



# **Pan American Health Organization**



*Regional Office of the  
World Health Organization*

## **HPV Vaccines: Background and Current Status**

**Bogota, Colombia, 2007**

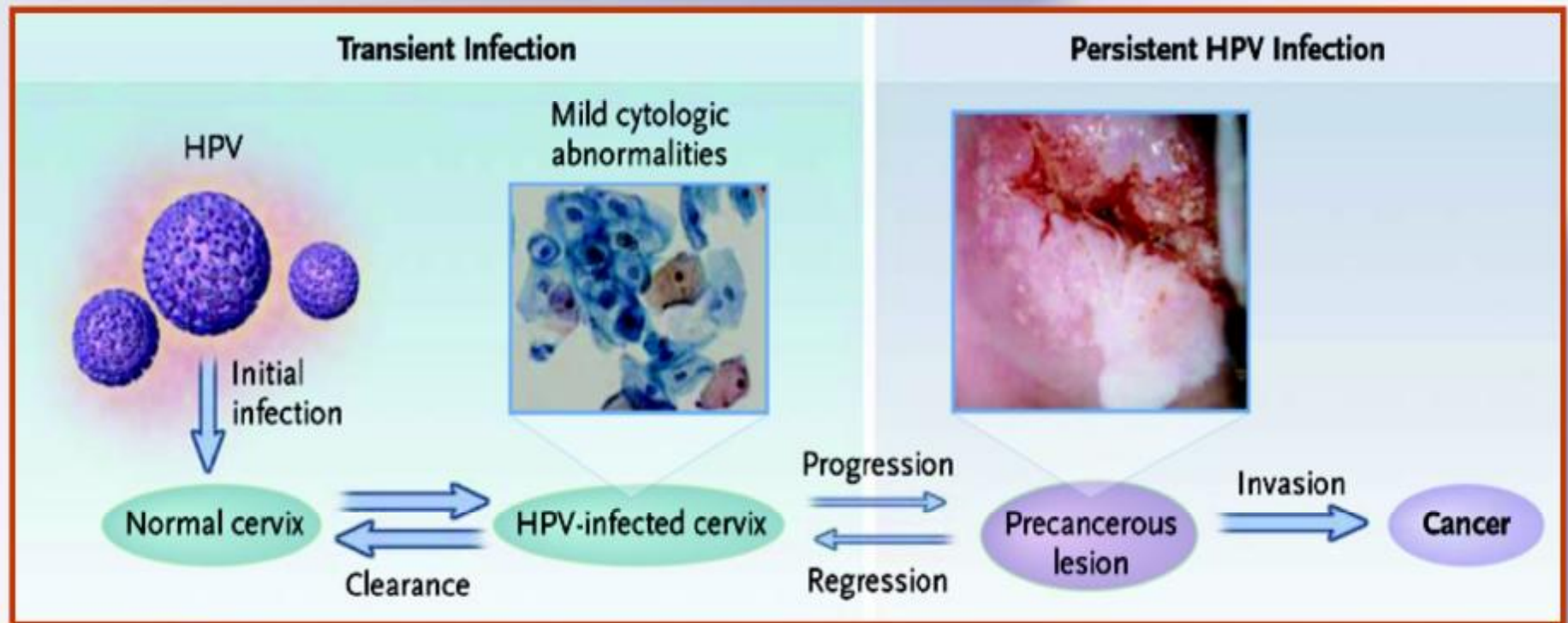
**Jon Kim Andrus, MD**

# HPV and Cervical Cancer

Evidence that HPV is essential:

- Documented molecular studies of cervical cancer
- Case-control studies of women with cancer with age-matched controls
- Prospective follow-up studies
- Experimental evidence

# Natural History of HPV Infections



Wright and Schiffman (2003) *NEJM*

# Integrated cervical cancer prevention and control

- Challenges encountered in trying to improve coverage and quality of services for cervical cancer screening
- Recent development of 2 safe and efficacious vaccines
- Opportunity with new technology to improve integrated and comprehensive cervical cancer prevention and control program

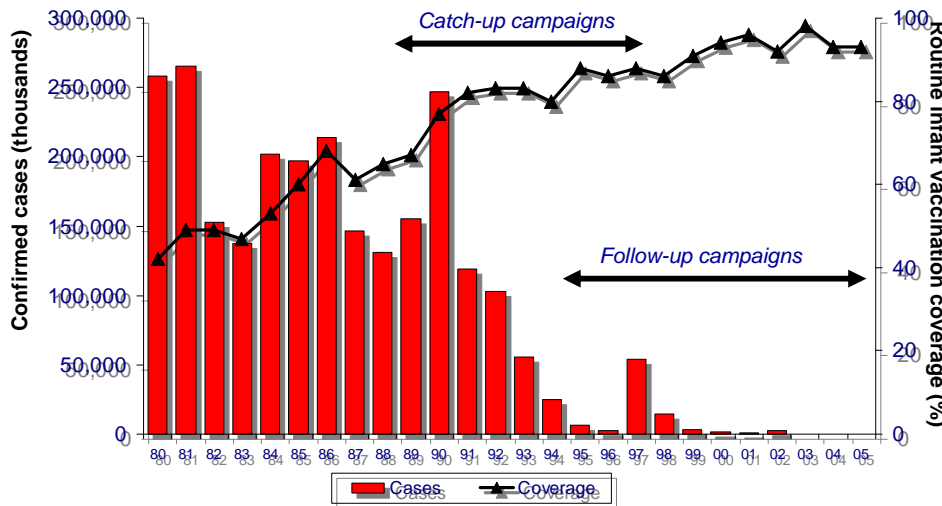
# Impact of Vaccines

## *Corynebacterium diphtheriae*

- *1900 - diphtheria killed more Americans than cancer*
- *1990's - averaged only 3 cases per year in United States*

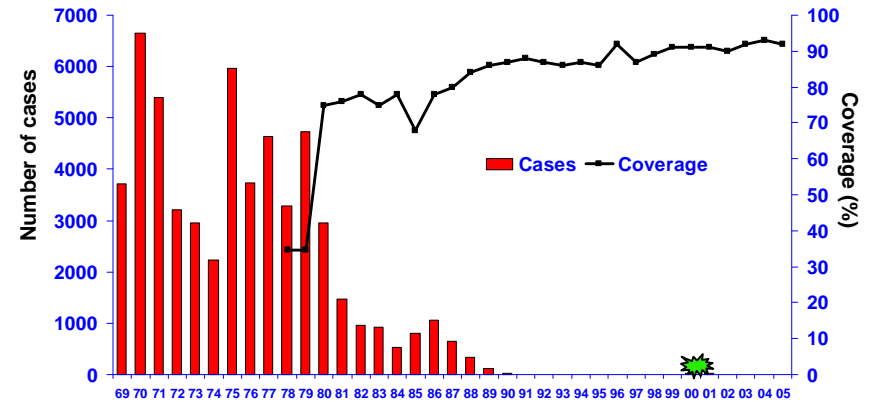
# Vaccination successes in LAC

## Measles elimination



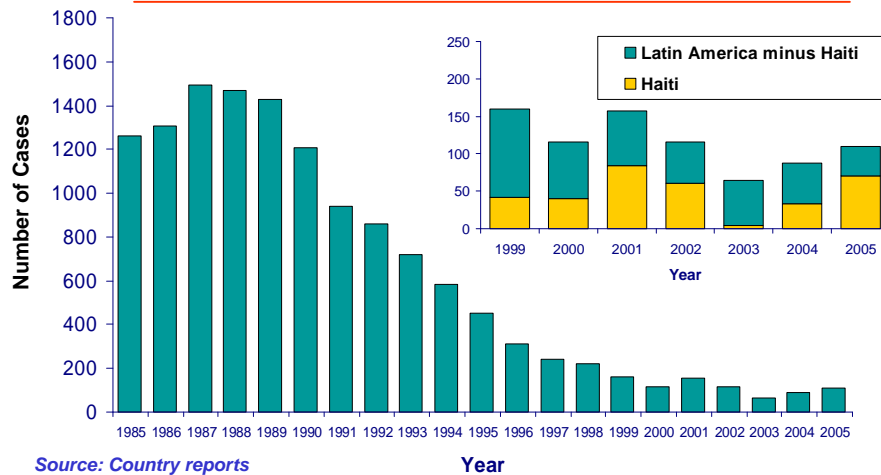
Note: 81 confirmed cases in 2005

## Polio Eradication



★ Type 1 vaccine derived virus in 2000 and 2001: 21 cases

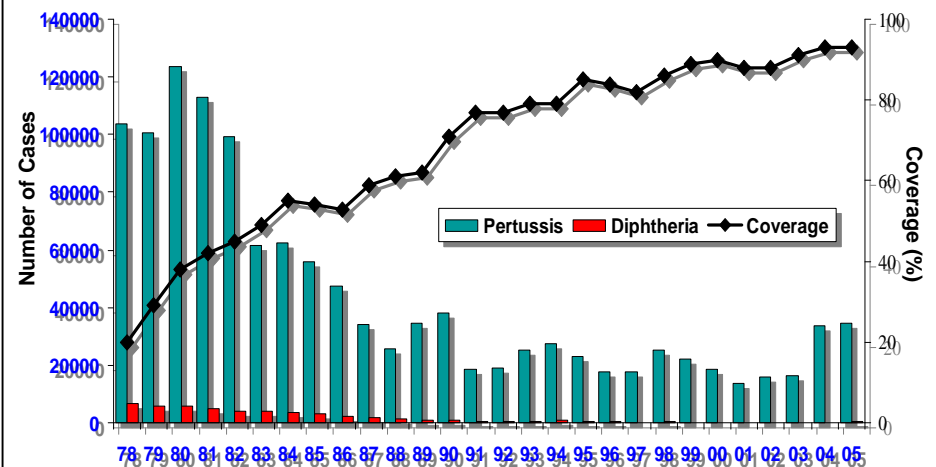
## Neonatal Tetanus Elimination



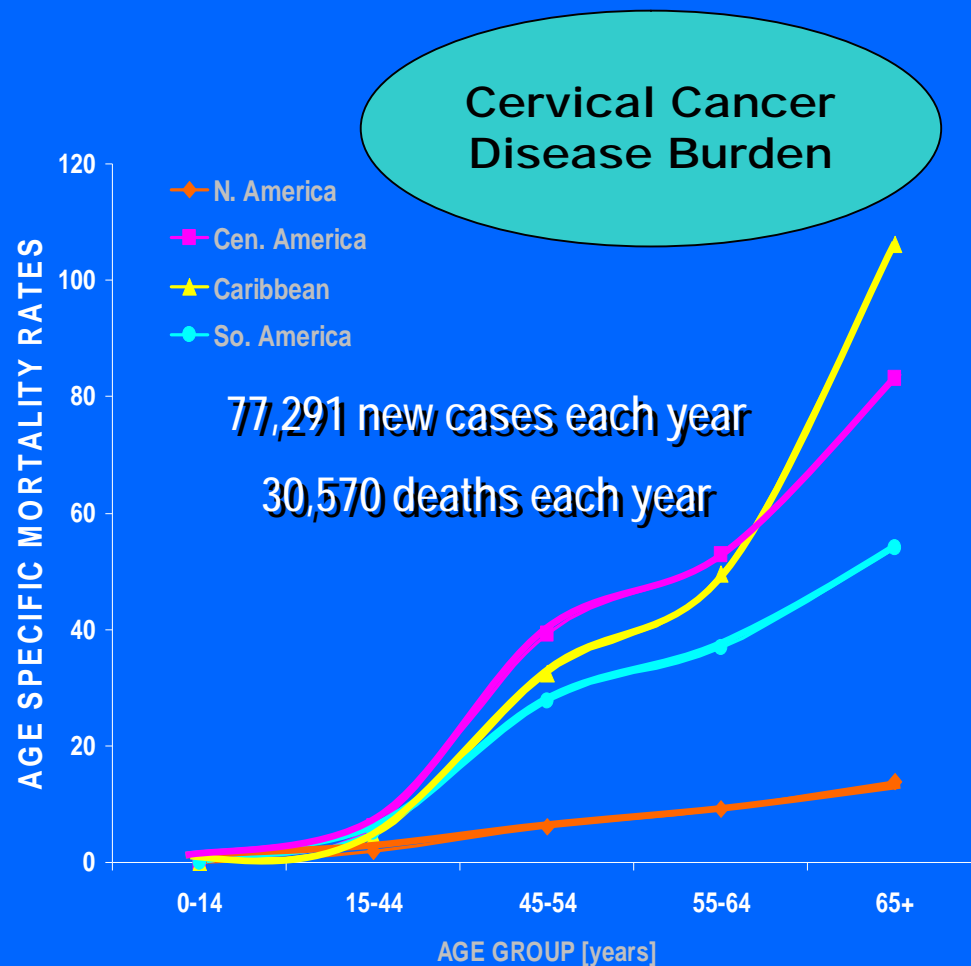
Source: Country reports

Countries with cases in the last 3 years: Argentina, Bolivia, Brazil, Colombia, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru and Venezuela

## Diphtheria and Pertussis



# Regional Challenge



- Taking advantage of new technologies while sustaining national immunization programs within national health priorities
- Reducing the developing country uptake lag time of two decades

## Status of Gardasil HPV Vaccine Licensure, 2007\*

<i>WHO Region</i>	<i>Countries that have licensed Gardasil™</i>
<i>Africa</i>	<i>Chad, DR Congo, Kenya, Mauritius, Togo</i>
<i>Americas</i>	<i>Argentina, Aruba, Bermuda, Brazil, Canada, Chile, Colombia, Costa Rica, Curaçao, Dominican Republic, Ecuador, Guatemala, Mexico, Perú, Trinidad and Tobago, USA</i>
<i>Europe</i>	<i>Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, UK</i>
<i>Eastern Mediterranean</i>	<i>Morocco, UA Emirates</i>
<i>Southeast Asia</i>	<i>Indonesia, Thailand</i>
<i>Western Pacific</i>	<i>Australia, Hong Kong, Macau, Malaysia, New Zealand, Philippines, Singapore, Taiwan</i>



# Status of Cervarix HPV Vaccine Licensure, 2007

- First to license earlier in 2007: Australia, Kenya, and United Arab Emirates
- More recently, EMEA (Europe's licensure body) approved vaccine
- Now licensed in >27 European countries
- Submitted to WHO for pre-qualification
- US FDA approval expected by 1<sup>st</sup> quarter 2008

# Burden of Disease

## Burden of Disease – HPV 6, 11, 16, 18

- 16,18
  - 70% of cervical cancers,
  - 70% of anogenital cancers,
  - 52% of CIN 2,3 lesions and
  - Many abnormal PAPs
- 6,11
  - 90% of genital warts,
  - 90% of laryngeal papillomatosis

# HPV Vaccines

## *Types of vaccines*

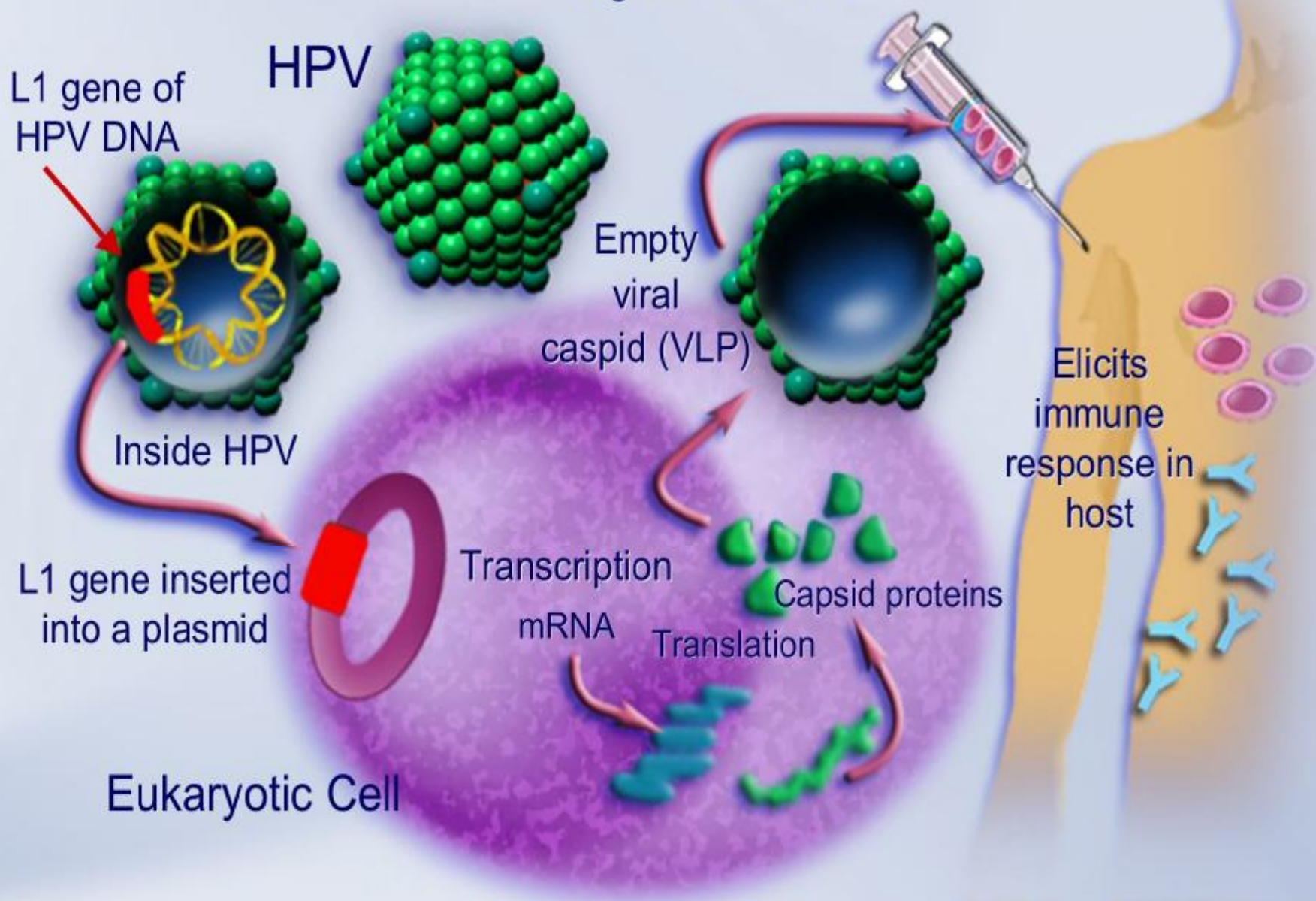
- *Prophylactic – will prevent infections*
- *Therapeutic – will treat established infections or lesions*

# HPV Vaccines

## *Current prophylactic vaccines:*

- Recombinant L1 HPV capsid proteins that form “virus-like” particles (VLP)
- Non-infectious
- Produce high levels of neutralizing antibodies
- Not expected to cause regression of established lesions

# HPV L1 Virus-Like-Particle (VLP) Vaccine Synthesis



# HPV VACCINES

Variables of Interest	Quadrivalent Gardasil™ (Merck)	Bivalent Vaccine Cervarix™ (GSK)
Subunit VLPs	6, 11, 16, 18	16, 18
Substrate	Yeast	Bactulovirus expression system using insect cells
Adjuvant	Alum	ASO4
Vaccine form and storage	Liquid at 2-8° C	Liquid at 2-8° C
Schedule	0.5 ml IM at 0,2,6 months	0.5 ml IM at 0,1,6 months

# HPV VACCINE EFFICACY MEASURES

End Points of Efficacy	Quadrivalent Vaccine Efficacy [95% CL]	Bivalent Vaccine Efficacy [95% CL]
Persistent Infection	96% [94.0-100] <i>Villa et al:2006</i>	96% [75.2-99.9] <i>Harper et al:2006</i>
CIN grade 2	100% [81-100] <i>Garland et al:2007</i>	100% [-7.7-100] <i>Harper et al:2006</i>
CIN grade 2+		90.4% [53.4-99.3] <i>Paavonen et al:2007</i>
CIN grade 3	100% [76-100%] <i>Garland et al:2007</i>	

# HPV VACCINES

<b>Variables of Interest</b>	<b>Quadrivalent Gardasil™ (Merck)</b>	<b>Bivalent Vaccine Cervarix™ (GSK)</b>
<b>Adverse Events</b>	<b>No serious vaccine-related adverse events Pain at injection site most common Others (swelling, redness, fever)</b>	<b>No widespread serious vaccine-related adverse events Pain at injection site most common</b>
<b>First licensed</b>	<b>1 June 2006, Mexico 8 June 2006, USA</b>	<b>Australia, Kenya, and UAE</b>
<b>Population group</b>	<b>Females, aged 9-26 years</b>	<b>Current studies with females aged 15-25 years</b>

# Projected Estimates of Vaccine Benefit: Invasive Cervical Cancer Cases Averted in 5 Latin America and Caribbean Countries (Goldie et al)

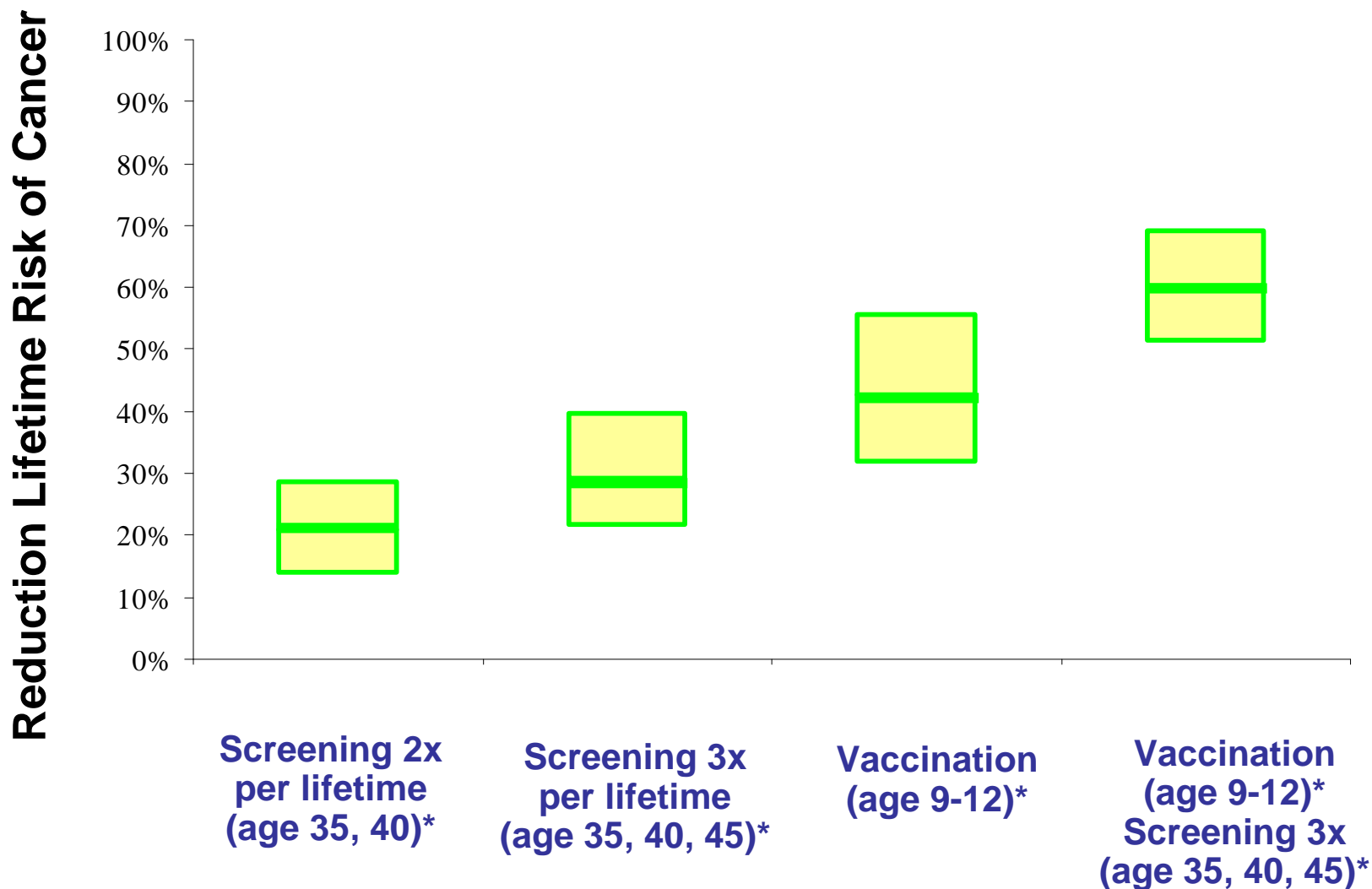
Country	Averted Cases (1 year)	Averted Cases (5 years)
<b>No screening:</b>		
<b>Colombia</b>	4,160	21,825
<b>Haiti</b>	1,190	6,262
<b>With screening:</b>		
<b>Brazil</b>	11,958	62,779
<b>Peru</b>	3,290	17,293
<b>Mexico</b>	7,630	40,083

**148,240 cases averted over a 5 yr period**



- Assuming 70% vaccine coverage and no screening in Haiti and Columbia
- Assuming 70% coverage of vaccine and screening in Peru, Brazil, and Mexico.

# Cervical Cancer Prevention in Brazil



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\*Assumes coverage 70%, VE 100%

Goldie, et al, unpublished

# Cost Effectiveness and Affordability

- Cost effectiveness attempts to define the value of an intervention
- Affordability refers to the implications on the actual budget
- Example (Goldie et al, South America, In Press):

Price per dose	Cost effectiveness	Budget*
\$ 5.00	< \$400 to avert DALY	\$360 million
\$12.25	< \$800	\$811 million
\$19.50	<\$1,400	\$1.26 billion

# Financial Requirements for Vaccines

	Vaccine	Cost		Vaccine Budget
Basic Vaccines (Fully immunized child)	BCG	\$0.10		Total X Birth Cohort
	OPV	\$0.66		
	Penta+Booster	\$12.37		
	MMR			
	<b>TOTAL</b>			
Underutilized Vaccines	Yellow Fever, Pediatric	<b>\$15.93</b>	1 doses	Doses X Cost X Children <1 yr
	Yellow Fever		1 doses	Cost X Adults at risk
	Influenza, Seasonal, Pediatric		2 doses	Doses X Cost X Children <1 yr
	Influenza, Seasonal, Adult		1 doses	Cost X Adults at risk
Supplemental Immunization	Rubella Elimination	\$0.43	1 doses	Cost X Women 15-39 yrs
New Vaccines	Rotavirus (Oral Vaccine Candidates)		2/3 doses	Cost X Doses X Birth Cohort
<b>TOTAL</b>	Routine Childhood Vaccines			<b>\$30.66</b> Total X Birth Cohort



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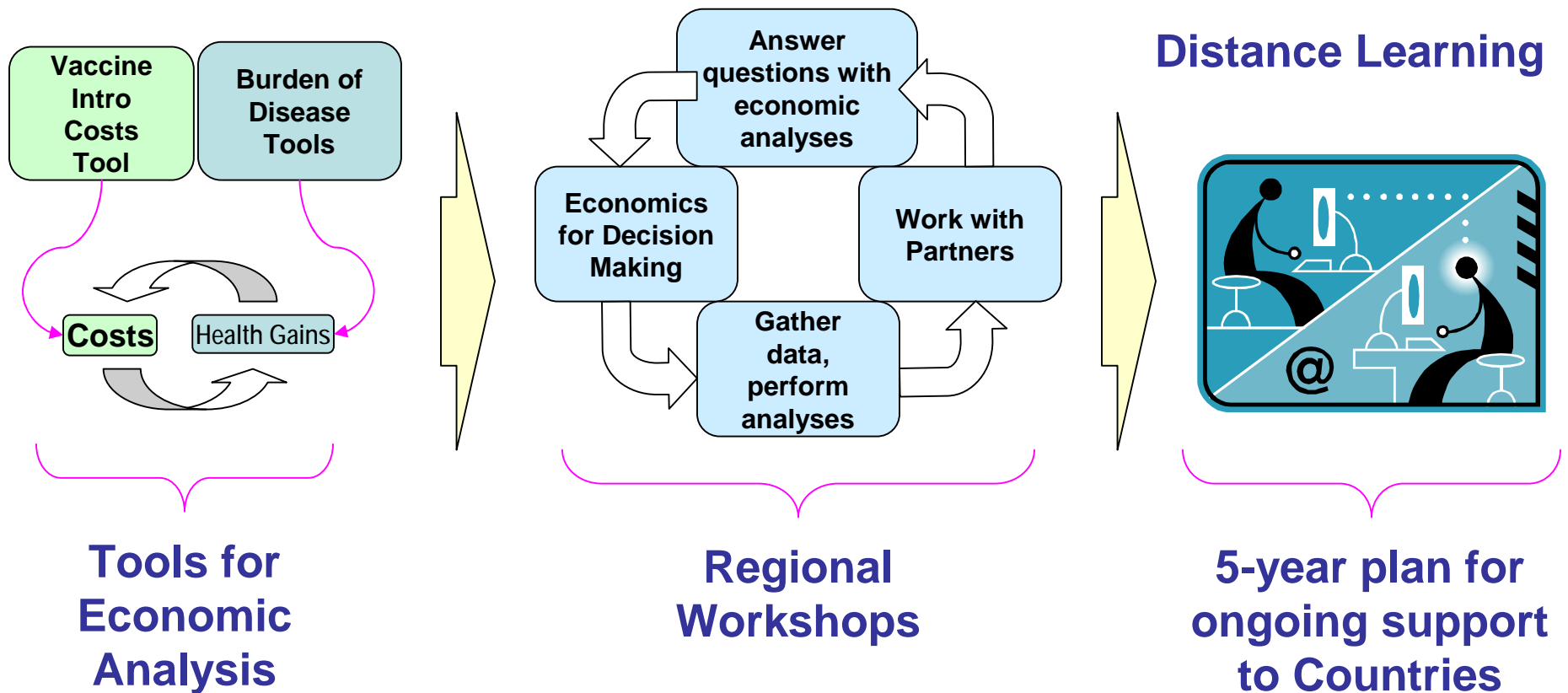
Average prices, RF - 2007

# **PAHO's Role to Promote Accelerated Access to HPV vaccine**

- HPV cervical cancer control partnership created
- Strategies for enhancing national capacity for evidence-based policy decisions being implemented (ProVac)
- Political commitment being mobilized
- Surveillance strategies being developed

# Pro-Vac

## Tools, Workshops, Long-term Support



# Summary (1)

- Safe, efficacious vaccines are available
- Many countries have licensed these vaccines
- Steps for pre-qualification are in place
- In anticipation of pre-qualification, PAHO has implemented policy for accelerating introduction using evidence-based processes outlined



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# Summary (2)

More effort is needed to assist countries with evidence-based decisions about vaccine introduction that account for:

- National health priorities
- Burden of disease
- Vaccine affordability and cost-effectiveness
- Capacity to sustain introduction, and
- How vaccination complements other prevention strategies



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# Conclusion

- We cannot accept a time lag of 20 years before HPV vaccines become affordable for use in developing countries
- Interventions must be supported by a broader base of partners that promote integrated, comprehensive cervical cancer prevention and control strategies



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# Acknowledgements

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