

Life



Health



Innovation



# Innovations in Human Papillomavirus Vaccine

1. Current HPV vaccines
2. New development
3. What's next?

# **PART I**

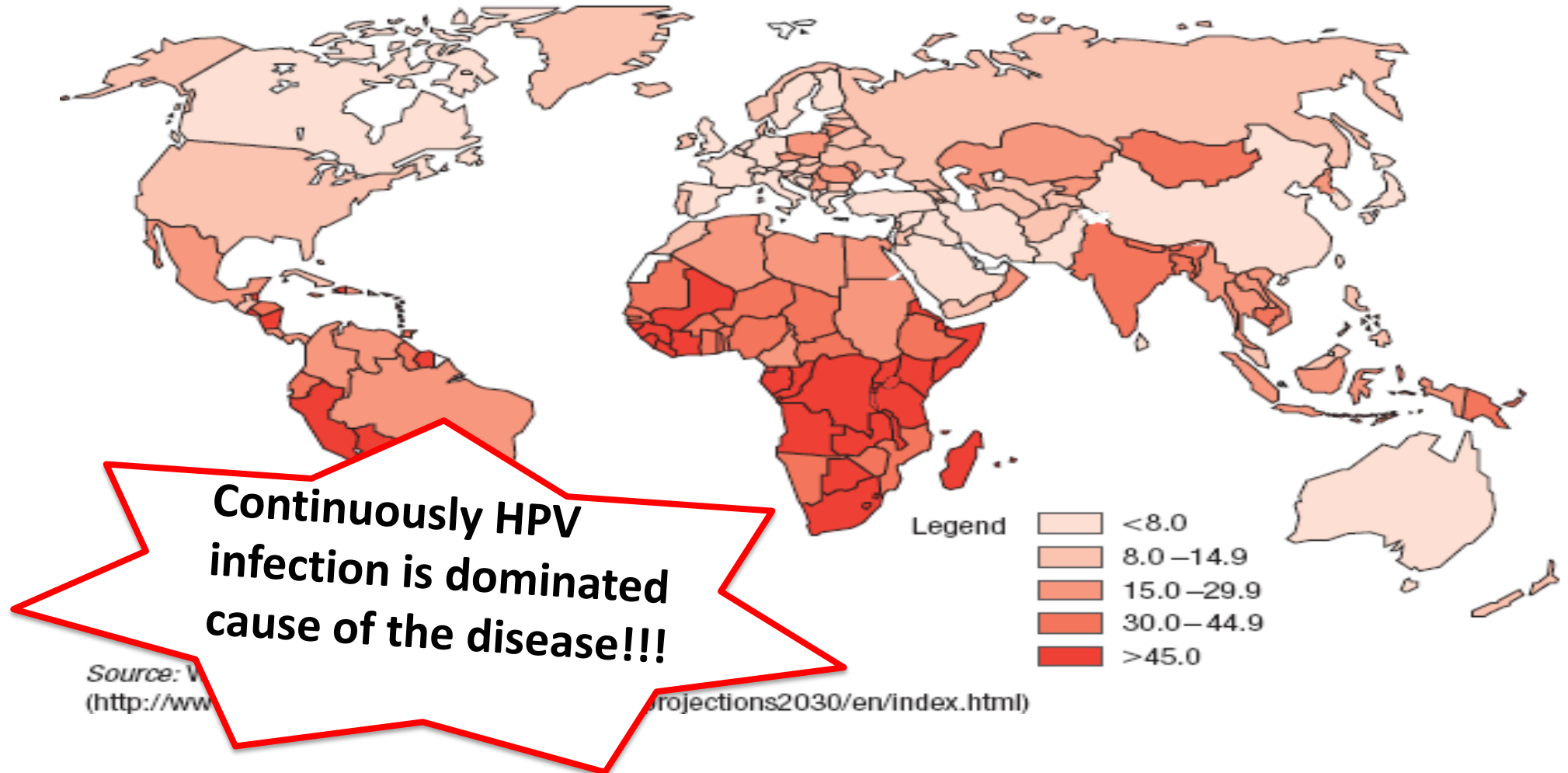
## **CURRENT HPV VACCINES**

# Worldwide incidence of cervical cancer

Worldwide incidence of cervical cancer per 100 000 females (all ages), age-standardized to the WHO standard population, 2005

2

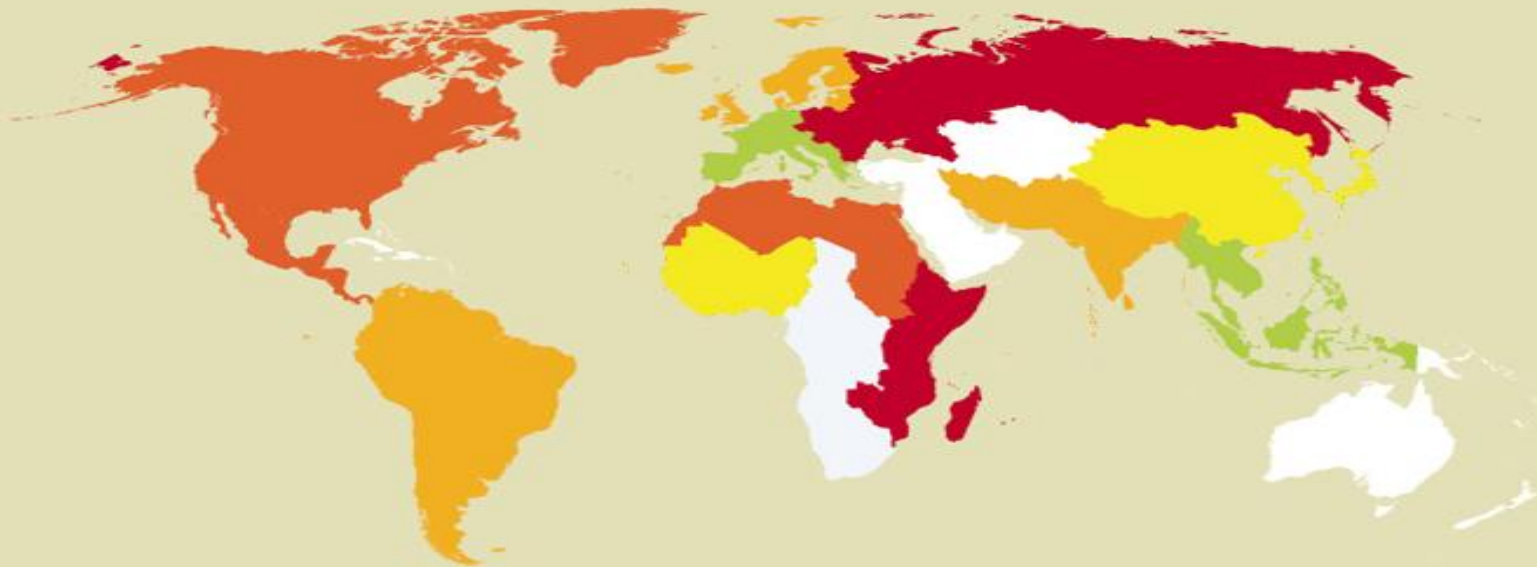
Current HPV  
Vaccines



# Human Papillomavirus types 16&18 (HPV16&18) ——causing **70%** of cervical cancer cases worldwide

2

**WORLDWIDE HPV-16 AND -18 PREVALENCE (%)**  
**AMONG WOMEN WITH NORMAL CYTOLOGY**  
A META-ANALYSIS OF 42,823 WOMEN AGED  $\geq 15$  YEARS



Quintile distribution of prevalence point estimates:

Not available

1.3 - 2.3

2.4 - 3.0

3.1 - 4.5

4.6 - 6.8

6.9 - 9.3

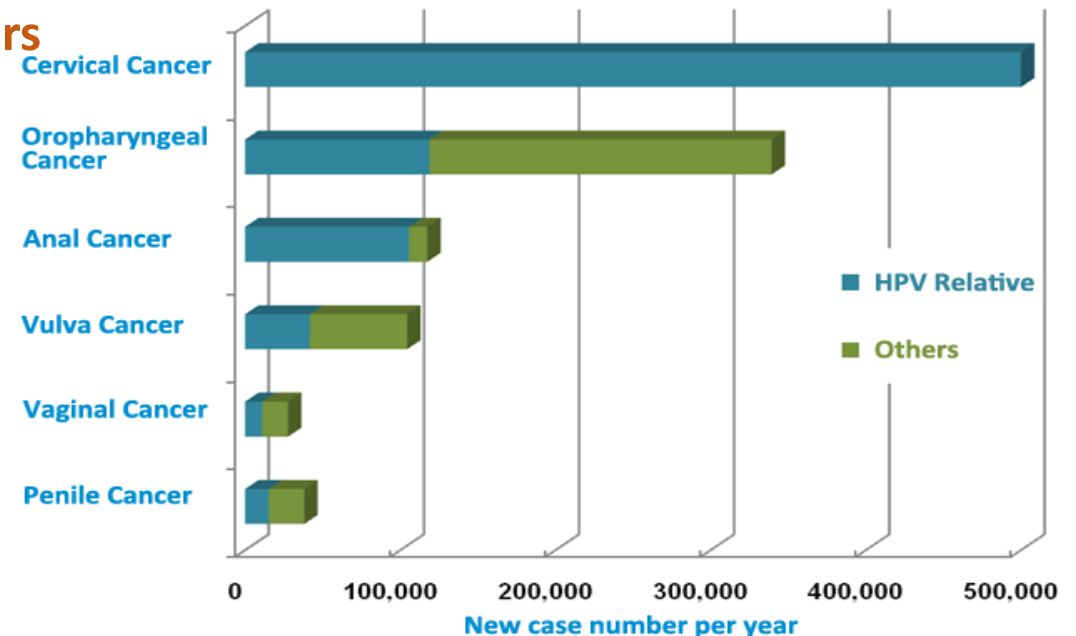
# Human Papillomavirus Vaccine (HPV)

## — World's first vaccine against cancer

1

### Current HPV Vaccines

- Persistent infection of certain high risk types of HPV can cause cervical cancer in women
  - More than 529,000 new cases each year worldwide
  - More than 274,000 deaths each year
  - > 85% deaths are in developing countries
  - Represents 13% of all female cancers
- HPV can also cause:
  - Anogenital cancer
  - Head and neck cancers
  - Genital warts



# HPV Vaccines

1

There are two HPV vaccines available on the market:

- Merck's Gardasil® (HPV 6/11/16/18)
- GlaxoSmithKline's Cervarix® (HPV 16/18)

By August 2014, 58 countries (30%) had introduced HPV vaccine in their national immunization program for girls, and in some countries also for boys.

Vaccine	Company	Market launch	2012 Sales (US\$)	2013 Sales (US\$)
Gardasil	Merck	Jan 2006	1.6 billion	1.8 billion
Cervarix	GSK	Sep 2007	362 million	230 million

Current HPV  
Vaccines

# **PART II**

## **NEW DEVELOPMENT**





## Increased Valences

- From 2-valent & 4-valent to 9-valent
- Increased coverage rate from 70% to 90% (next page)
- Phase III study completed, waiting for approval by US FDA
- 3-valent and 5-valent vaccines are also been developed

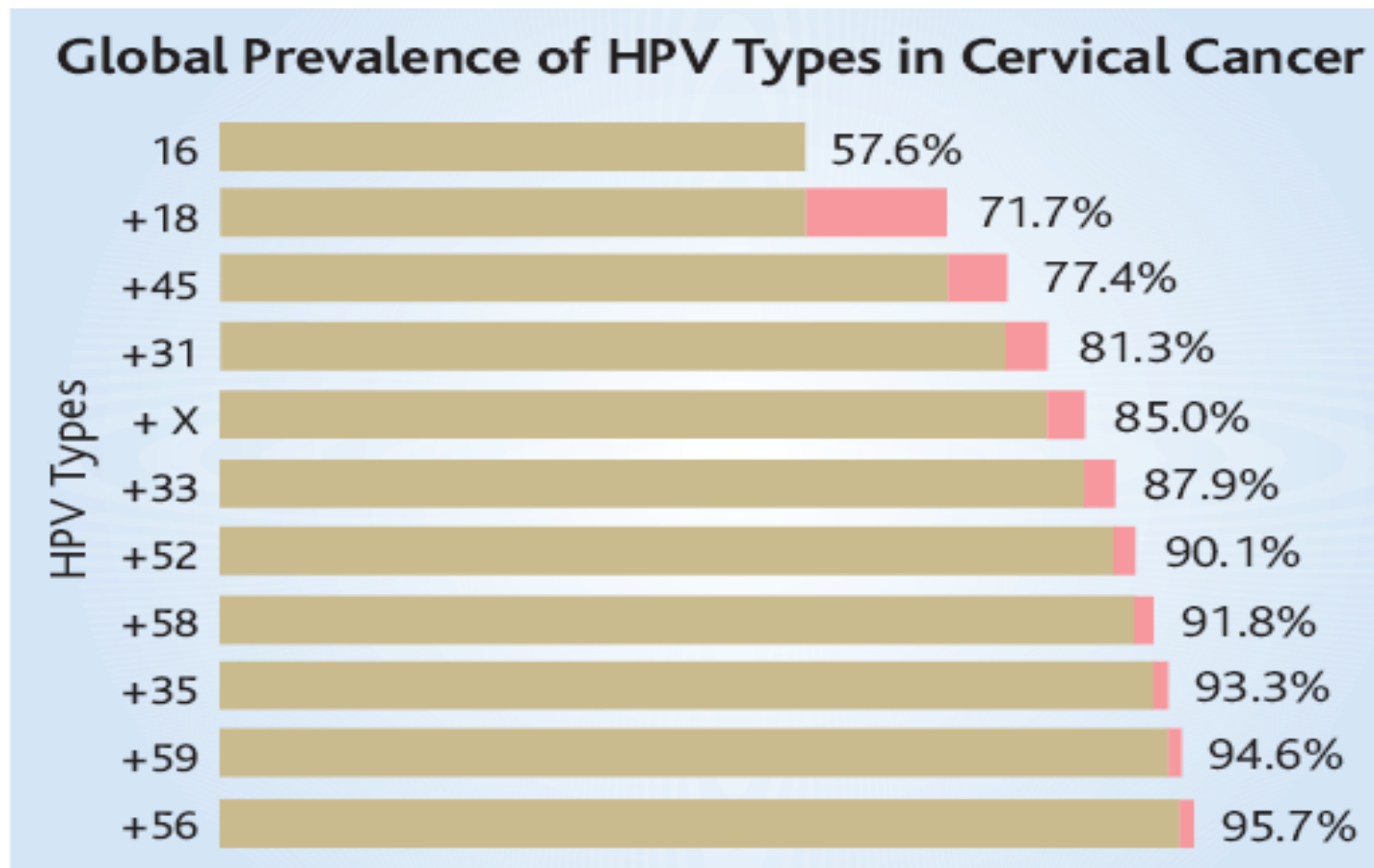
# 9-Valent HPV Vaccine

— Stronger protect against Cervical Cancer

2

New

development



— JON COHEN, 29 APRIL 2005 VOL 308 SCIENCE

## Reduced Injection

- From 3-dose regimen to 2-dose regimen
- WHO recommended using 2-dose regimen for routine immunization
- Shortened immunization schedule make it easier to administer
- New standard for new developers to match
  
- HPV has been recommended for routine immunizations in 40+ countries

# 2-dose regiment VS. 3-dose regiment

Results of a systematic review indicate that 2 doses of HPV vaccine in girls aged 9–14 years are non-inferior to 3 doses in terms of immunogenicity when compared to 3 doses in girls aged 9–14 years or 3 doses in women aged 15–24 years.

2

New

development

## Immunogenicity of 2 vs. 3 doses of HPV vaccination in immunocompetent girls

**Population :** Immunocompetent females  
**Intervention:** 2 doses of HPV vaccination in girls (9-14 years)  
**Comparison:** 3 doses of HPV vaccination in girls or women  
**Outcome :** Immunogenicity (GMT)

What is the scientific evidence of non-inferior immunogenicity of a 2 dose HPV vaccination schedule in girls (9-14 years) compared to a three dose schedule in girls or women?				
		Rating		Adjustment to rating
Quality Assessment	No. of studies/starting rating		4/ RCT 2/ observational <sup>I</sup>	4
	Factors decreasing confidence	Limitation in study design <sup>II</sup>	Serious	-1
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence		3	
Summary of Findings	Statement on quality of evidence		We are moderately confident in the estimate of effect on health outcome. The true effect is likely to be close to the estimate of the effect.	
	Conclusion		We are moderately confident that a 2-dose HPV schedule induces non-inferior immunogenicity compared to a 3-dose HPV schedule. Evidence from 3 RCTs as well as 2 non-randomized / non-controlled trials indicate that a two dose HPV schedule in girls induces non-inferior levels of GMT to HPV 16 and 18 than a three dose schedule in girls or women. Bridging studies allow assumption of efficacy of a 2-dose	

## Efficacy of 2 vs. 3 doses of HPV vaccination in immunocompetent girls

**Population :** Immunocompetent females  
**Intervention:** 2 doses of HPV vaccination in girls (9-14 years)  
**Comparison:** 3 doses of HPV vaccination in girls or women  
**Outcome :** Cervical Cancer

What is the scientific evidence of non-inferior immunogenicity of a 2 dose HPV vaccination schedule in girls (9-14 years) compared to a three dose schedule in girls or women?				
		Rating		Adjustment to rating
Quality Assessment	No. of studies/starting rating		4/ RCT 2/ observational <sup>I</sup>	4
	Factors decreasing confidence	Limitation in study design <sup>II</sup>	Serious	-1
		Inconsistency	None serious	0
		Indirectness <sup>III</sup>	Serious	-2
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence		1	
Summary of Findings	Statement on quality of evidence		We have very little confidence in the estimate of the effect on the health outcome.	
	Conclusion		No data vaccine efficacy against cervical cancer is available using a 2-dose HPV schedule despite non-inferior immunogenicity compared to a 3-dose HPV schedule. Evidence from 3 RCTs as well as 2 non-randomized / non-controlled trials indicate that a two dose HPV schedule in girls induces non-inferior levels of GMT to HPV 16 and 18 than a three dose schedule in girls or women. Bridging studies allow assumption of efficacy of a 2-dose vaccination schedule in girls (9-14 years).	

## 2-dose regiment VS. 3-dose regiment

2

New

development

Results of a systematic review indicate that 2 doses of HPV vaccine in girls aged 9–14 years are non-inferior to 3 doses in terms of immunogenicity when compared to 3 doses in girls aged 9–14 years or 3 doses in women aged 15–24 years.

Gardasil (Quadrivalent HPV vaccine): For girls and boys aged 9–13 years this vaccine can be administered according to a 2-dose schedule (0.5 mL at 0 and 6 months). If the second vaccine dose is administered earlier than 6 months after the first dose, a third dose should be administered.

Cervarix (Bivalent HPV vaccine): For girls aged 9–14 years a 2-dose schedule (0.5 mL at 0 and 6 months) is recommended. The second dose can be given between 5 and 7 months after the first dose.

# **PART III**

## **WHAT'S NEXT?**



## What's Next

# What's Next?

- More valences?
- Combos?
- Global efforts to expand routine immunizations: efforts from GAVI, Gates Foundation, etc.
- Immunizing males – is single-sex immunization going to work?

# Revised WHO position on human papillomavirus vaccines

3

What's next?

Updated position paper published on 24 Oct. 2014. WHO revised the number of doses recommended for human papillomavirus (HPV) vaccines for different age groups. Furthermore, WHO reiterates its recommendation that HPV vaccines should be included in national immunization programmes.





What's next?

3



## Upcoming events

WHO Informal consultation on Recommendations to assure the quality, safety and efficacy of recombinant human papillomavirus virus-like particle (HPV-VLP) vaccines

11-12 November 2014, Geneva, Switzerland

## The Supply Issue – Who's Providing the Vaccine?

3

What's next?

- Two companies supplying so far
- Two more companies in Phase 3 trials
- Several more in earlier stage
  
- Can these 4 companies supply the world?
- Needs for innovative ways to supply?

**INNOVAX**  
厦门万泰

4

Innovax

Established at

2005 03

Focus on --

Developing, manufacturing and marketing innovative vaccines, bioactive materials, and medical devices.

Committed to--

Increase the availability of high quality innovative Vaccines and Diagnostic reagents to combat infectious diseases globally.



# Innovax – Products and Pipeline

4

Innovax

## Launched Product:

- Hepatitis E vaccine (*E. coli*)

## Pipeline:

- Varicella, Registration
- HPV 2-valent (*E. coli*), Phase 3
- HPV multi-valent, pre-clinical

## Company Information

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Thanks !

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