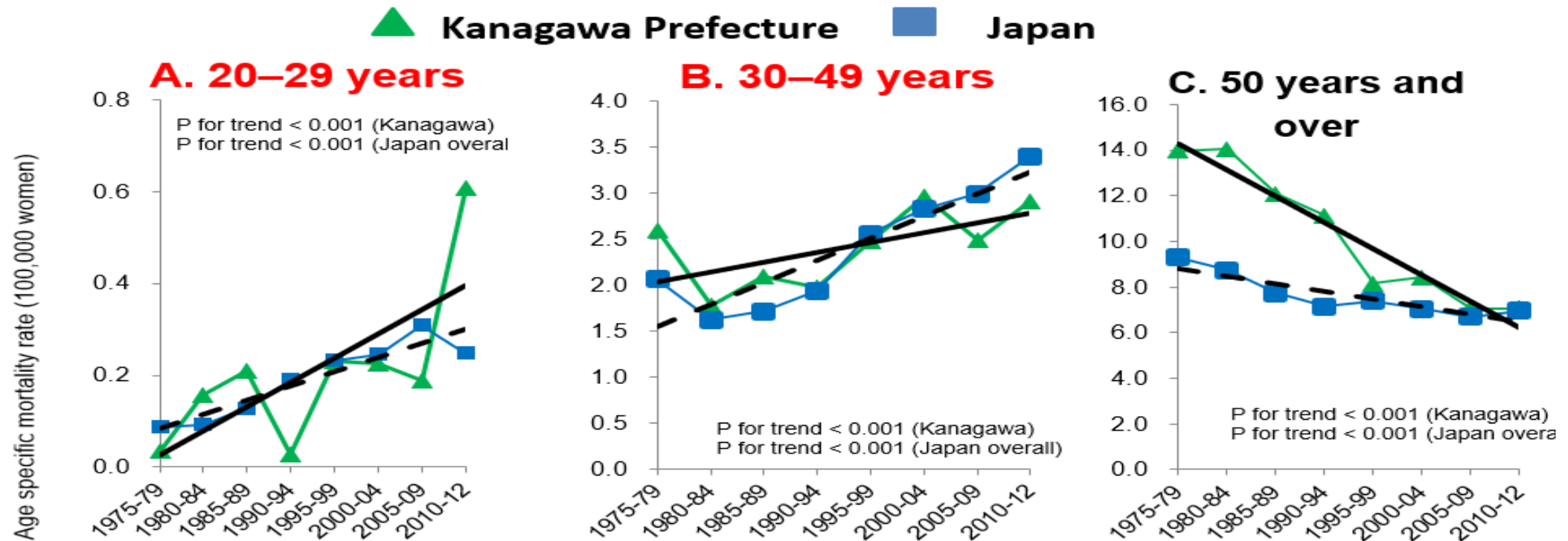
according to the sources.  
2018/8/2

<https://www.japantimes.co.jp/news/2018/08/02/>

Do you think Japan is  
one of the **real** developed countries?

Also In terms of cervical cancer prevention, I say “**No**”.

**Increasing trends in CC mortality rates  
among young women in Japan: 1975–2012**

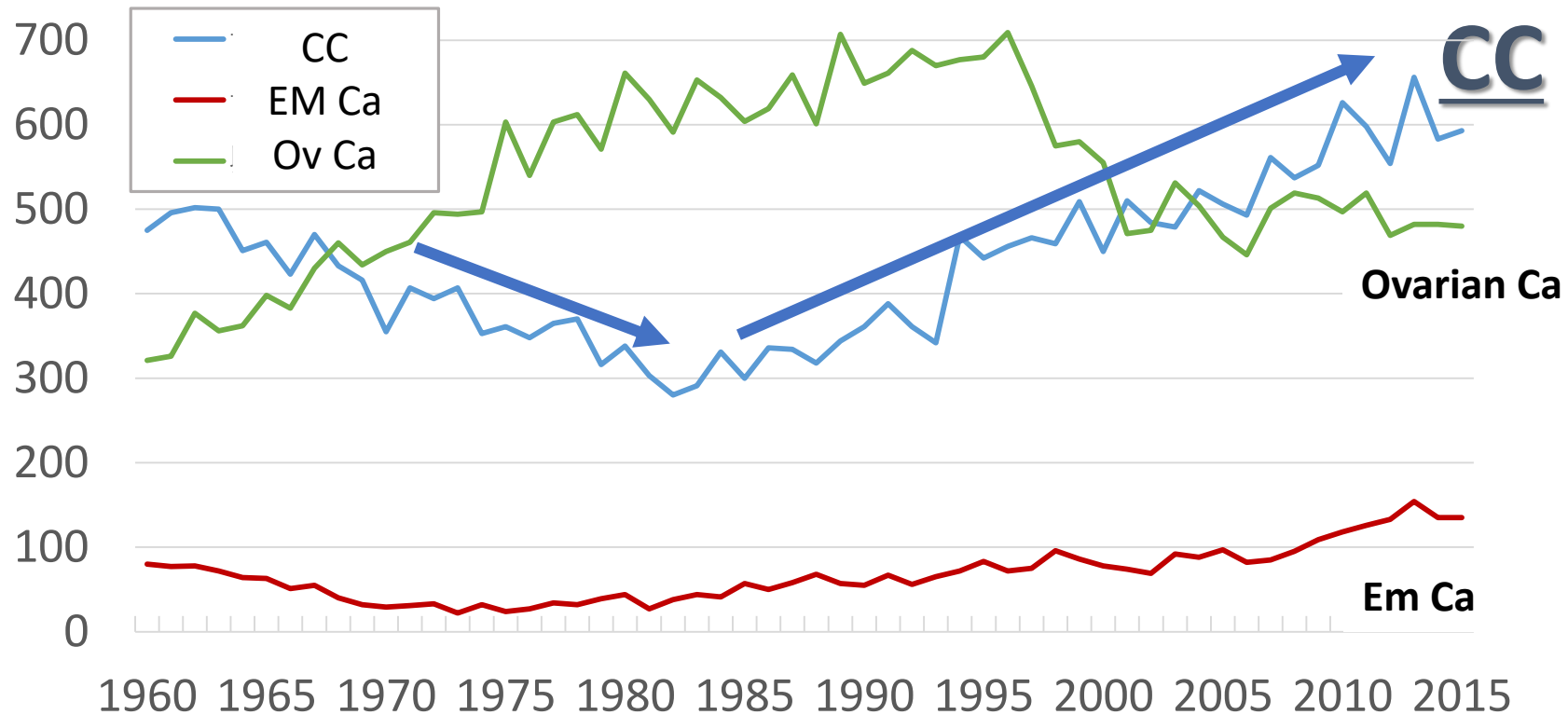


**I have seen many young patients die of CC every year!**

(Motoki, Miyagi et al. Cancer Epidemiology 2015; 39: 700-6)



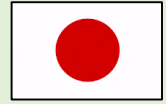
# Increasing number in CC mortality among under 50 years old women in Japan



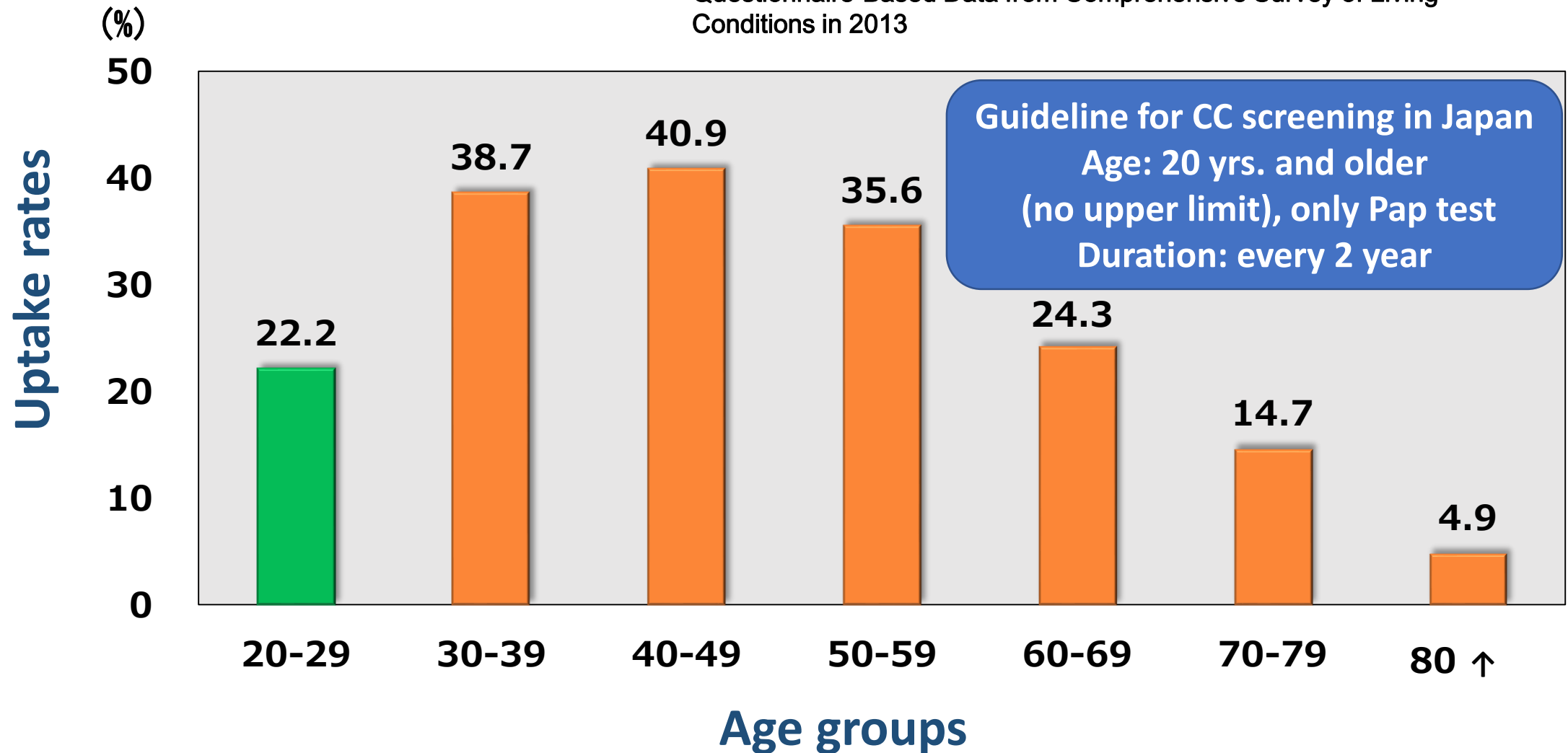
(Source: Center for Cancer Control and Information Services, National Cancer Center, Japan)

**Increasing trend in CC death is because of low uptakes of CC screening among young women and the failure of the system**

# Cervical cancer screening (Pap test) uptakes by age groups in Japan



Questionnaire-Based Data from Comprehensive Survey of Living  
Conditions in 2013



# Agenda

- 1. Partnership between Cambodian and Japan Societies of OB & Gyn through cervical cancer screening project**
- 2. Promotion of cervical cancer prevention with HPV vaccination & screening in the world as well as WHO strategy.**
- 3. Risk communication issues in promoting cervical cancer prevention in Japan**
- 4. Our research results about self-sampling HPV testing**



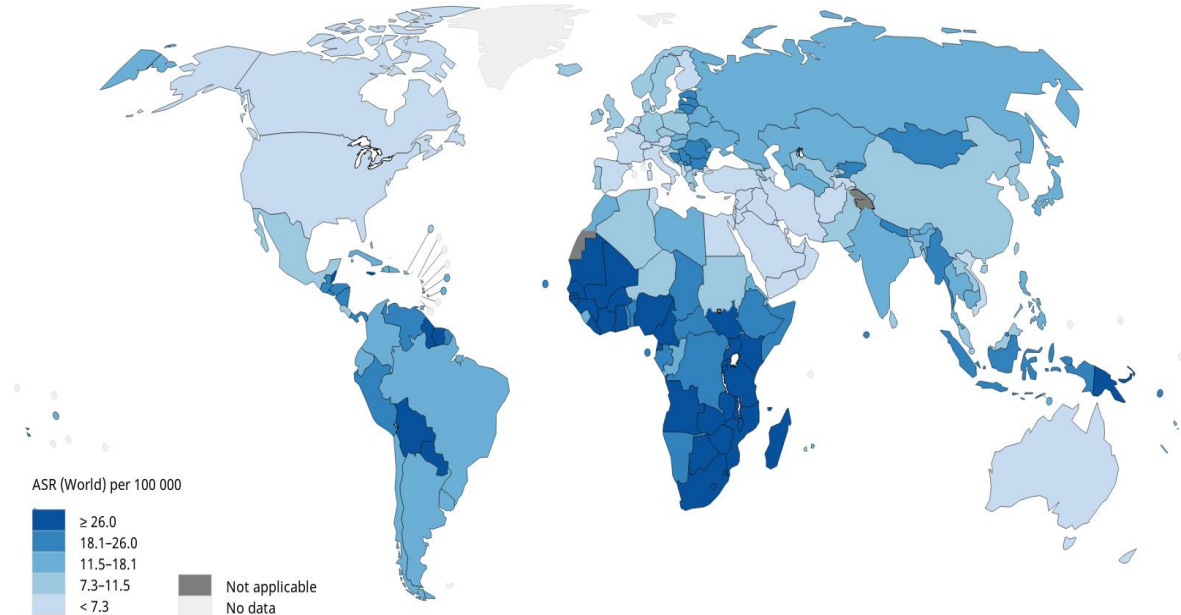
# Agenda

- 1. Partnership between Cambodian and Japan Societies of OB & Gyn through cervical cancer screening project**
2. Promotion of cervical cancer prevention with HPV vaccination & screening in the world as well as WHO strategy.
3. Risk communication issues in promoting cervical cancer prevention in Japan
4. Our research results about self-sampling HPV testing

# Incidence and mortality of CC

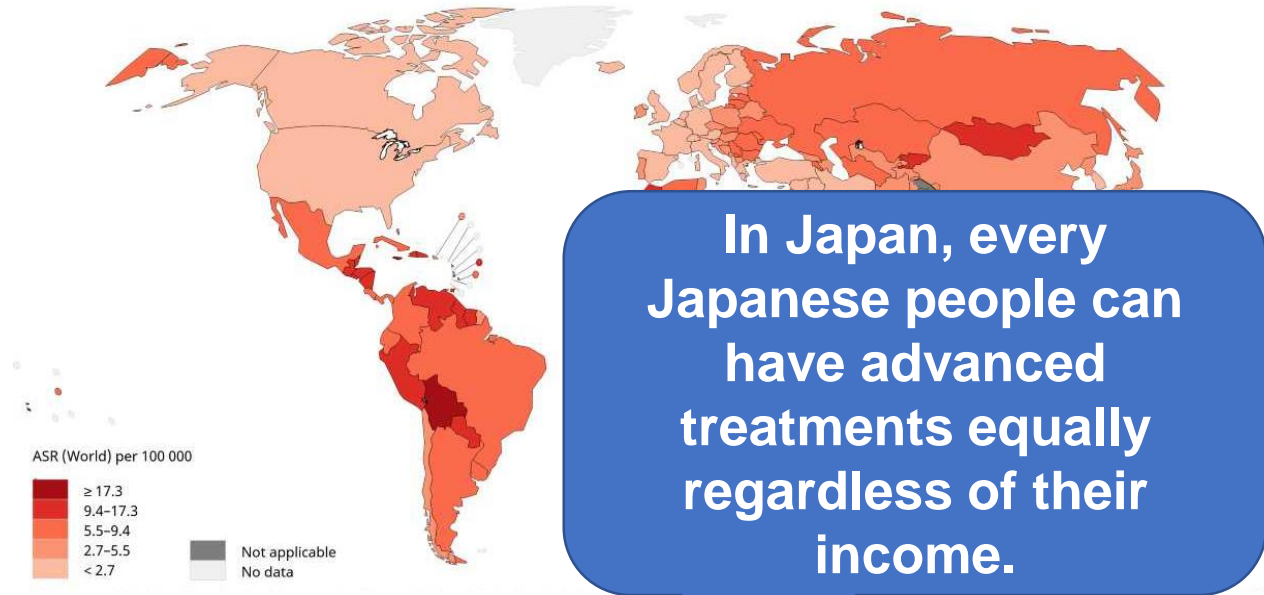


## Incidence



<b>Global</b>	<b>13.1 per 100,000 women</b>
<b>Cambodia</b>	<b>23.8 per 100,000 women</b>
<b>Japan</b>	<b>11.0 per 100,000 women (2015)</b>

## Mortality



<b>6.9 per 100,000 women</b>
<b>13.4 per 100,000 women</b>
<b>2.0 per 100,000 women (2017)</b>

In Japan, every Japanese people can have advanced treatments equally regardless of their income.

# SCGO-JSOG Joint Project - Women's Health and Cervical Cancer-



**Prof. Kimura (Osaka University)  
was JSOG vice-President in 2015  
and JSOG President now.**

**On 29 July, 2015  
Signing of Minutes of  
Memorandum of the  
Project  
at the Ministry of Health,  
Cambodia**

**Funded by the JICA Grassroots Technical Cooperation Project**

**This slide was kindly provided by Dr. Noriko Fujita**

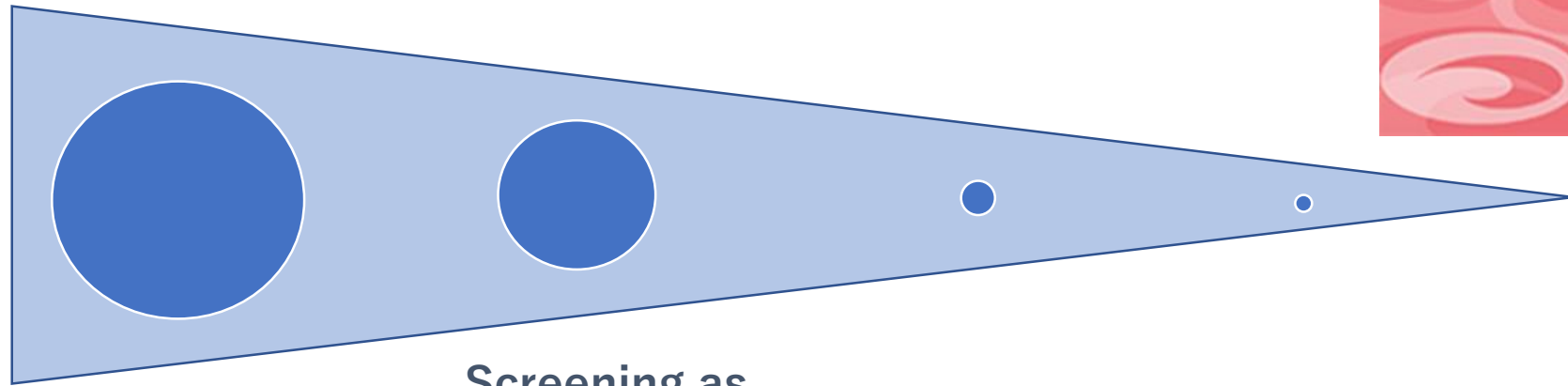
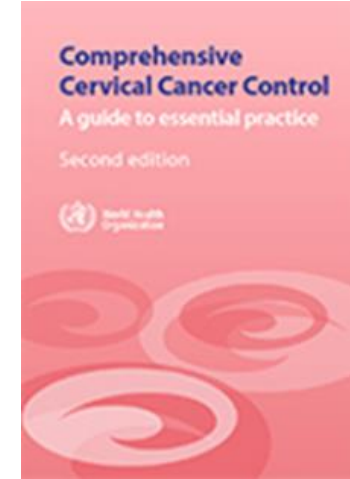


# Situation in Cambodia (as of 2015)

- 1. Cervical cancer has been a priority in Noncommunicable disease (NCD) since 2007**
- 2. “Screen and treat” with VIA and cryotherapy was recommended as the nationwide strategy**
- 3. Small pilot programs were running with the support of different NGOs**
- 4. Identified problems:**
  - Lack of technical expertise in VIA**
  - Limited supply of gas for cryotherapy**
  - Difficulty in collaboration and harmonizing clinical practice**
  - Extremely limited capacity of pathology (4 pathologists in the country)**
  - No real data on cervical cancer (but most women presenting to hospital in advanced stage)**

Sources: Cambodian MOH National Strategy for the Prevention and Control of NCDs 2007–2010,  
Cambodian MOH National Strategic Plan for the Prevention and Control of NCDs 2013-2020

# Project's Strategic Focus



Primary Prevention

Screening as  
secondary  
Prevention  
-VIA

Treatment of  
precancerous lesions

Management of  
invasive cancer

Factory-based

-Health education

-HPV testing

- LEEP

Hospital-based  
(3 National hospitals)

-HPV vaccine

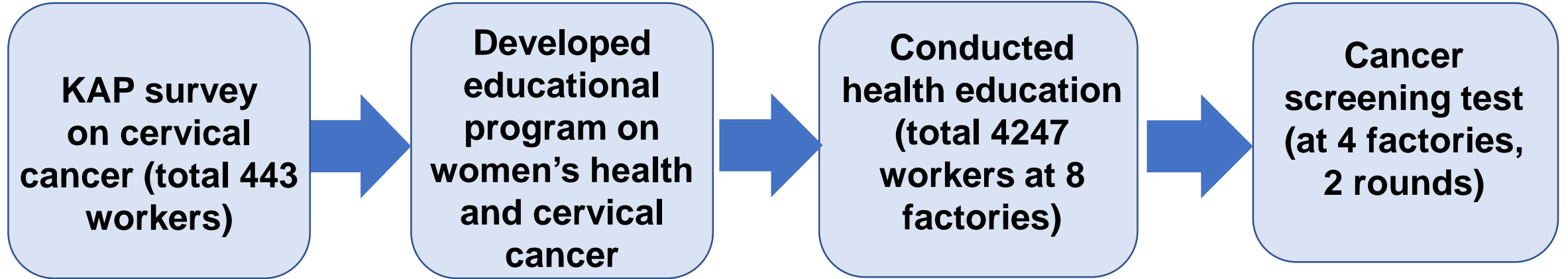
-Cytology

- Cryotherapy

-Surgery  
-Radiotherapy  
-Chemotherapy  
-Palliative care

Gavi support

# Health Education



**This slide was kindly provided by Dr. Noriko Fujita**



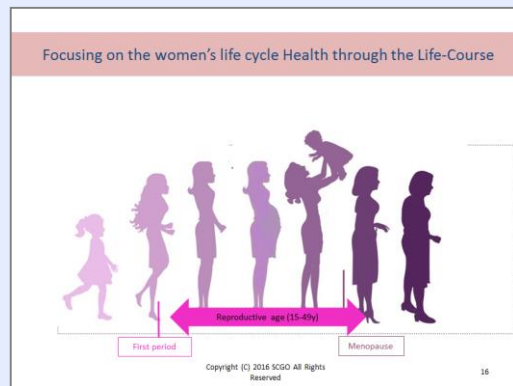
# Educational program

## Contents

1. Basic hygiene and women's body
2. Family planning
3. Care during pregnancy
4. Cervical cancer
5. Cervical cancer screening



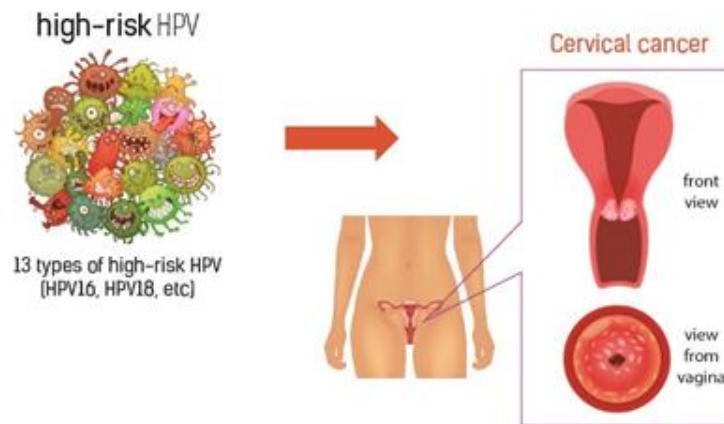
Flip charts



Slides (Power point)



Cervical cancer is caused by a virus, called HPV.





# Factory-based screening



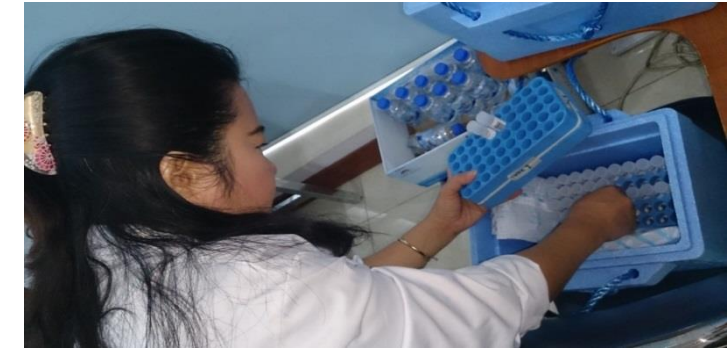
Set up



Registration



Check HPV samples



Laboratory check



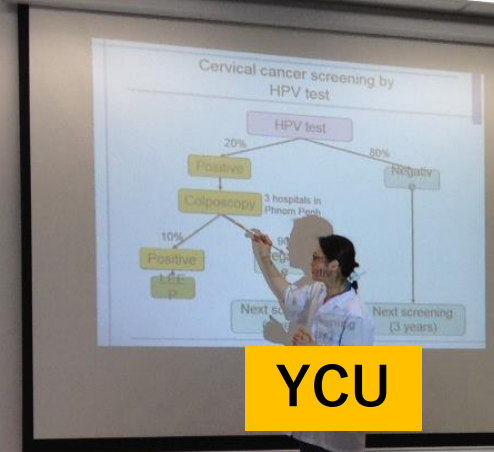
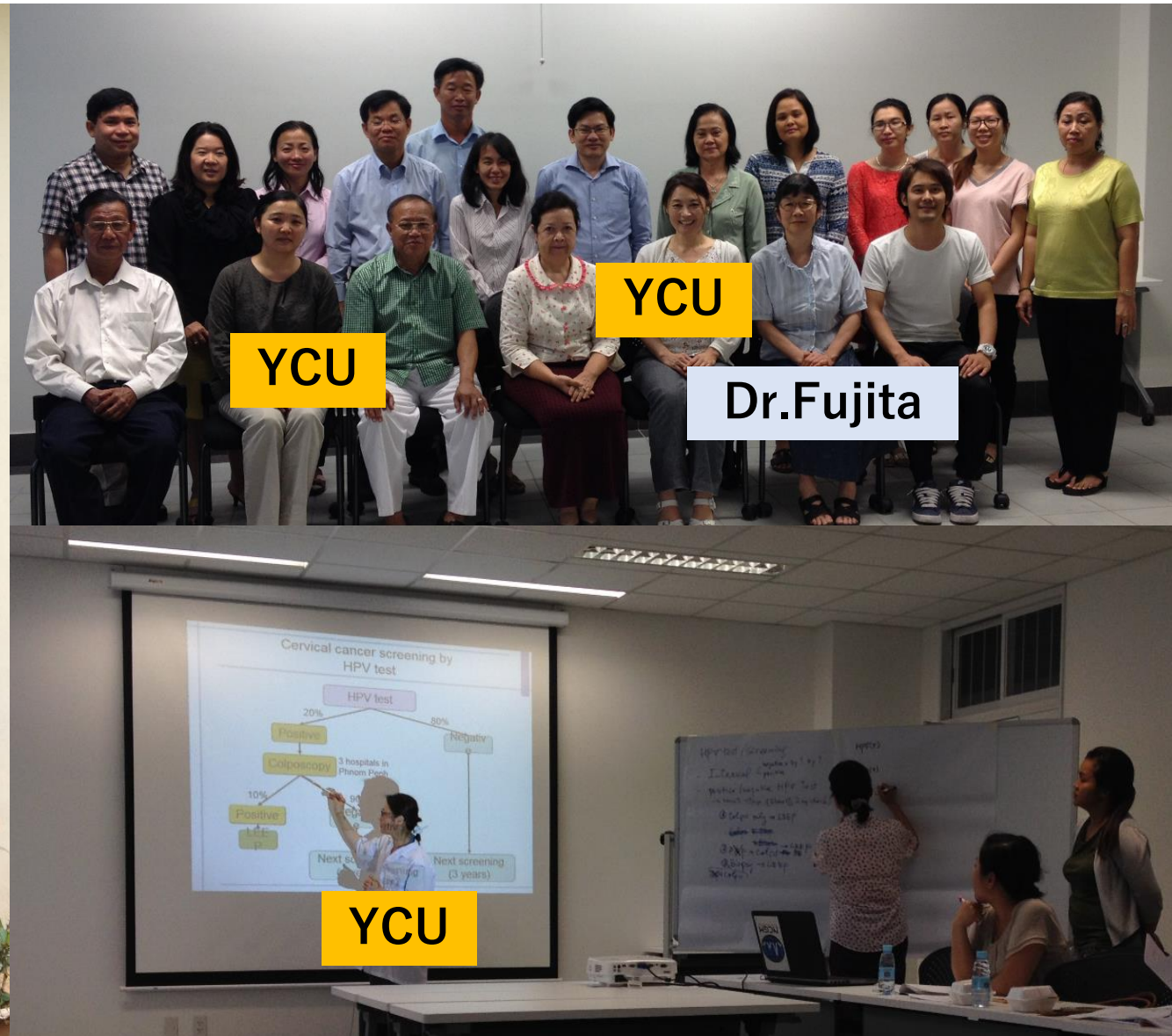
Post-screening health education  
Factory workers by Tuk Tuk

**This slide was kindly provided by Dr. Noriko Fujita**





# Two Female Doctors from Yokohama City University (YCU) participated in the Educational Program



# A pilot project of HPV-test based screening and treatment of precancerous lesions by professional societies of Cambodia and Japan **(HPV test – colposcopy – LEEP)**



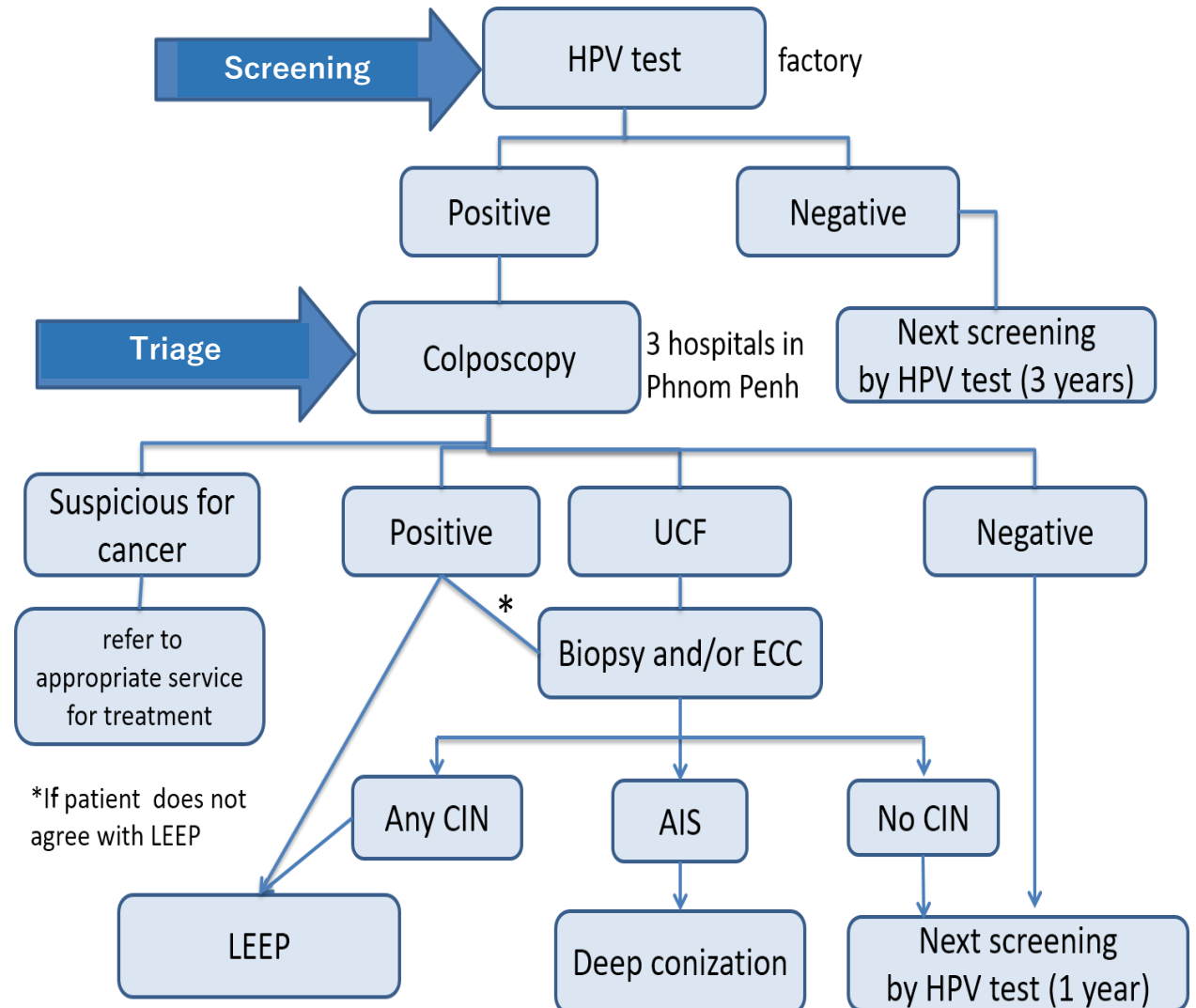
3 National hospitals, 15 gynecologists

- Trained on colposcopy and LEEP
- Developed standard protocol

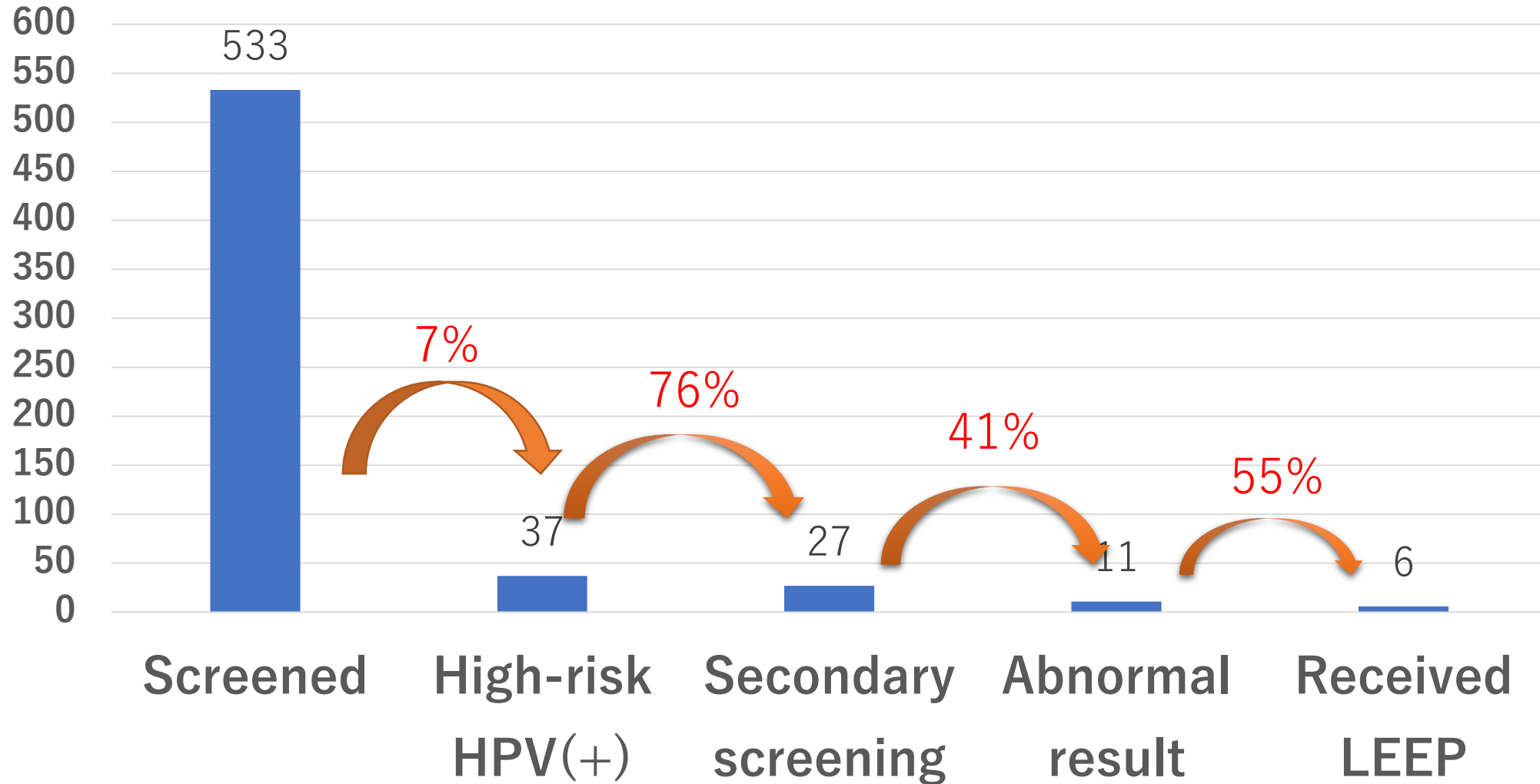
Eligible criteria for screening:  
older than 25 y/o, ever married  
(with no reliable age-specific prevalence of high-risk HPV)

- Factory-based screening: 128 women (screening at factory, triage and treat at hospitals)
- Hospital-based screening: 315 women (screening, triage and treat at hospitals)

**This slide was kindly provided by Dr. Noriko Fujita**



# Screening results (factory + hospital)





# HPV test applied in the project

1. *CareHPV*: detects 14 high risk HPV types. Obtained WHO Prequalification in Sep 2018.
2. Cost of *CareHPV*: **5.4 US\$ per test** when conducting 90 samples per time, excluding personnel cost.
3. Field applicability: It took only one month for laboratory technicians to properly handle HPV test, having test results within 3 hours.
4. **Quality control: HPV genotyping was analyzed in Japan for 352 random samples by PCR-based method detecting 31 HPV types.**

Accuracy	326/352 (92.6%)
False-positive	5/352(1.4%)
<b><u>False-negative</u></b>	<b><u>21/352 (6.0%)</u></b>

This slide was kindly provided by Dr. Noriko Fujita

Genotyping  
National I  
HPV DNA

The 2019  
12.

**Assume problems  
related to the  
sensitivity of the HPV  
testing**

System used in  
proficient in the  
work.

Genotyping in  
28/JCM.00840-

Y. Ueda, et al. Development and Evaluation of a Cervical Cancer Screening System in Cambodia: A Collaborative Project of the SCGO and JSOG. JOGR 2019

**A variety of HPV testing methods available in Japan (Above 50 US\$ per test)**  
**HPV testing is used for ASC-US triage, not recommended for Screening at Present**

Name	HPV DNA Qiagen HCII®	Cobas®4800	Acugene®HPV	Aptima® m-HPV	BD Onclarity™ HPV
Method	Hybrid Capture	Real-time PCR	Real-time PCR	TMA Method	Real-time PCR
Target HPV Genotypes	16.18.31.33.35.39. 45.51.52.56.58.59.68 (13 types)	16.18.31.33.35.39. 45.51.52.56.58.59.68 + 66 (14 types)	16.18.31.33.35.39. 45.51.52.56.58.59.68 + 66 (14 types)	16.18.31.33.35.39. 45.51.52.56.58.59.68 + 66 (14 types)	16.18.31.33.35.39. 45.51.52.56.58.59.68 + 66 (14 types)
Target Genes	HPV whole genome	L1 gene	L1 gene	E6/E7 mRNA	E6/E7 DNA
HPV 16+18 genotyping	×	○	○	×	○
Genotyping Other than 16+18	×	X	X	×	○
Cut-Off level	100,000 copies/mL (5,000 copies/test)	Depending on Genotypes	Depending on Genotypes	Depending on Genotypes	Depending on Genotypes
Internal Control	×	○	○	○	○

# Agenda

1. Partnership between Cambodian and Japan Societies of OB & Gyn through cervical cancer screening project
- 2. Promotion of cervical cancer prevention with HPV vaccination & screening in the world as well as WHO strategy.**
3. Risk communication issues in promoting cervical cancer prevention in Japan
4. Our research results about self-sampling HPV testing

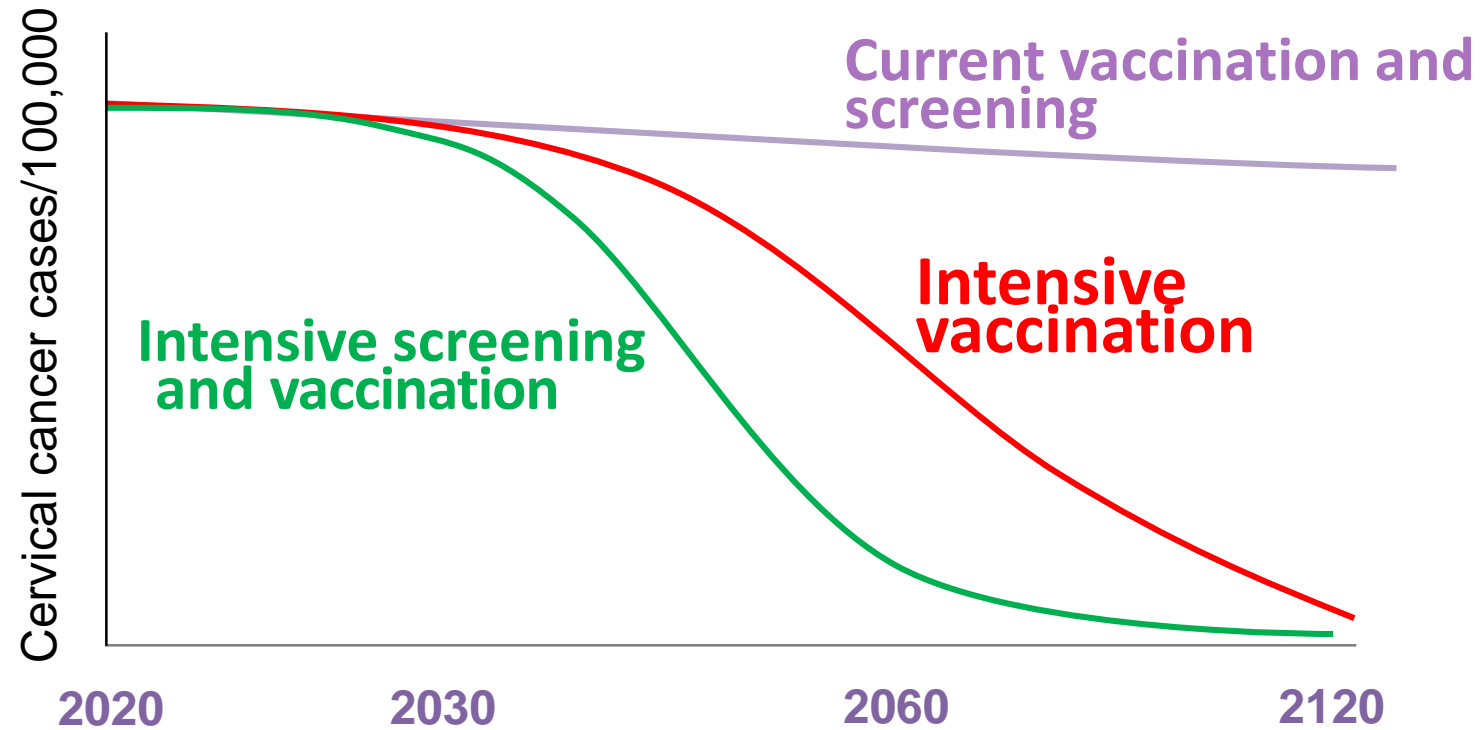


# ELIMINATION OF CERVICAL CANCER AS A GLOBAL PUBLIC HEALTH PROBLEM

**“Consign cervical cancer to  
the history books “**



# CERVICAL CANCER ELIMINATION: CONCEPTUAL FRAMEWORK





# THE ARCHITECTURE TO ELIMINATE CERVICAL CANCER:

VISION: A world without cervical cancer

THRESHOLD: All countries to reach < 4 cases 100,000 women-years

## 2030 CONTROL TARGETS

**90%**

of girls fully vaccinated  
with HPV vaccine  
by 15 years of age

**70%**

of women screened with  
an high precision test at  
35 and 45 years of age

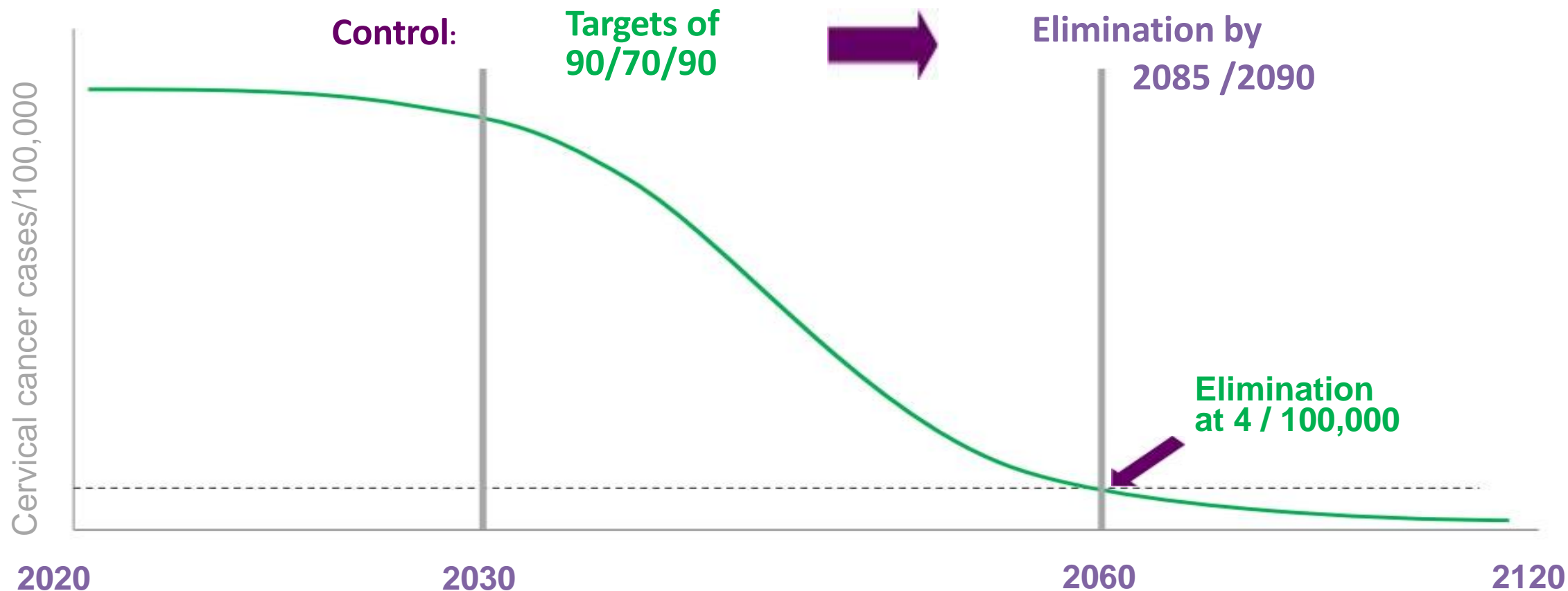
**90%**

of women identified with  
cervical disease receive  
treatment and care

**2030: 30% reduction in mortality from cervical cancer**

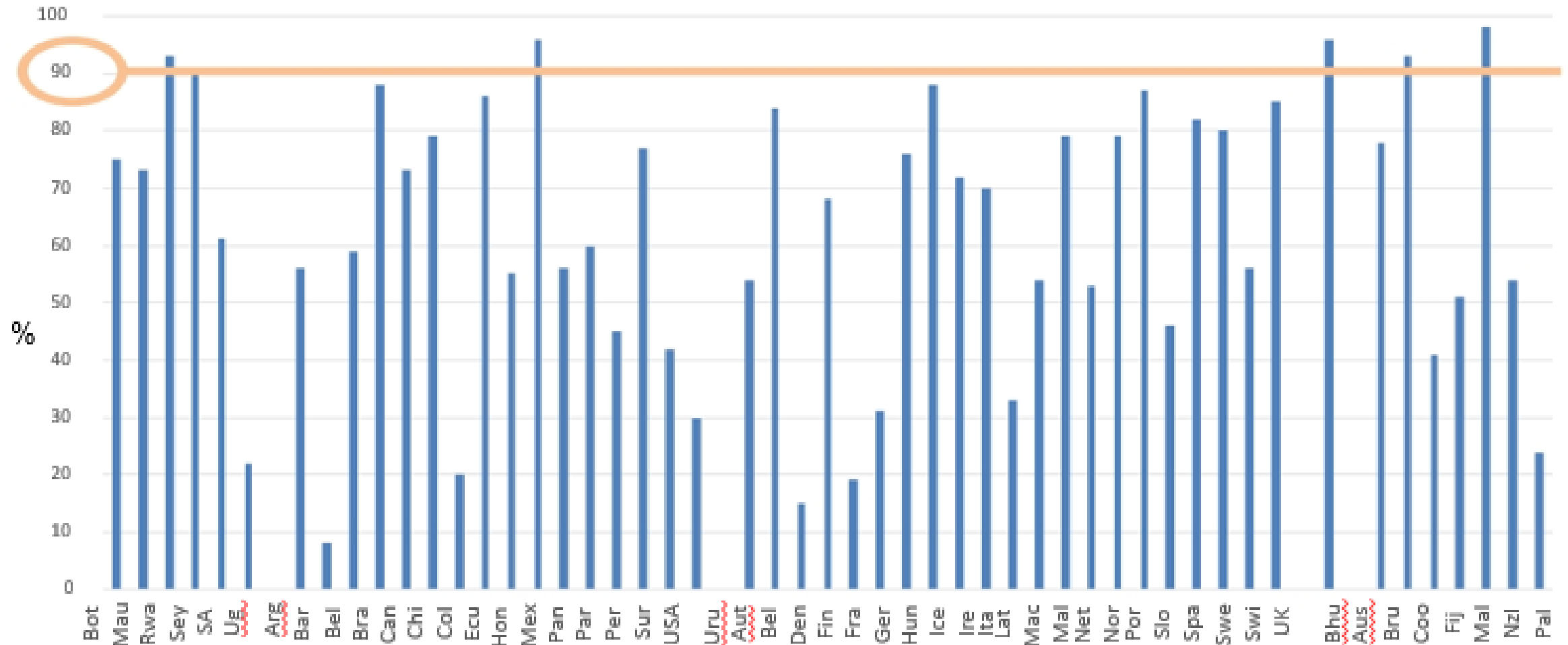
The 2030 targets and elimination threshold are subject to revision depending on the outcomes of the modeling and the WHO approval process

## INCREASING ACCESS TO INTERVENTIONS 2030 VACCINATION, SCREENING & TREATMENT COVERAGE TARGETS



# Reported HPV vaccine coverage of various ages, 2014-2016

90% coverage is achievable, but most countries are far behind



# ACHIEVING 70% COVERAGE OF SCREENING AND TREATMENT OF PRECANCER LESIONS

## WHO recommendations

- Women aged 30-49 be screened at least once in their lifetime for cervical cancer, and rescreened every 5 years.
- Women living with HIV should be screened every 3 years.
- Immediate treatment where possible

## Challenges *for low- and middle-income contexts*

- *Expensive and complex screen and treat technologies complicate scaling-up new or optimized service and delivery methods*

## ACHIEVING 70% COVERAGE OF SCREENING AND TREATMENT OF PRECANCER LESIONS



### Accelerators to achieve 70% coverage of CC screening

- ◆ Sufficient, affordable supply of screening and treatment technologies & products
  - Prompt certification of new products
  - Price reductions
- ◆ National scale-up of screening & treatment
  - Simple algorithms need to be introduced for different settings
- ◆ Increased quality and coverage of service delivery
  - Detailed implementation plans to introduce and scale-up products and delivery models
- ◆ Strengthen patient retention and linkage to treatment



# Recent Action of the Japan Society of Obstetrics and Gynecology ~Introduction of WHO Strategy for the Elimination of CC~



公益社団法人 **日本産科婦人科学会**  
Japan Society of Obstetrics and Gynecology

検索

English >

HOME

② 会員・医療関係の皆様へ

② 医学生・研修医の皆様へ

② 一般の皆様へ

関連リンク

サイトマップ

産科・婦人科の病気

Human+

Babyプラス

専門医を探す

イベント情報

公開情報

寄附について

HOME > 公開情報 > 子宮頸がんとHPVワクチンに関する正しい理解のために

**公開情報**

[臨床研究について](#)

子宮頸がんとHPVワクチン

[周産期の広場](#)

[声明](#)

**子宮頸がんとHPVワクチンに関する正しい理解のために**

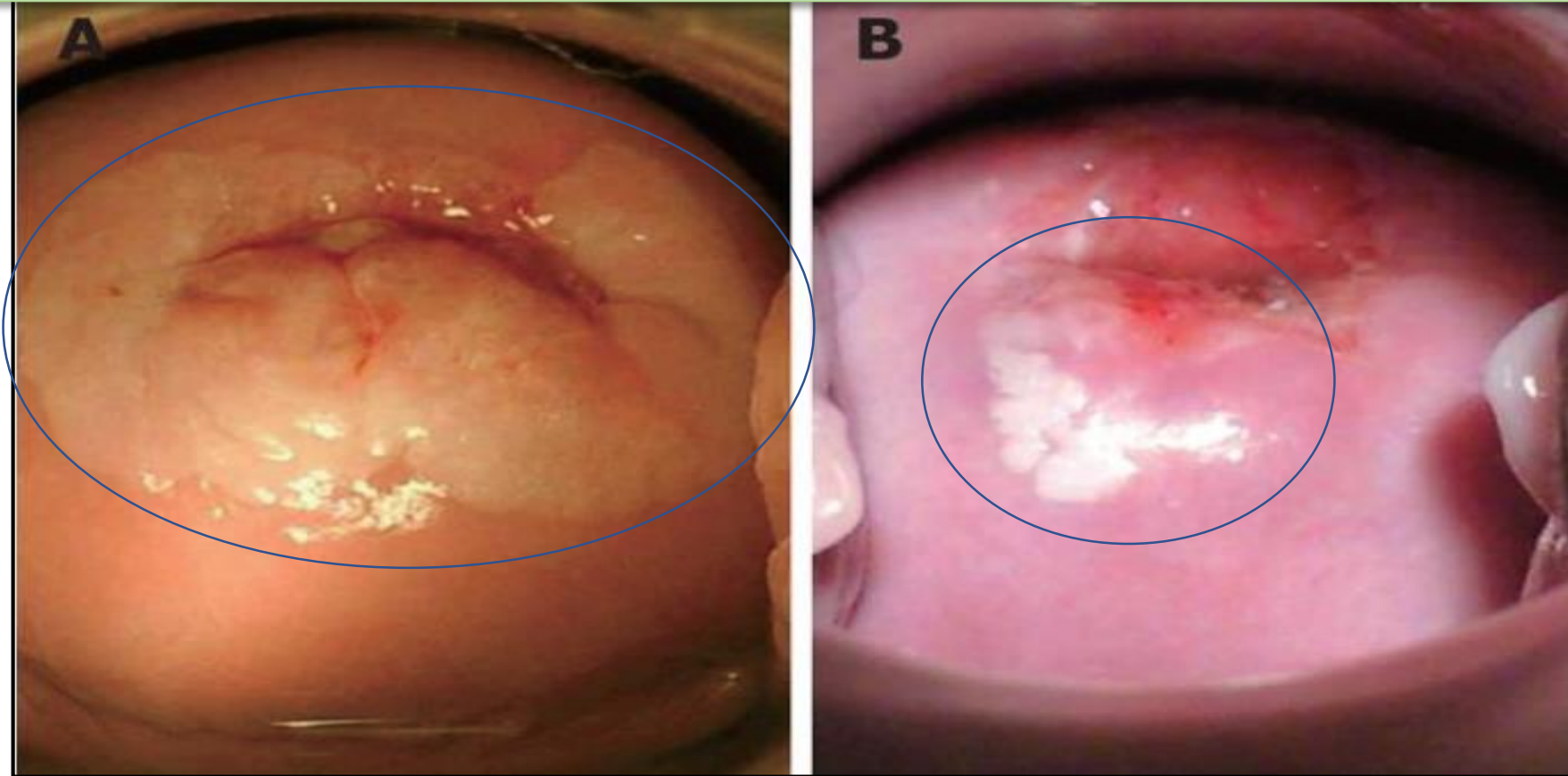
更新日時：2019年9月9日

 [世界的な公衆衛生上の問題「子宮頸がんの排除」に向けたWHOスライド](#)の日本語翻訳版を掲載しました。以下のバナーからパワーポイントスライドをダウンロードし、ご利用下さい。



We have translated the WHO slides into Japanese.  
Now, everyone can download the Japanese PPT slides.

## What do you think is the most cost-effective strategy to promote CC prevention ?

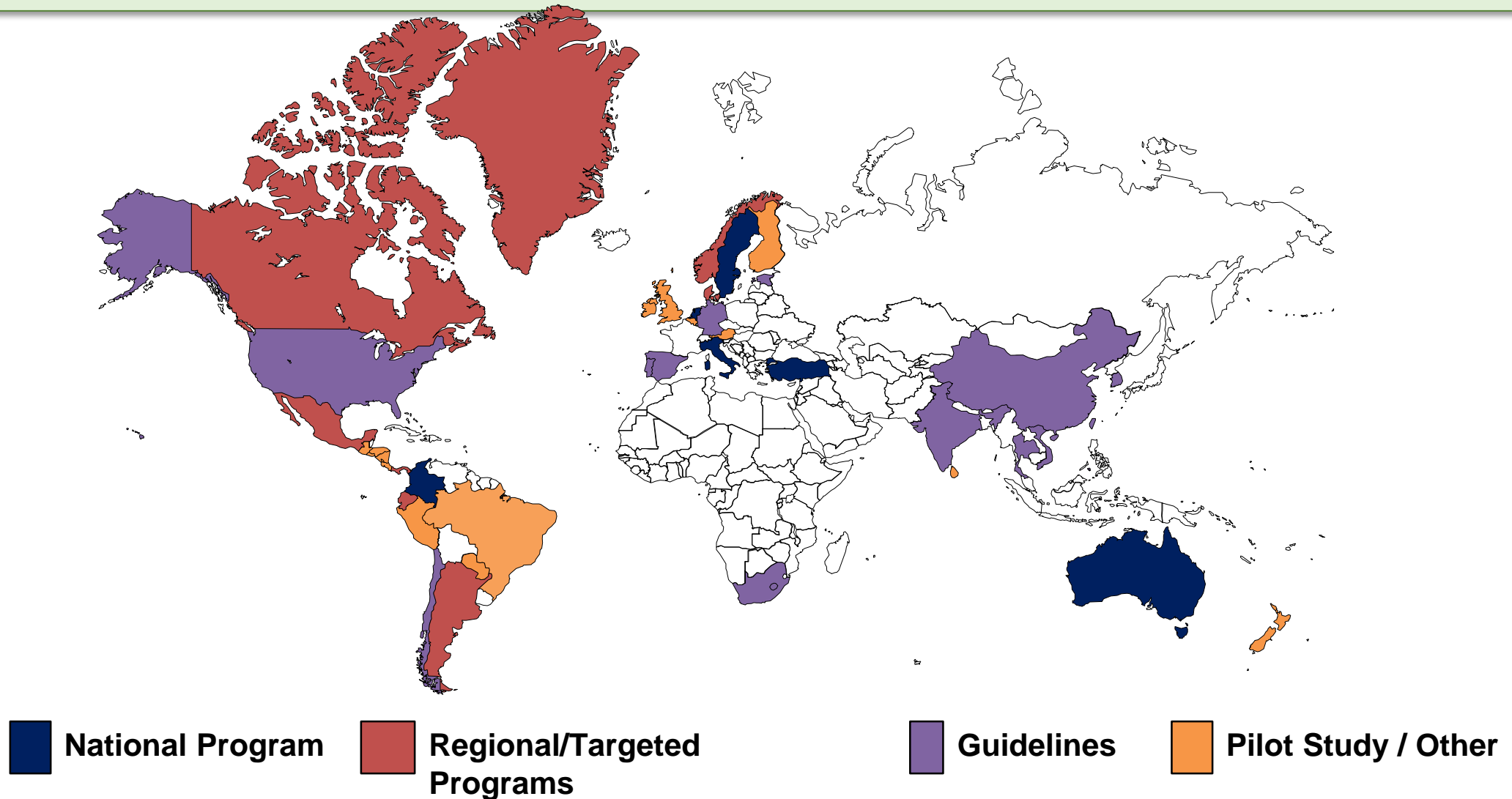


World J Obstet Gynecol.  
Dec 10, 2012

**Maintain 90%↑ HPV vaccination, hopefully 9-valent, by the age of 15.**

→All women have only one-time HPV testing → HPV positive women have colposcopic examination or Visual Inspection with Acetic Acid (VIA)→High quality pictures are sent to a distant specialist or AI→LEEP will be performed certainly in a same day!

# HPV DNA primary screening is spreading rapidly around the world



Current to the best of our knowledge on Aug 2018; South Korea, Taiwan & Germany support co-testing not stand-alone HPV screening

# **HPV DNA primary screening: Status Around The World**

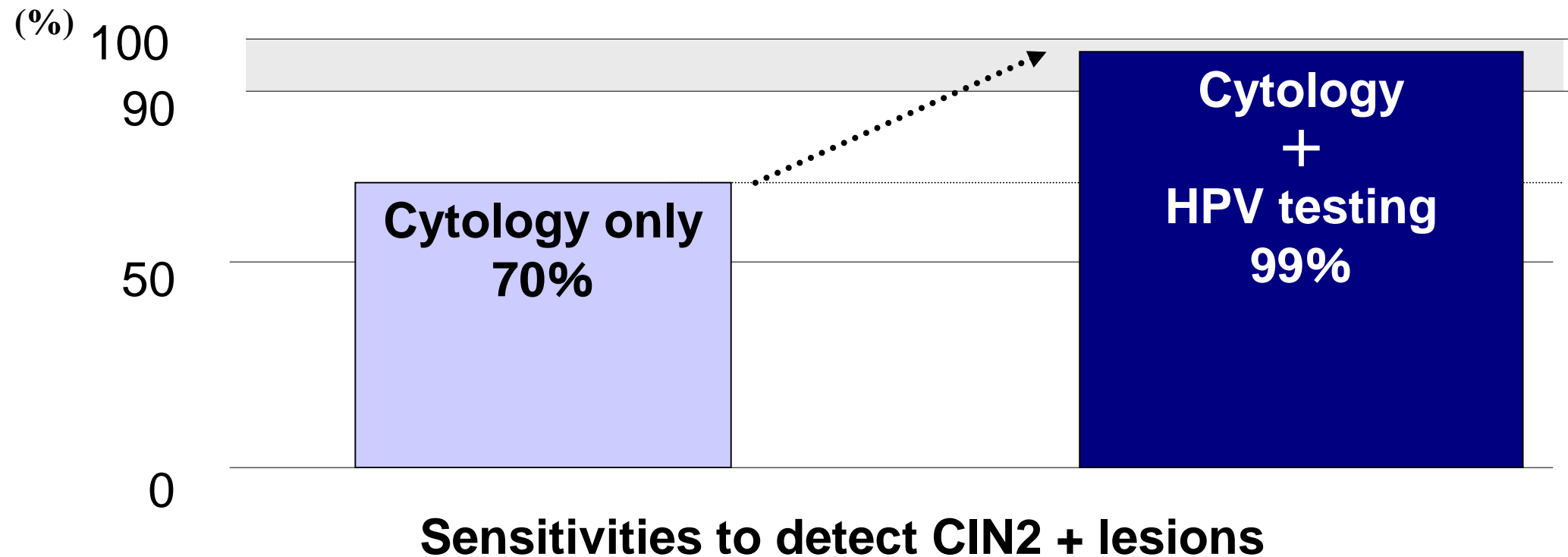
Type of Program	Country
Implemented	Italy, Mexico, Denmark, Turkey, Argentina, Ecuador, Canada, Netherlands, <b>Australia</b> , Sweden, Isle of Man, Colombia
Guidelines	ASCO, Chile, China, Estonia, EU, Germany*, Hong Kong, India, Portugal, South Africa, South Korea*, Spain, Taiwan*, Thailand, <b>USA, WHO</b>
Guidelines under review	Austria, Singapore, Barbados, <b><u>Japan</u> (HPV primary or co-testing or Pap only)</b>
Pilot programs	England, Norway, Scotland, New Zealand, Vietnam, El Salvador, Nicaragua, Paraguay, Peru, Brazil, Costa Rica, Guatemala, Honduras, Sri Lanka, <b><u>Cambodia</u></b>

\*Co-testing, but not stand-alone primary screening

# Advantages and disadvantages of HPV DNA co-testing with Pap test

**Advantages:** Almost no false negative cases, Detection of HPV negative rare CC

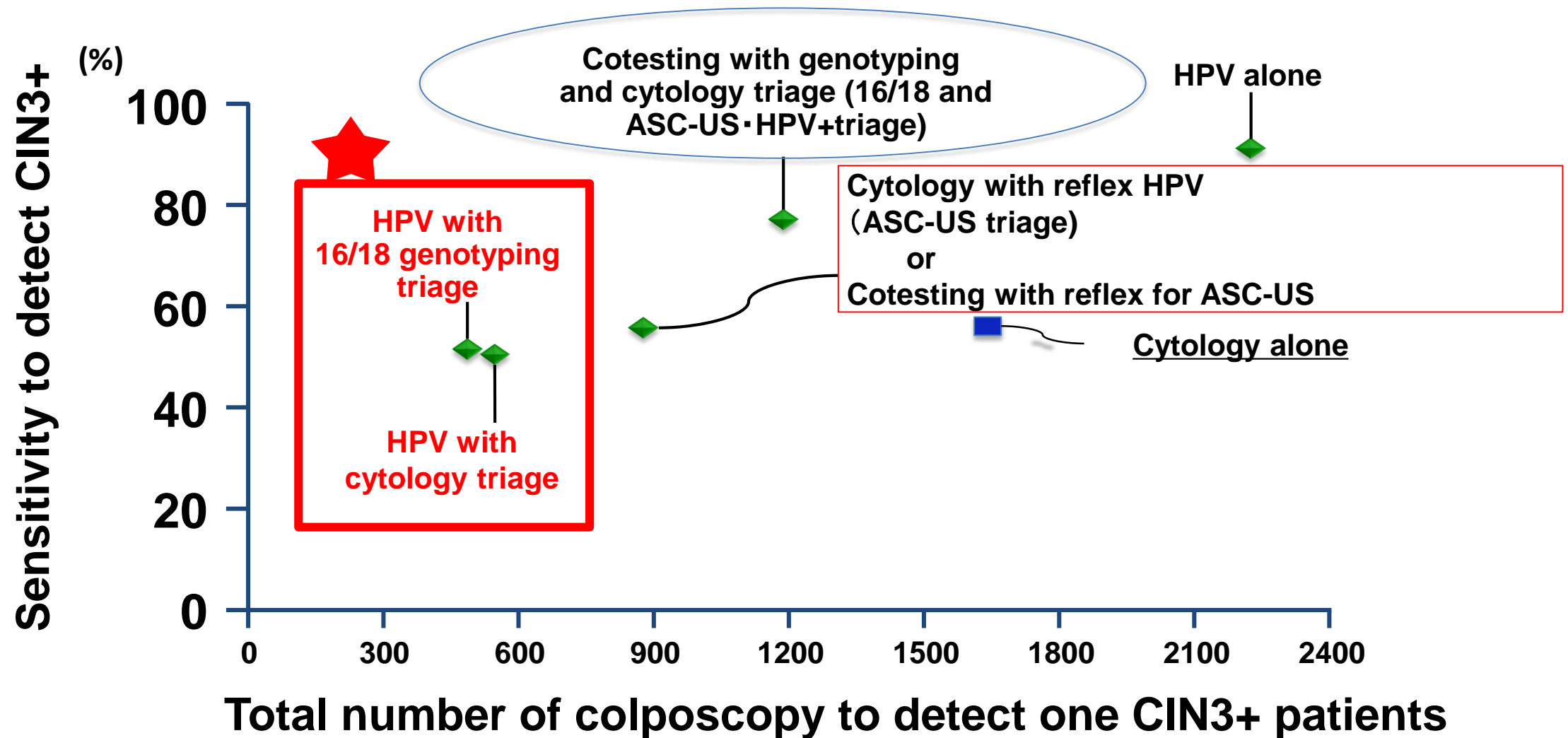
**Disadvantages:** Higher cost, Many false positive cases among young women, Needs of complex algorithms





# Strategies for cost-effective CC screening

## (Results from the ATHENA HPV study)





# Most advancing CC prevention program in Australia



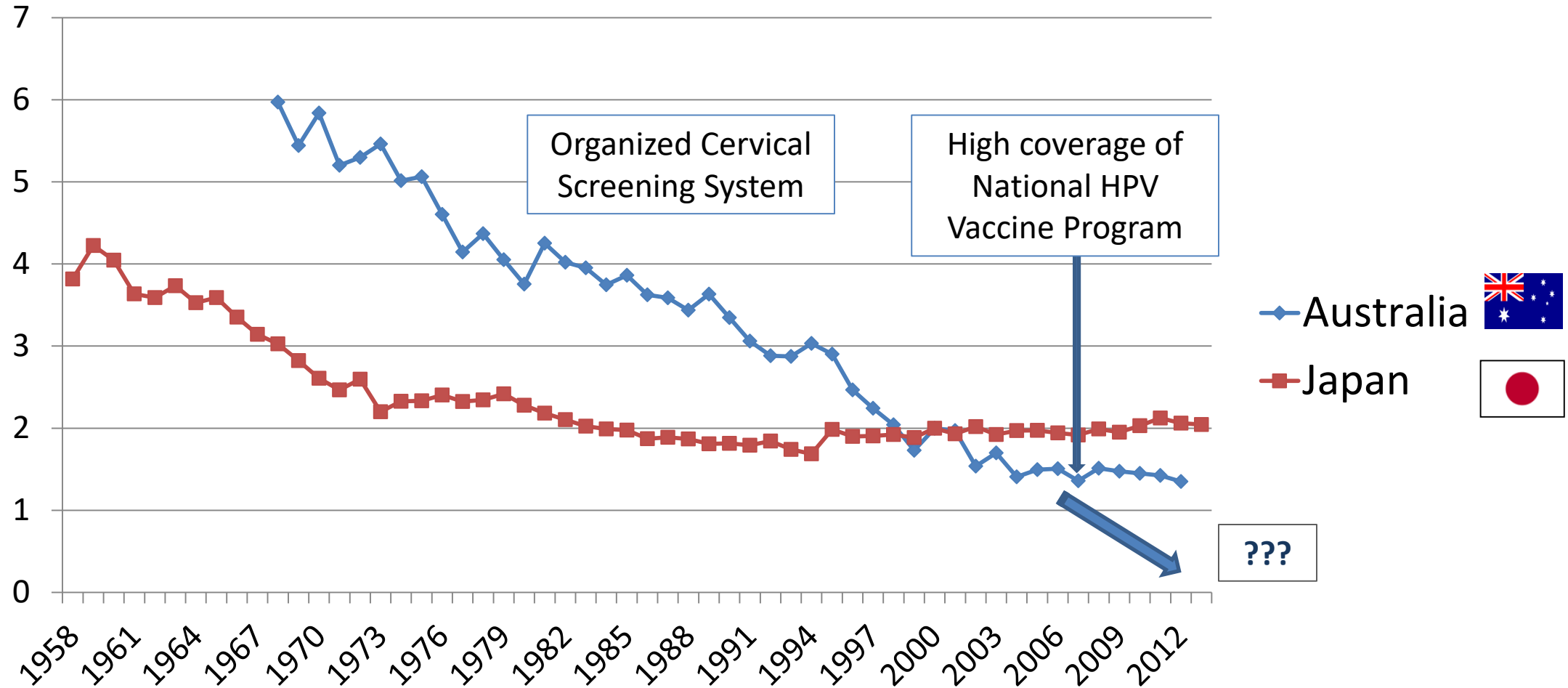
Morning conference in Melbourne in 2016



Lecture of Prof. Suzanne Garland @ YCU in July 2019

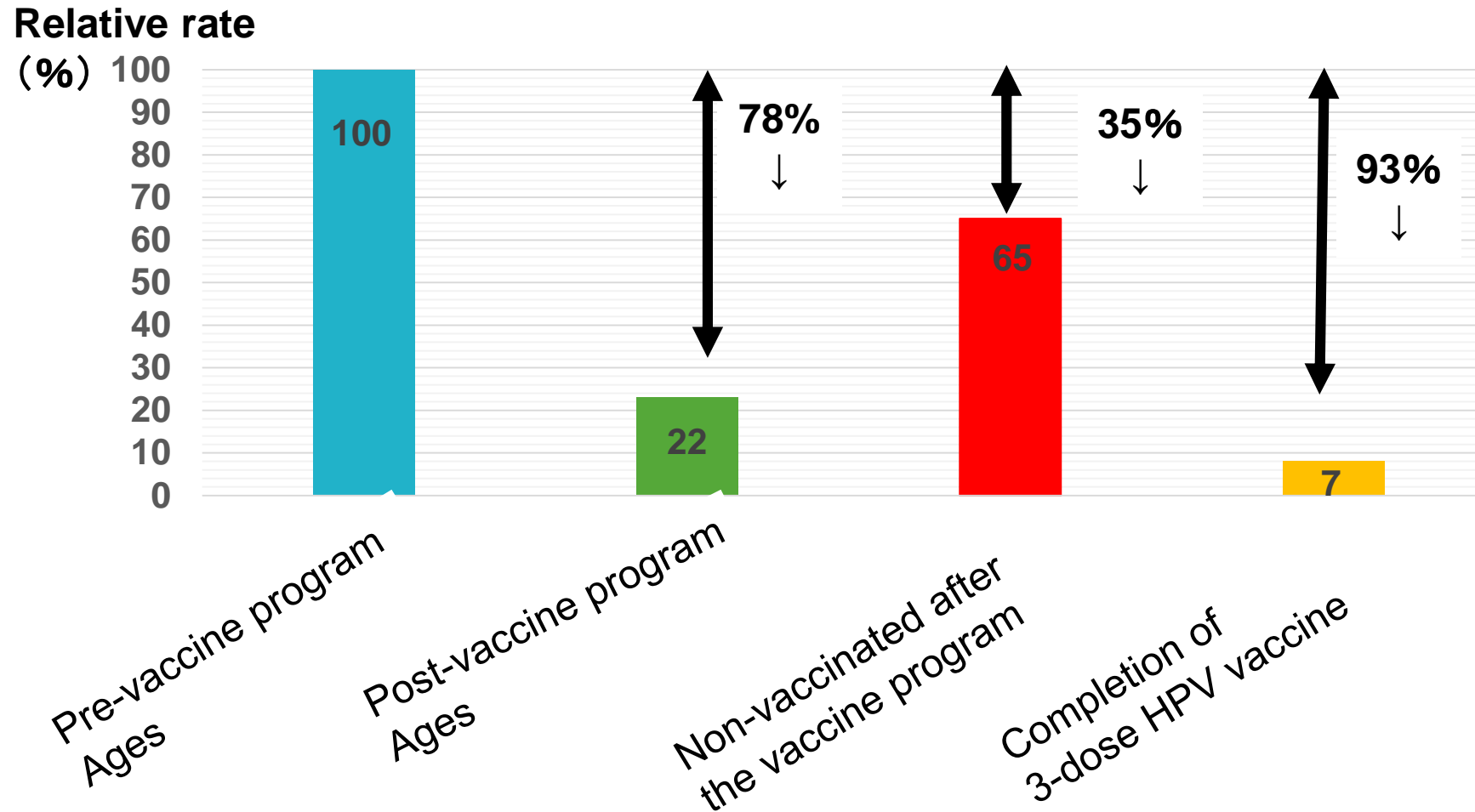
# Age standardized mortality rates of CC in Australia & Japan

(:100,000 women)



# HPV vaccine impact in Australia

## Drastic decreases in HPV 6, 11, 16, 18 infection among young women



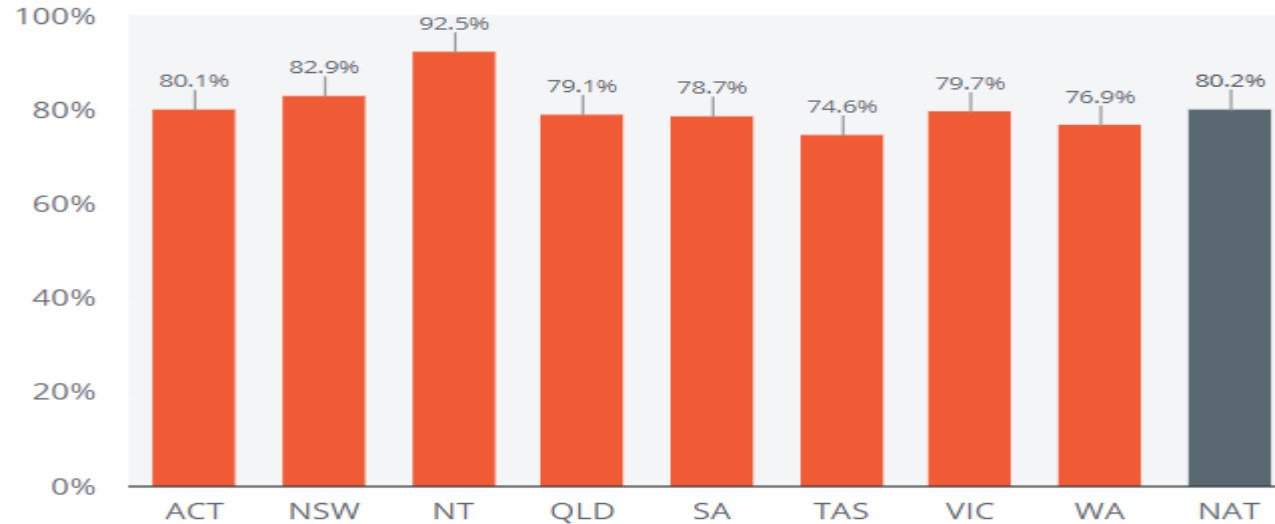
Tabrizi SN et al.  
Lancet Infect Dis.  
(2014)

**Herd immunity was verified in Australia.**

# High Coverages of HPV vaccination in Australia as the results of gender free vaccination program in 2017

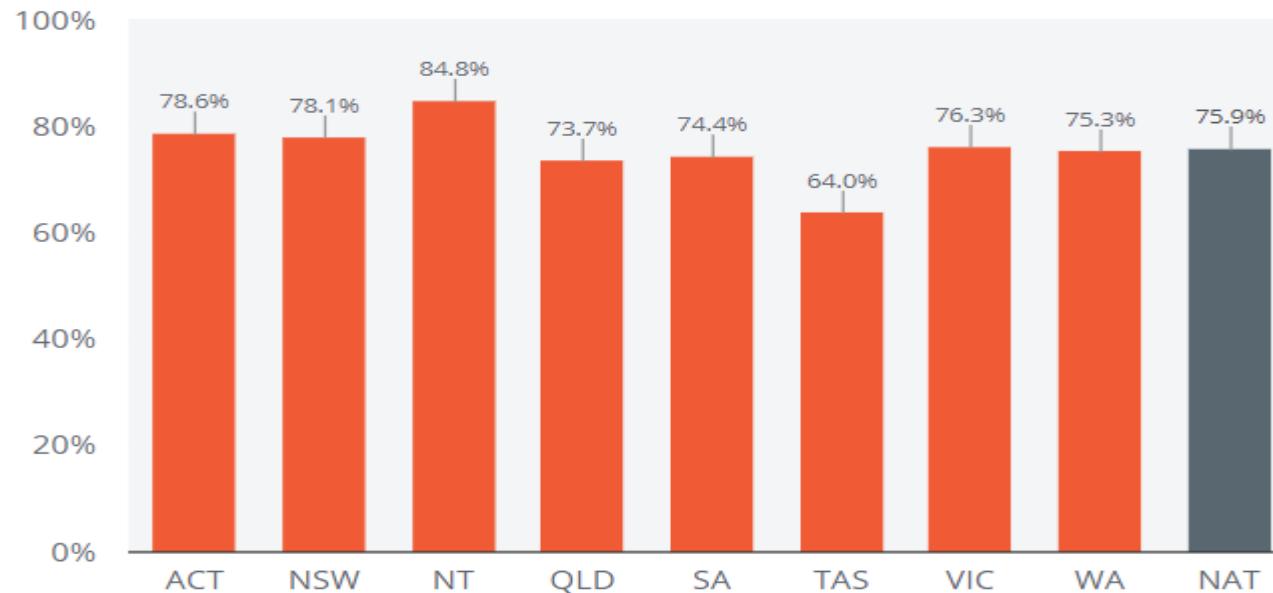
## Girls

3 Dose HPV Vaccination Coverage

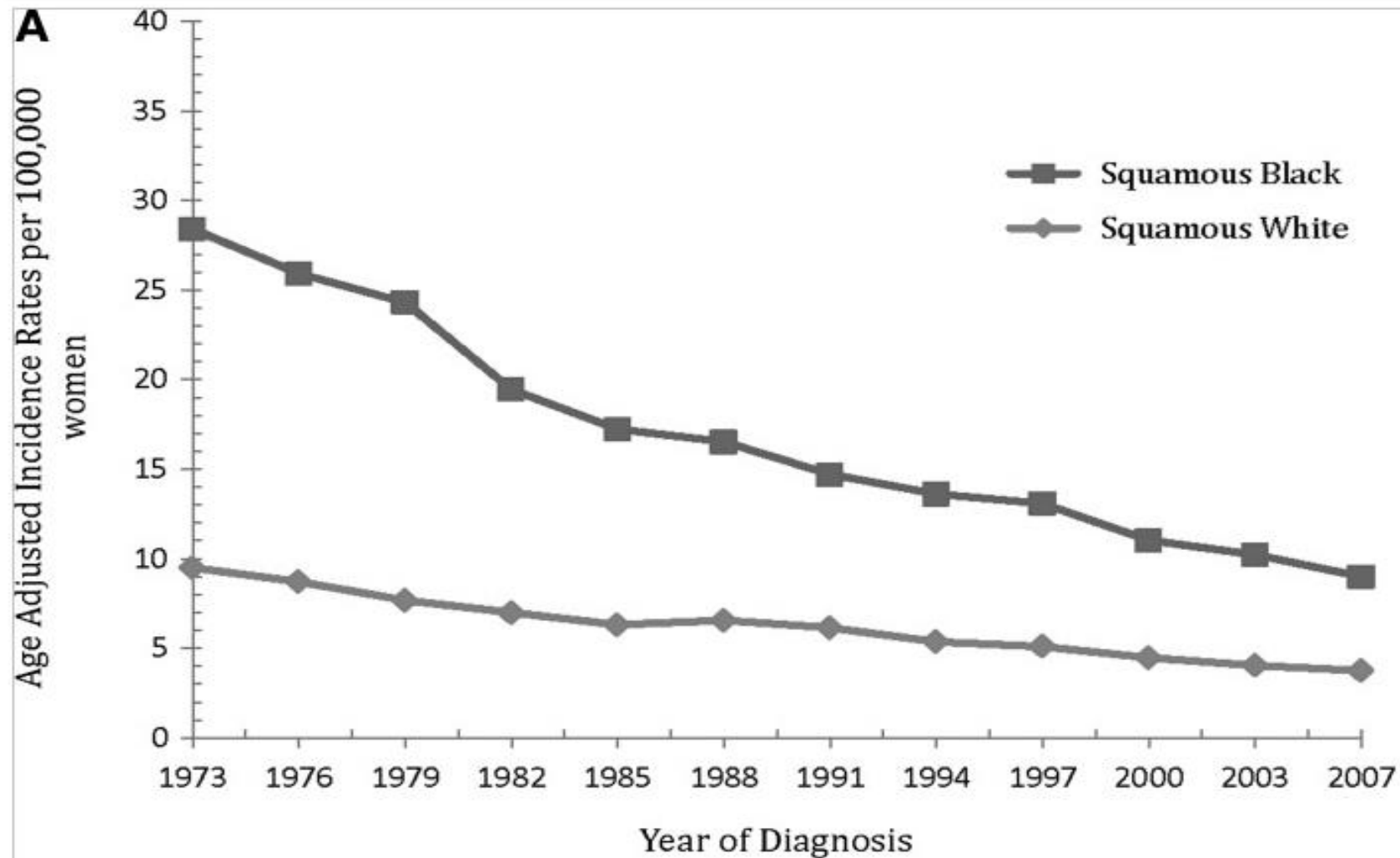


## Boys

3 Dose HPV Vaccination Coverage



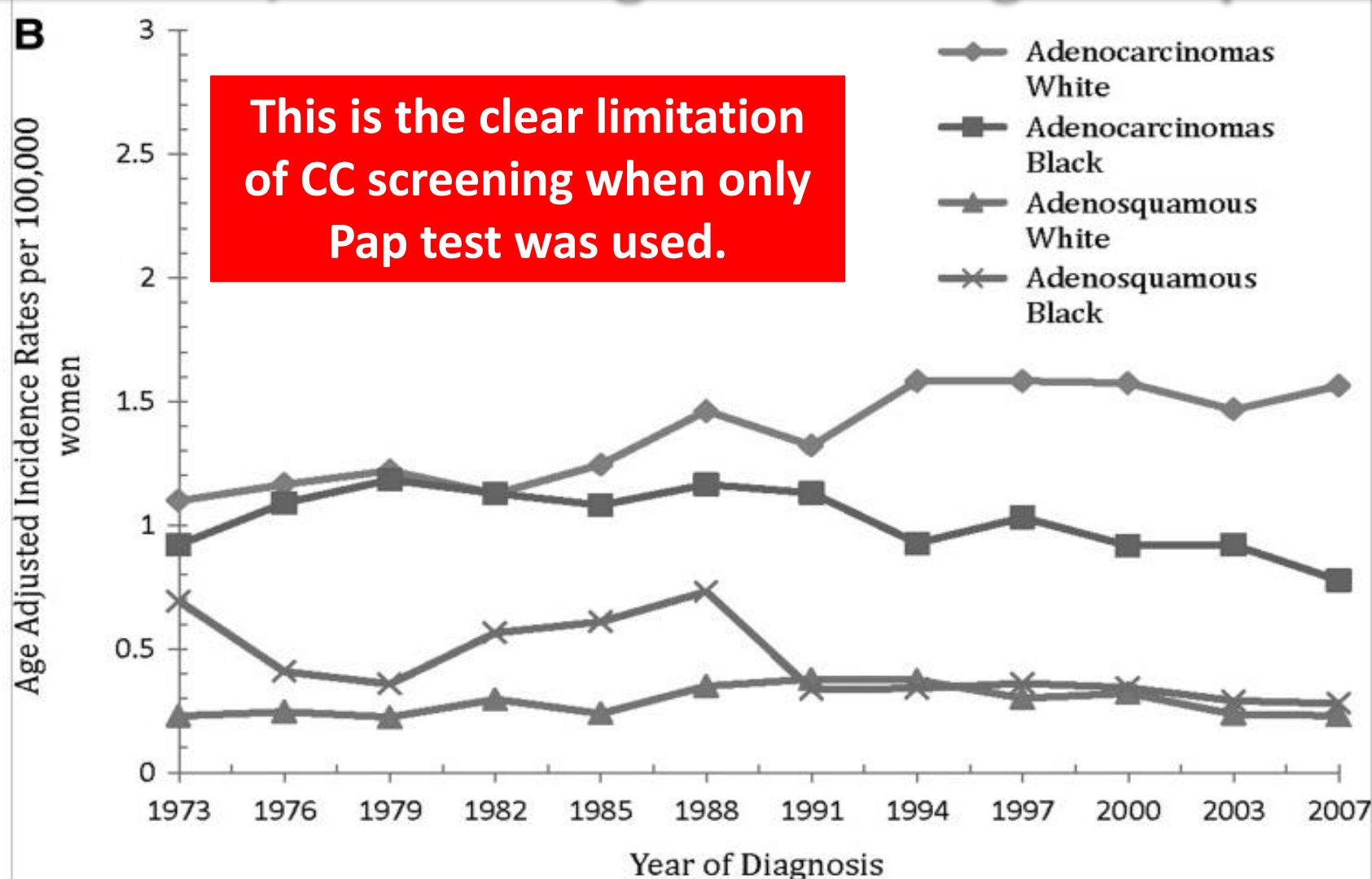
## Decreasing trends of Squamous cell carcinoma of the cervix in both black and white women in the US



Adegoke O, et al. J Womens Health (Larchmt). 2012 Oct;21(10):1031-7. doi: 10.1089/jwh.2011.3385. Epub 2012 Jul 20. Cervical cancer trends in the United States: a 35-year population-based analysis.



# No decreasing trends of adenocarcinoma of the cervix in the US, even having 90% coverage of Pap test



Adegoke O, et al. J Womens Health (Larchmt). 2012 Oct;21(10):1031-7. doi: 10.1089/jwh.2011.3385. Epub 2012 Jul 20. Cervical cancer trends in the United States: a 35-year population-based analysis.

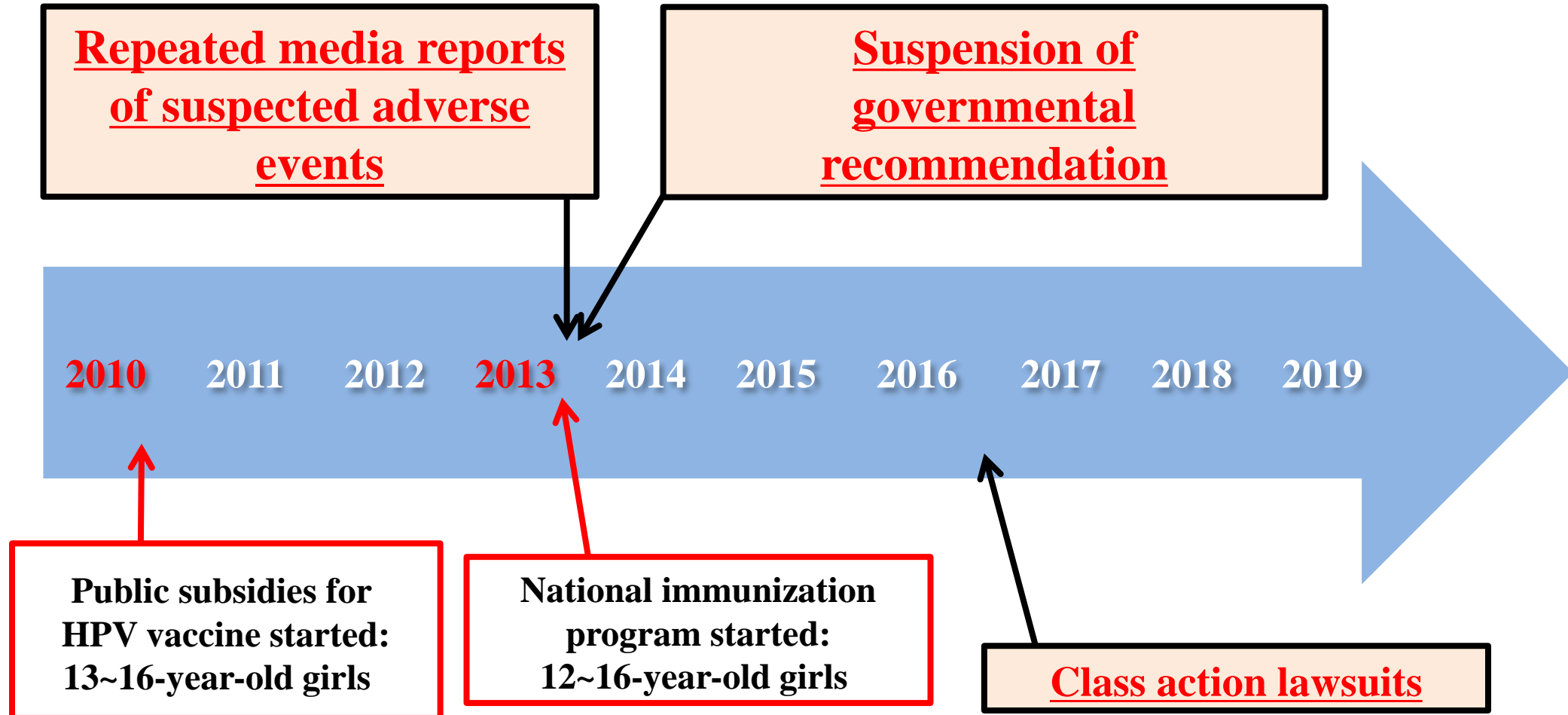
# Agenda

1. Partnership between Cambodian and Japan Societies of OB & Gyn through cervical cancer screening project
2. Promotion of cervical cancer prevention with HPV vaccination & screening in the world as well as WHO strategy.
- 3. Risk communication issues in promoting cervical cancer prevention in Japan**
4. Our research results about self-sampling HPV testing

# Background

- The incidence/mortality rates of cervical cancer are in increasing trends among women younger than 50 years old in Japan.
- Japanese government has suspended proactive recommendation of HPV vaccines in July 2013, following repeated media reports of adverse events after the vaccination.
- Although the restart of governmental recommendations for HPV vaccines is a minimum requirement to normalize the national HPV vaccine program in Japan, no official statement has been made yet.

# Policies and events related to HPV vaccine program in Japan



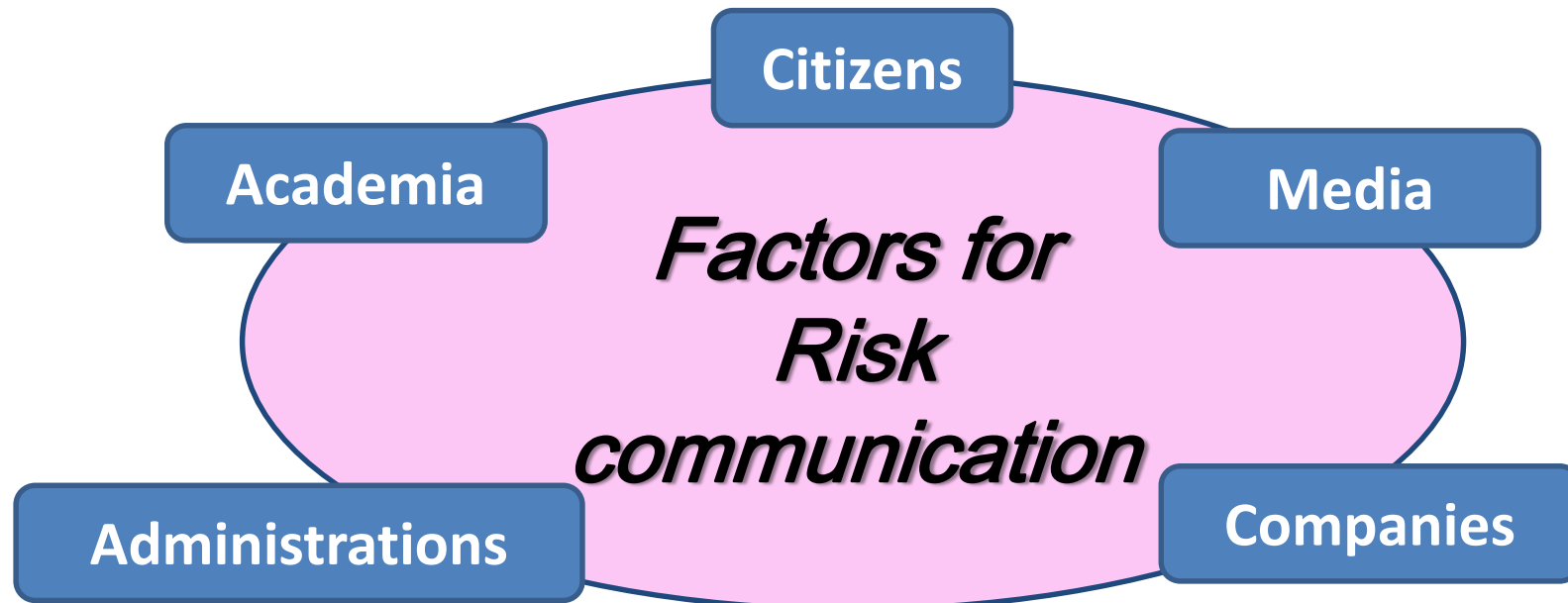
**Young Japanese women are faced with the immediate risks of cervical cancer**

■ **Low coverage of CC screening** ■

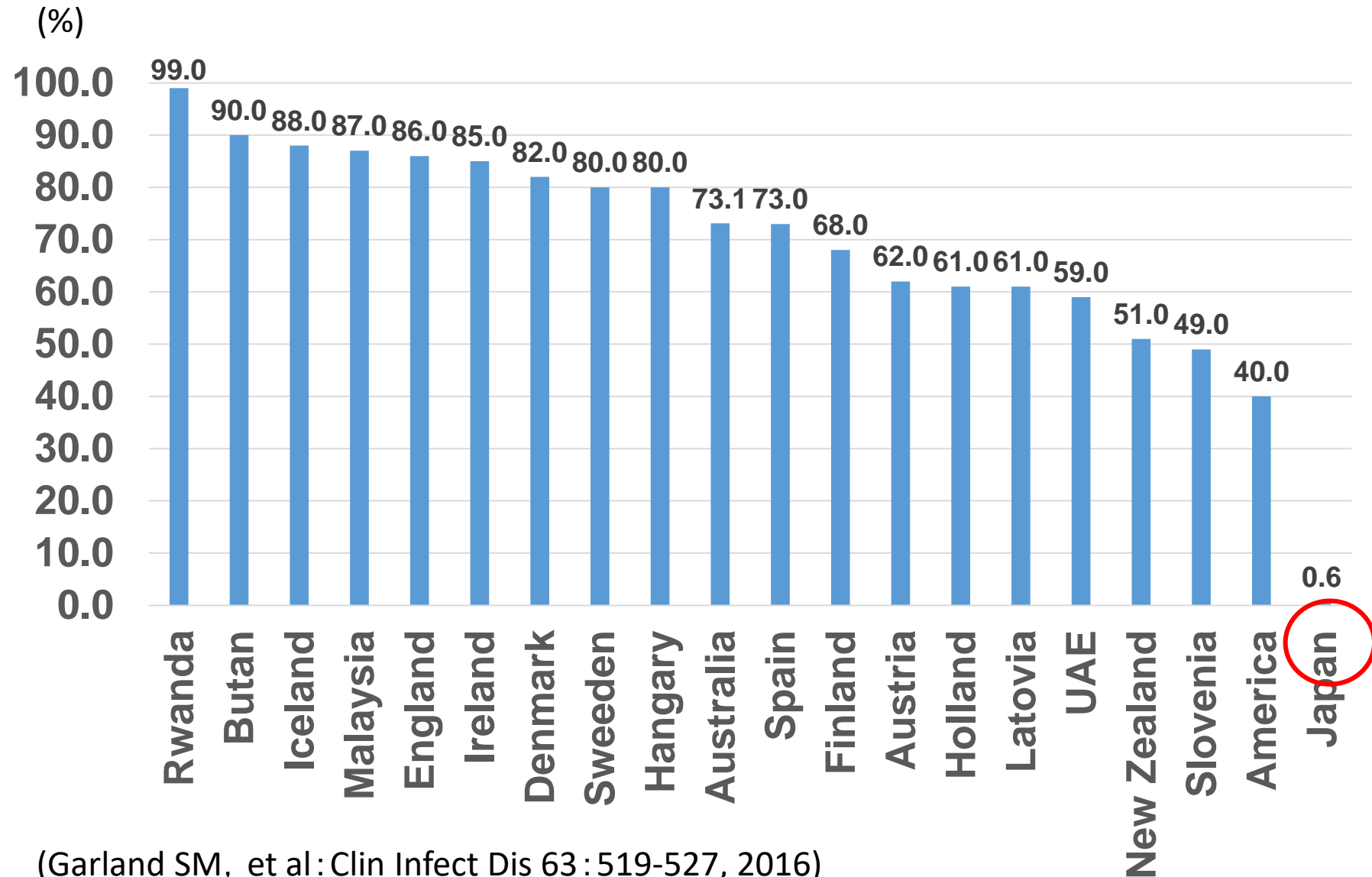
■ **Substantially stopped HPV vaccination program** ■



**Risk Communication Breakdown**



# HPV vaccine coverage rate by nation



(Garland SM, et al: Clin Infect Dis 63:519-527, 2016)



## □ ORIGINAL ARTICLE □

**Peripheral Sympathetic Nerve Dysfunction in Adolescent Japanese Girls Following Immunization with the Human Papillomavirus Vaccine**

Chronic regional pain syndrome (CRPS) alone	5 cases	Kinoshita M, Ikeda S. et.al. Internal Medicine 2014; 53; 2185–2200)
CRPS & Orthostatic hypotension	5 cases	
CRPS & Orthostatic disorder	5 cases	
CRPS & Postural orthostatic tachycardia syndrome (POTS)	3 cases	(Kinoshita M, Ikeda S. et.al. Internal Medicine 2014; 53; 2185–2200)
Orthostatic hypotension alone	3 cases	
Orthostatic disorder alone	7 cases	
POTS only	1 cases	
Others	11 cases	
<b>Total</b>	<b>40 cases</b>	

**A controversial case series reported by the Japanese neurologists, who treated girls suffering from various symptoms after HPV vaccination. Such kinds of papers accelerated anti-HPV vaccine movements in Japan.**

## Nation-wide epidemiological study on safety

The number of patients with diverse symptoms, mainly pain or movement disorders, among young Japanese girls and boys between ages of 12-18

Girls after HPV vaccination: 27.8/100,000

Boys, all without HPV vaccination: 20.2/100,000

Girls without HPV vaccination and unknown history: 46.2/100,000

### Conclusion

There are a certain number of unvaccinated patients with similar symptoms observed after HPV immunization.



Contents lists available at ScienceDirect

## Papillomavirus Research

journal homepage: [www.elsevier.com/locate/pvr](http://www.elsevier.com/locate/pvr)

# No association between HPV vaccine and reported post-vaccination symptoms in Japanese young women: Results of the Nagoya study

Sadao Suzuki\*, Akihiro Hosono

Department of Public Health, Graduate School of Medical Sciences, Nagoya City University, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 466-8601, Japan

**Table 6**

Age-adjusted odds ratios of association of vaccination with symptom, hospital visit, and current symptom after excluding subjects with early-onset symptoms.

Symptom	Occurrence of the symptom		Hospital visits		Persistent and constant symptom	
	OR	95% CI	OR	95% CI	OR	95% CI
1 Menstrual irregularity	0.98	(0.91–1.06)	1.34	(1.14–1.59)	1.18	(1.01–1.39)
2 Abnormal amounts of menstrual bleeding	1.11	(0.97–1.27)	1.54	(1.15–2.06)	1.54	(1.15–2.06)
3 Pain in the joints or other parts of the body	0.84	(0.74–0.95)	1.44	(1.09–1.90)	0.68	(0.49–0.94)
4 Severe headache	0.98	(0.88–1.10)	1.41	(1.16–1.72)	1.22	(0.84–1.78)
5 Fatigue	0.82	(0.74–0.91)	1.60	(1.19–2.15)	0.92	(0.73–1.15)
6 Poor endurance	0.91	(0.82–1.00)	1.64	(1.17–2.29)	1.08	(0.88–1.32)
7 Difficulty concentrating	0.85	(0.75–0.96)	1.71	(1.09–2.68)	0.84	(0.64–1.09)
8 Abnormal field of vision	0.81	(0.64–1.03)	1.25	(0.77–2.02)	0.90	(0.43–1.89)
9 Abnormal sensitivity to light	0.95	(0.81–1.13)	1.19	(0.80–1.79)	0.95	(0.65–1.38)
10 Sudden vision loss	0.85	(0.75–0.97)	1.07	(0.90–1.27)	1.13	(0.88–1.47)
11 Dizziness	0.86	(0.78–0.96)	1.33	(1.06–1.67)	1.03	(0.76–1.41)
12 Cold feet	0.80	(0.72–0.88)	1.34	(0.78–2.29)	0.96	(0.80–1.16)
13 Difficulty falling asleep	.68	(0.60–0.76)	1.09	(0.75–1.58)	0.75	(0.58–0.98)
14 Abnormally long duration of sleep	.90	(0.81–0.99)	1.30	(0.85–1.99)	1.12	(0.92–1.37)
15 Skin problems	0.83	(0.75–0.92)	1.01	(0.88–1.16)	0.97	(0.81–1.15)
16 Hyperventilation	0.83	(0.69–0.99)	1.06	(0.76–1.47)	0.20	(0.04–0.87)
17 Memory decline	0.94	(0.77–1.14)	1.69	(0.75–3.77)	0.71	(0.49–1.01)
18 Loss of ability to do simple calculations	0.68	(0.49–0.95)	4.95	(1.03–23.78)	0.32	(0.18–0.56)
19 Loss of ability to remember fundamental Kanji	0.66	(0.53–0.82)	6.15	(1.32–28.75)	0.39	(0.22–0.67)
20 Involuntary uncontrollable body movement	1.40	(0.97–2.01)	1.99	(0.89–4.47)	1.12	(0.36–3.49)
21 Loss of ability to walk in a normal way	1.45	(0.75–2.82)	2.65	(1.02–6.91)	1.44	(0.23–8.99)
22 Becoming dependent on a walking stick or wheelchair	0.90	(0.37–2.22)	1.02	(0.30–3.52)	0.70	(0.14–3.41)
23 Sudden loss of strength	1.13	(0.85–1.50)	2.61	(1.16–5.87)	0.79	(0.17–3.63)
24 Weakness in the hands and feet	1.41	(1.09–1.82)	2.00	(1.11–3.61)	1.24	(0.42–3.68)

# Statements from Japanese Academic Societies

*THE JOURNAL OF*  
**Obstetrics and Gynaecology Research**

doi:10.1111/jog.12912

*J. Obstet. Gynaecol. Res. Vol. 41, No. 12: 1859–1860, December 2015*



## Declaration to demand the resumption of recommendations for human papillomavirus (HPV) vaccination for cervical cancer prevention

Tomoyuki Fujii, MD, PhD  
*Chairperson of the Executive Board*

*Japan Society of Obstetrics and Gynecology (JSOG)*

Vaccine 35 (2017) 2291–2292



Contents lists available at [ScienceDirect](#)

Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)



Commentary

Consensus statement from 17 relevant Japanese academic societies on the promotion of the human papillomavirus vaccine



Satoshi Iwata<sup>a</sup>, Kenji Okada<sup>b</sup>, Kei Kawana<sup>c,\*</sup>, on behalf of the Expert Council on Promotion of Vaccination<sup>1</sup>

<sup>a</sup> Department of Infectious Diseases, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan

<sup>b</sup> Section of Pediatrics, Department of Medicine, Division of Oral and Medical Management, Fukuoka Dental College, 2-15-1 Tamura, Sawara-ku, Fukuoka, Japan

<sup>c</sup> Department of Obstetrics and Gynecology, Nihon University School of Medicine, 30-1 Oiyaguchi-kamicho, Itabashi-ku, Tokyo 173-8610, Japan

# YOKOHAMA HPV PROJECT

- Our new project to let Japanese citizens and media know the latest information about HPV vaccination and cervical cancer prevention.
- **We are focusing on the understanding of HPV infection in Japanese males, as a critical factor for the risk communication about HPV-related diseases.**

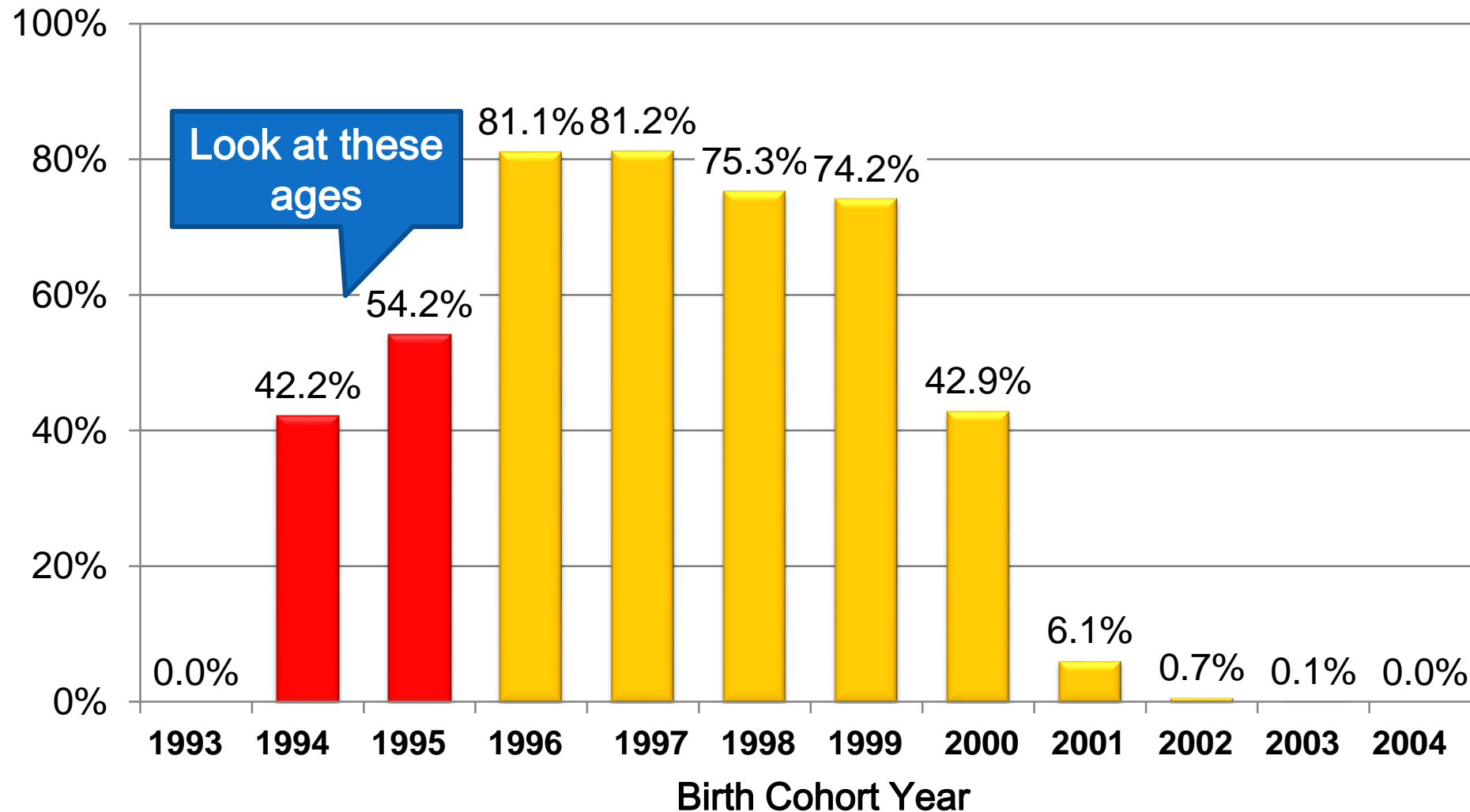
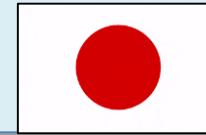


<http://dev.kanagawacc.jp/>





# HPV vaccination rates in young Japanese women

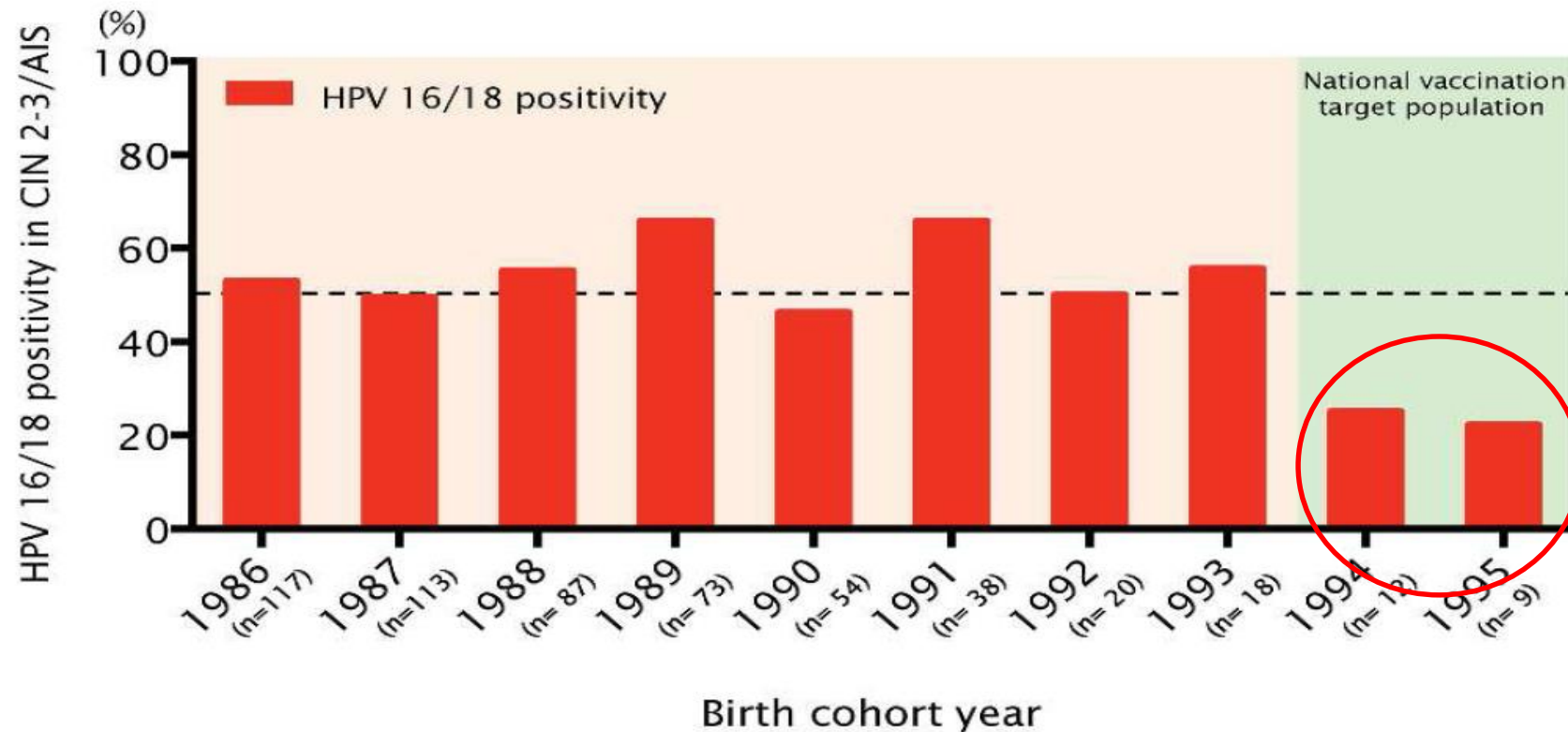


( Report from the 26<sup>th</sup> Vaccine Adverse Reactions Review Committee of MHLW, 2017, revised)

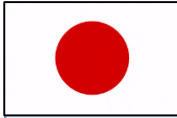
## Monitoring the impact of a national HPV vaccination program in Japan (**MINT Study**): interim analysis



Positive rates for HPV16/18 in CIN2-3/AIS were significantly reduced in the patients born in 1994-1995 (**23.8%: 5/21**), compared to those born in 1986-1993 (**54.6%: 284/520**).



Early impact of the Japanese immunization program implemented before the HPV vaccination crisis  
(Matsumoto K, et al. Int J Cancer. 2017, 141)



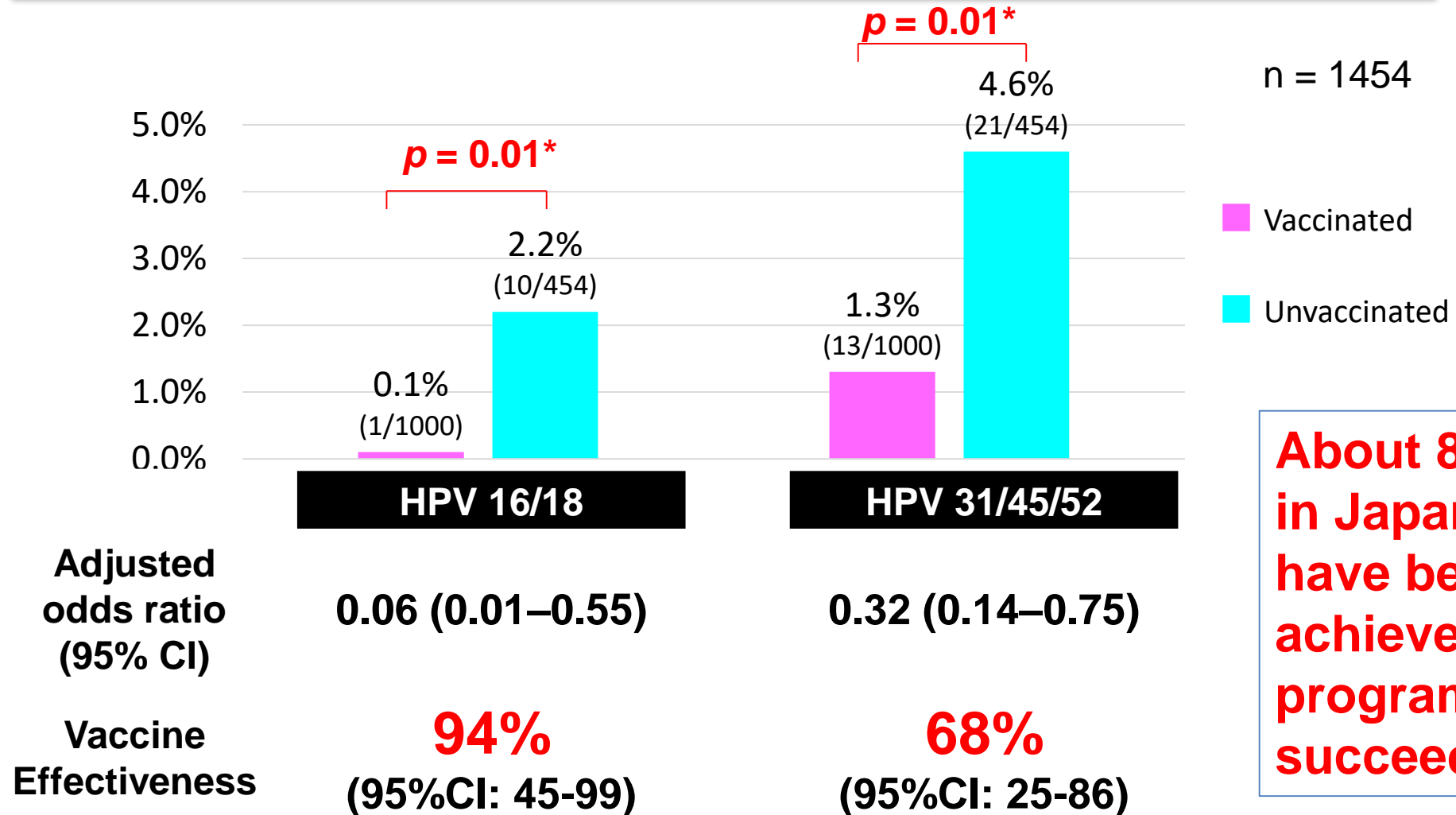
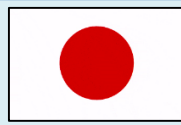
## Evaluation of vaccine effectiveness (Interim Analysis in **Osaka Study**)

### HPV Infection (20-year-old)

	High-risk HPV infection	HPV-16·18 infection
Unvaccinated	<b>19.7% (173 / 877)</b>	<b>4.9% (43 / 877)</b>
Vaccinated	<b>12.9% (22 / 170)</b>	<b><u>0.0% (0 / 170)</u></b>
p-value (Fisher's exact test)	<b>0.041</b>	<b>&lt; 0.001</b>

(This data is kindly provided by Dr. Ueda Y from Osaka University)

# Adjusted vaccine effectiveness against pooled HPV 16/18, HPV31/45/52 (**Niigata Study**) (In the cases of sexual-debut-after-vaccination group)



**About 80% of ICC in Japan might have been achieved, if the program succeeded.**

\*Logistic regression test: Adjusted for number of sex partner and birth year

Kudo R, et al. The Journal of Infectious Diseases. in press

# Agenda

1. Partnership between Cambodian and Japan Societies of OB & Gyn through cervical cancer screening project
2. Promotion of cervical cancer prevention with HPV vaccination & screening in the world as well as WHO strategy.
3. Risk communication issues in promoting cervical cancer prevention in Japan
- 4. Our research results about self-sampling HPV testing**





## *Validity of Self-Sampling Human Papillomavirus Testing in Japanese Women with Abnormal Cervical Cytology*

Etsuko Miyagi<sup>1</sup>, Aiko Kawano-Yashiro<sup>1</sup>, Yoko Motoki<sup>1</sup>, Ryoko Asano<sup>1</sup>, Yasuyo Maruyama<sup>1</sup>, Yukio Suzuki<sup>1</sup>, Mari Saito-Oba<sup>2</sup>, Takeharu Yamanaka<sup>2</sup>, Mikiko Asai-Sato<sup>1</sup>



<sup>1</sup>Department of Obstetrics and Gynecology,  
Yokohama City University Hospital, Japan

<sup>2</sup>Department of Biostatistics, Yokohama  
City University Graduate School of  
Medicine, Yokohama, Japan.

## Objectives

- The purpose of this study was to compare the performances of self-collected vaginal samples (sHPV) for HPV testing with cervical samples collected by physicians (pHPV) from Japanese women with a past and/or present history of abnormal cervical cytology.
- In addition, acceptability of self-sampling HPV testing was also assessed using a questionnaire.

# Methods

- **Patients:** women, between the ages of 20-69, underwent gynecological examination at Yokohama City University Hospital for the follow-up of abnormal cervical cytology (CC High risk group)
- **Recruitment period:** April 2014 ~January 2015
- **Physician-collected cervical samples (pHPV):** taken after conventional cytology, before colposcopic examination
- **Self-collected vaginal samples (sHPV):** taken at home with Evalyn Brush within 7-days after their examinations at the hospital, and mailed with the answer sheet about self-sampling acceptability

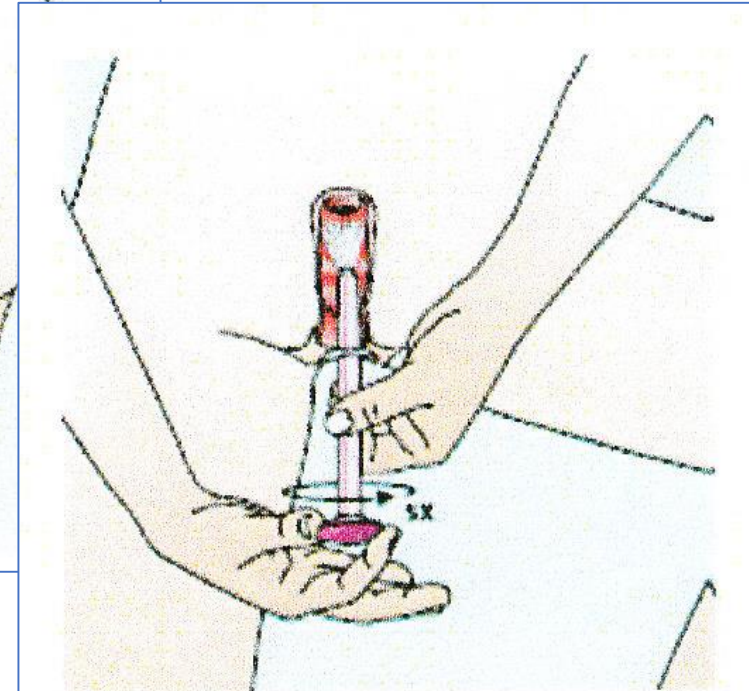
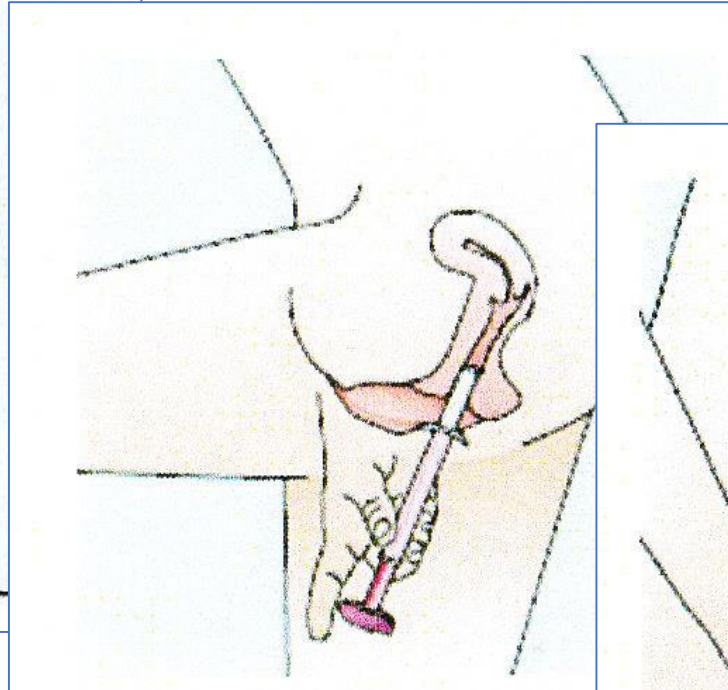
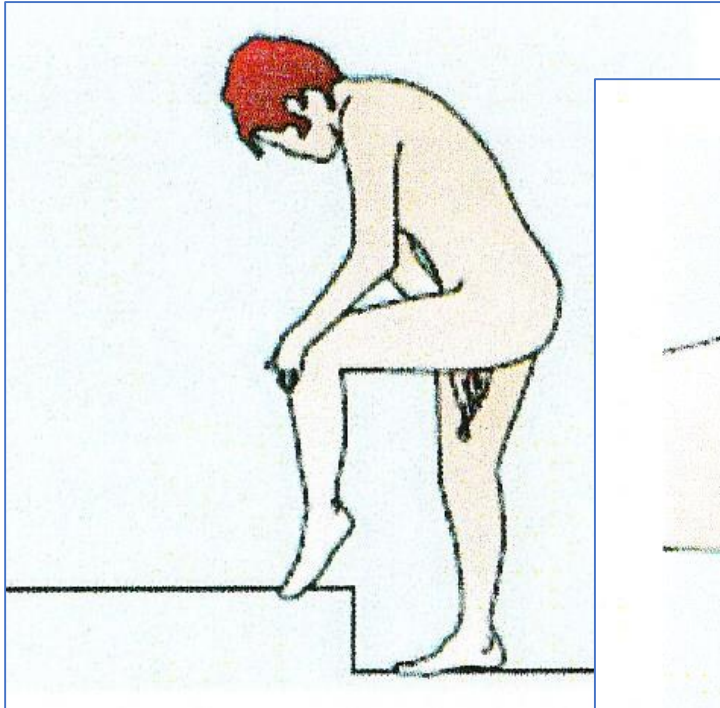
**\*HC2 was used for both HPV testing.**

# Instruction for sHPV

## Figures

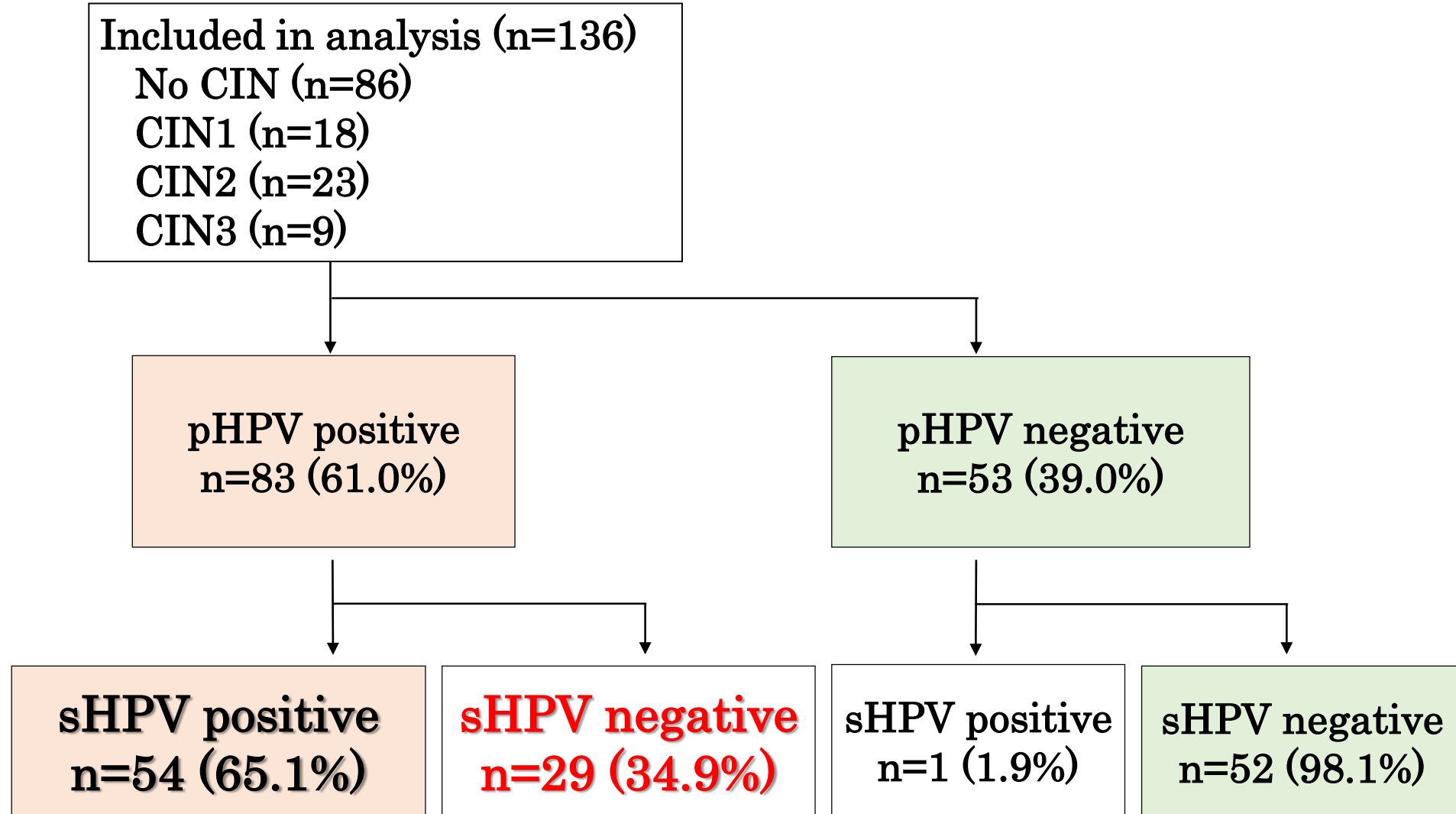


Evalyn Brush<sup>®</sup>



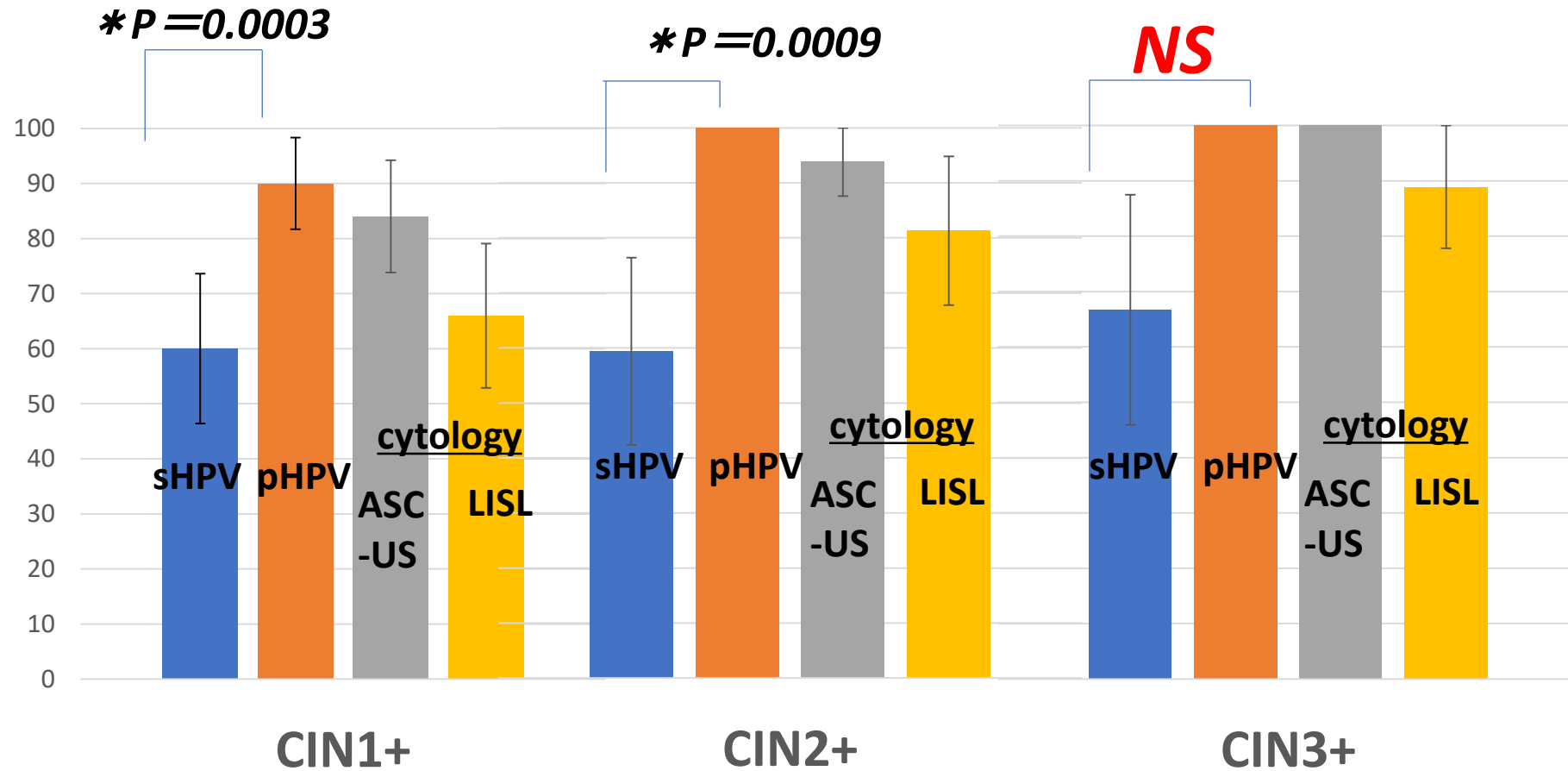
The instruction was written in plain Japanese.

# Result 1 : sHPV results vs pHPV results

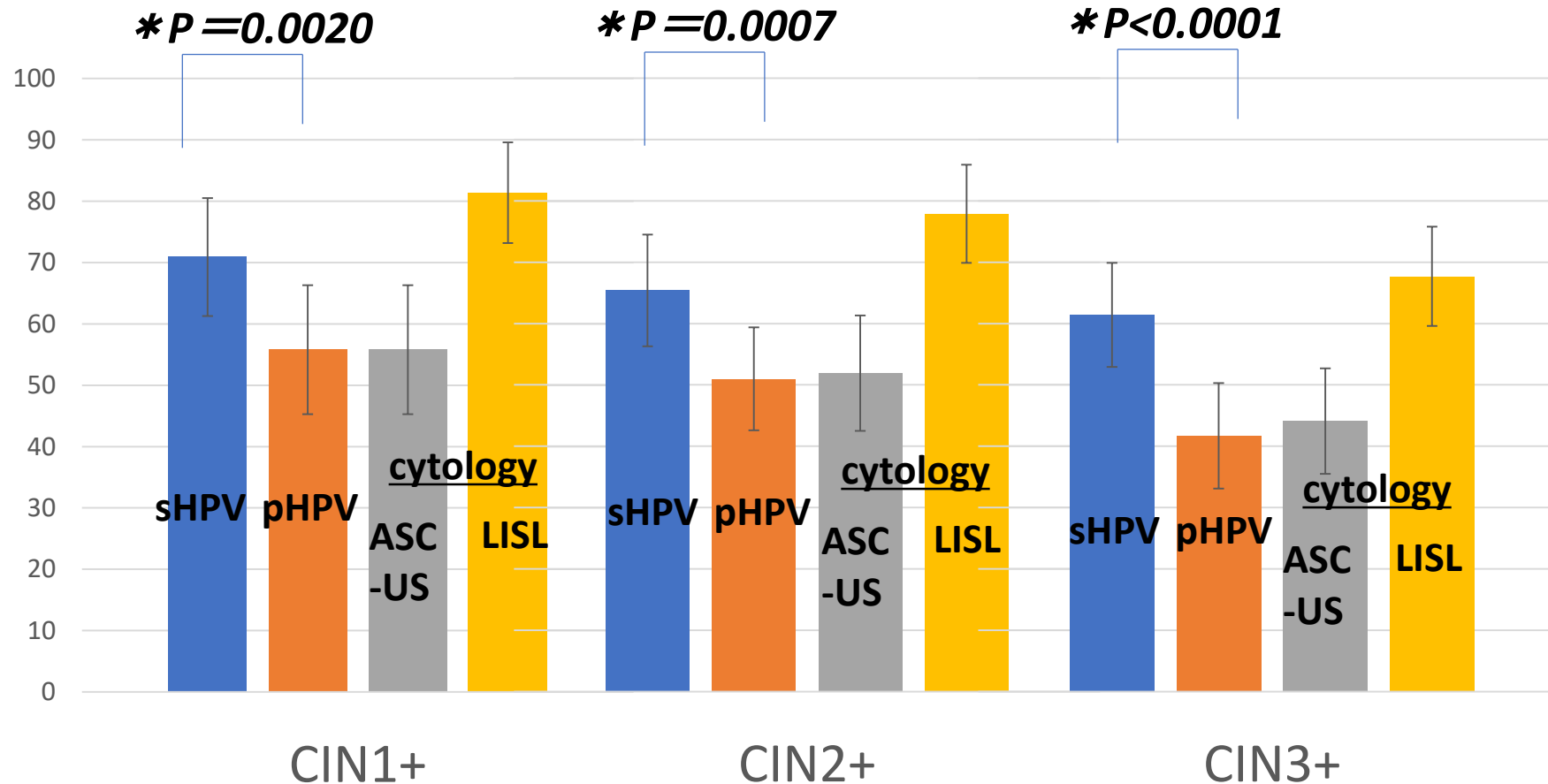




## Result 2 : Comparison of Sensitivities



## Result 3 : Comparison of Specificities



## Result 4 -1: Acceptability of sHPV versus pHPV

Outcome	sHPV test n (%)	pHPV test n (%)	p value
Easy to understand instructions			
Very easy	66 (48.5)	NA	
Easy	44 (32.3)		
Difficult	15 (11.0)		
Very difficult	3 (2.2)		
Easy to use			
Very easy	82 (60.2)	NA	
Easy	36 (26.4)		
Difficult	10 (7.3)		
Very difficult	0 (0)		
Embarrassment			
Not embarrassing at all	93 (68.3)	17 (12.5)	<0.001
Not so embarrassing	32 (23.5)	37 (27.2)	
Embarrassing	8 (5.8)	55 (40.4)	
Very embarrassing	0 (0)	24 (17.6)	

N/A; not applicable

J Obstet Gynaecol Res. 2017 Apr;43(4):710-717

## Result 5 : Acceptability of sHPV versus pHPV

Outcome	sHPV test n (%)	pHPV test n (%)	p value
Pain			
No pain at all	81 (59.5)	15 (11.0)	<0.001
Not so painful	40 (29.4)	46 (33.8)	
Painful	9 (6.6)	53 (38.9)	
Very painful	2 (1.4)	20 (14.7)	
Concern about accuracy			
No concern at all	2 (1.4)	60 (44.1)	<0.001
Not so concerned	36 (19.1)	55 (40.4)	
Concerned	73 (53.6)	14 (10.2)	
Very concerned	22 (16.1)	3 (2.2)	

## Lower sensitivities in sHPV testing; Why?

- **The combination of Evalyn Brush and HC2?**
  - ⇒ Generally, sensitivity of sHPV < pHPV except for some PCR-based HPV testing.
- **Inappropriate self-sampling procedures?**
  - ⇒ With limited experience of tampon-use (about 30%?)
- **The sampling order?**
  - ⇒ However, there is a trial, which showed that it did not influence the result (Harper DM, et al. J Fam Pract. 1999;48(7):531-535).



## **Conclusion of our pilot study about the validation of self-sampling HPV testing**

**Self-HPV testing has the potential to improve very low cervical cancer screening uptakes in Japan, because of good acceptability.**

**However, sensitivities to detect CINs must be improved to substitute for conventional cytology or HPV testing taken by gynecological doctors.**

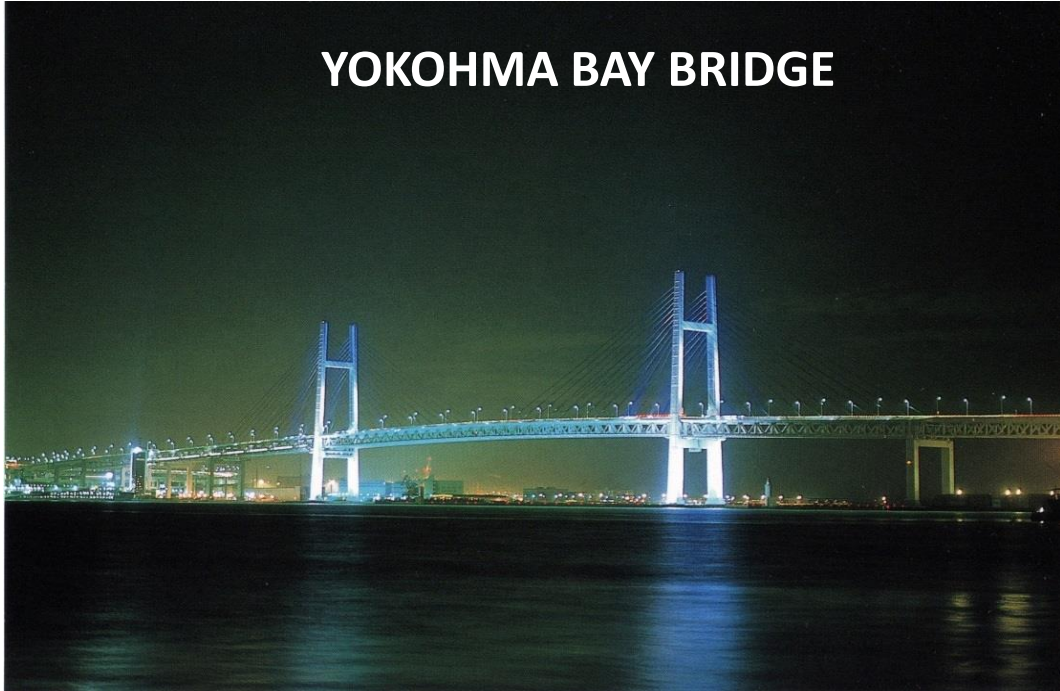
## Summary of my presentation

- As the cervical cancer screening innovation, primary HPV testing with cytology triage is implemented or planned in many developed countries.
- In the developing countries, the method with HPV testing and LEEP treatment in the same day may work effectively, instead of training cytoscreeners, under the very high prevalence of HPV vaccination.
- In Japan, academic societies are actively united to restore the credibility of HPV vaccines, although the HPV vaccine problem has become a political issue.
- Improvement of risk communications about HPV vaccination is crucial for the further progress of cervical cancer prevention all over the world.

*Thank you for your kind attention.*

Please keep your eyes on the world CC prevention,  
and also 2020 Olympic Games in Japan!

YOKOHMA BAY BRIDGE



**Special thanks to  
Prof. Kanal,  
all the SCGO committee  
members,  
Dr. Fujita and Dr.  
Haruyama.**

YOKOHMA CITY NIGHT VIEW

