

Recent findings from the NCI Costa Rica HPV-16/18 Vaccine Trial

Aimée R. Kreimer, Ph.D.

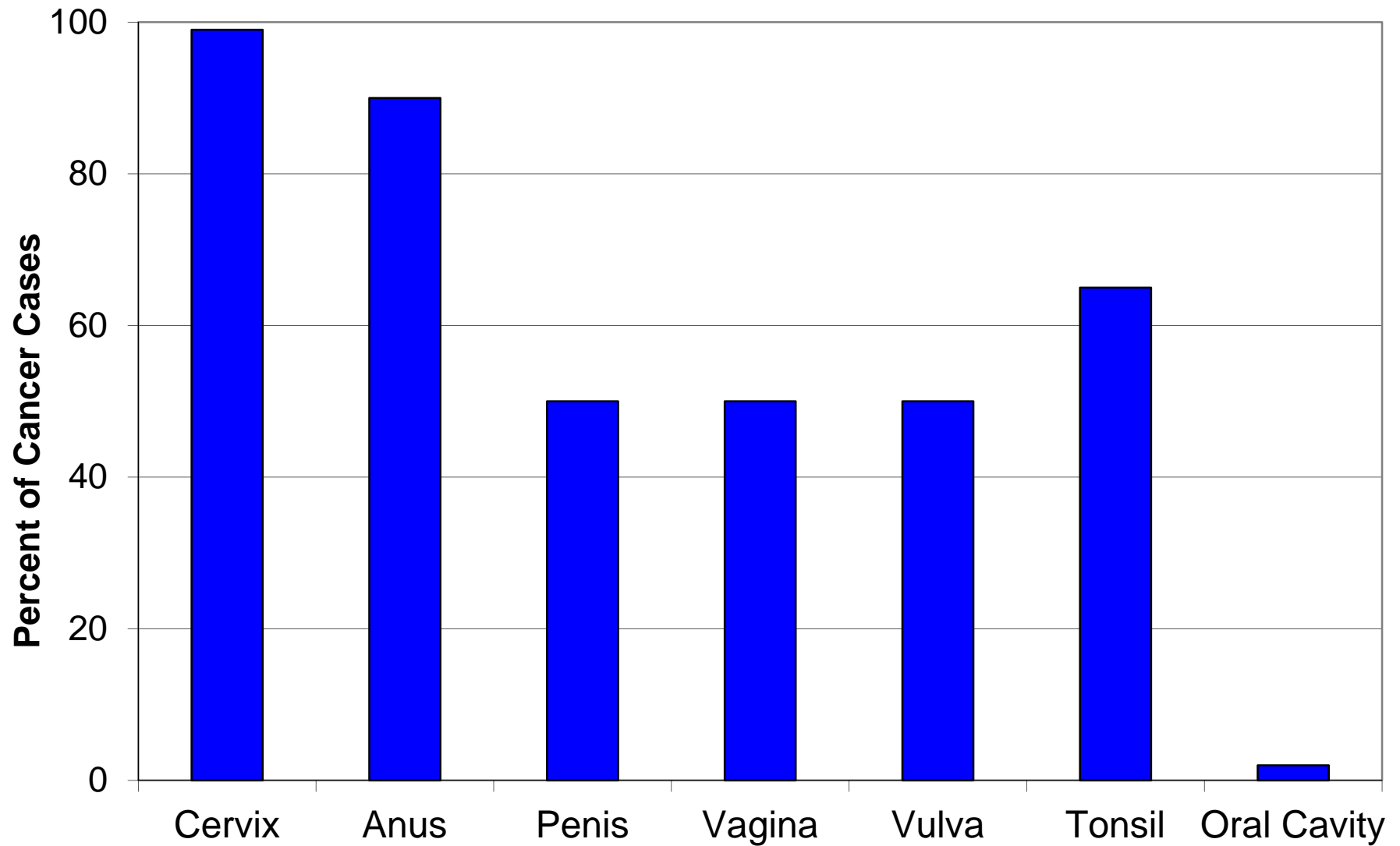
Investigator

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National Cancer Institute

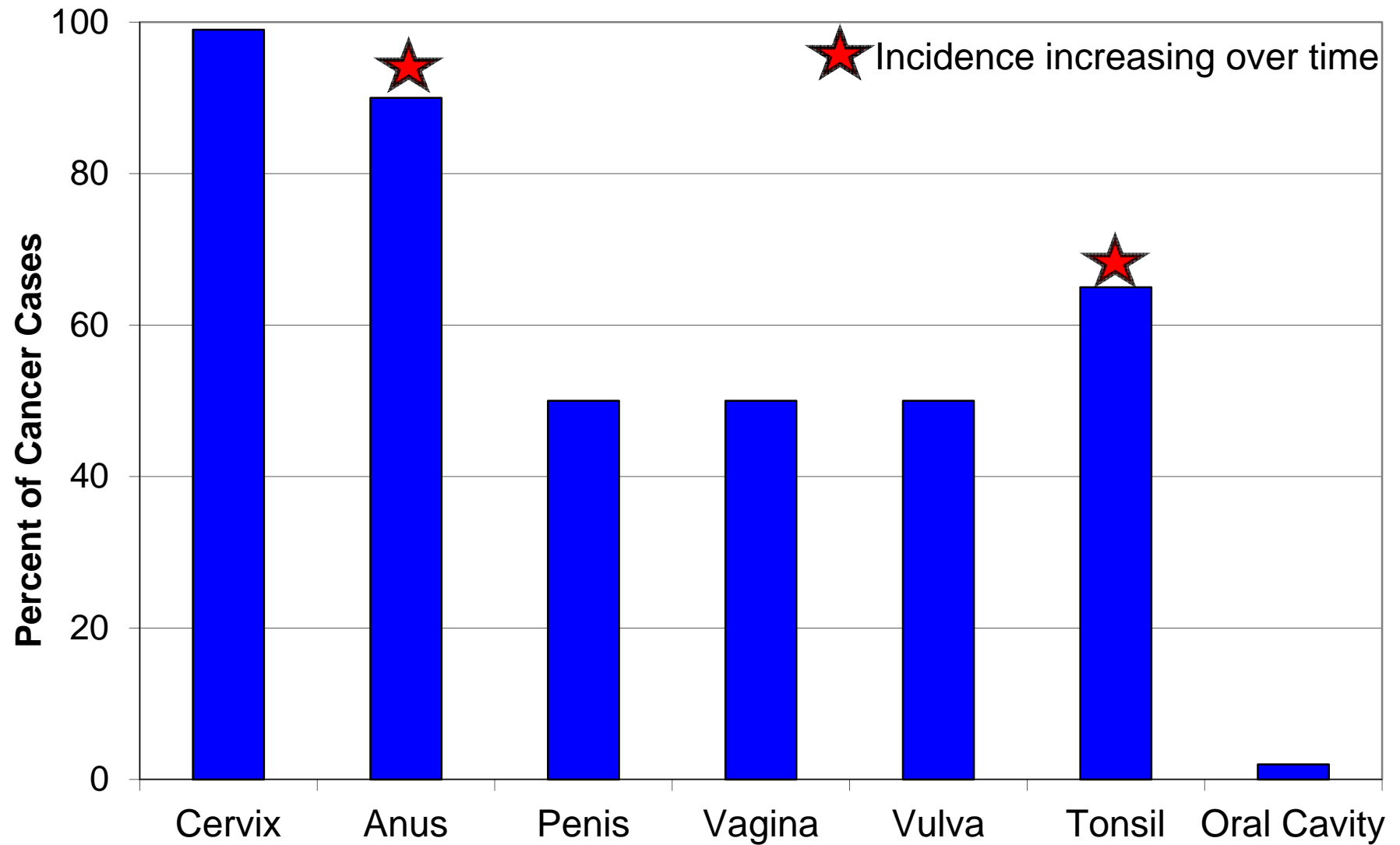
Cervical Cancer

- Worldwide incidence and mortality
 - 500,000 new cases per year
 - 250,000 deaths per year
- Incidence and survival rates vary by geographical region
 - 85% occur in developing nations
- HPV is a necessary cause of cervical cancer

HPV-associated cancers: US



HPV-associated cancers: US



Estimated burden of HPV-associated cancers

Cancer Site	WORLDWIDE		UNITED STATES	
	<u>Females</u>	<u>Males</u>	<u>Females</u>	<u>Males</u>
Cervix	530,000	-	8,540	-
Anus	53,460	35,640	2,640	2,310
Vulva/Vagina	16,000	-	2,480	-
Penis	-	10,520	-	500
Tonsil	12,050	28,000	880	3,360
TOTAL	611,510	74,160	14,540	6,170

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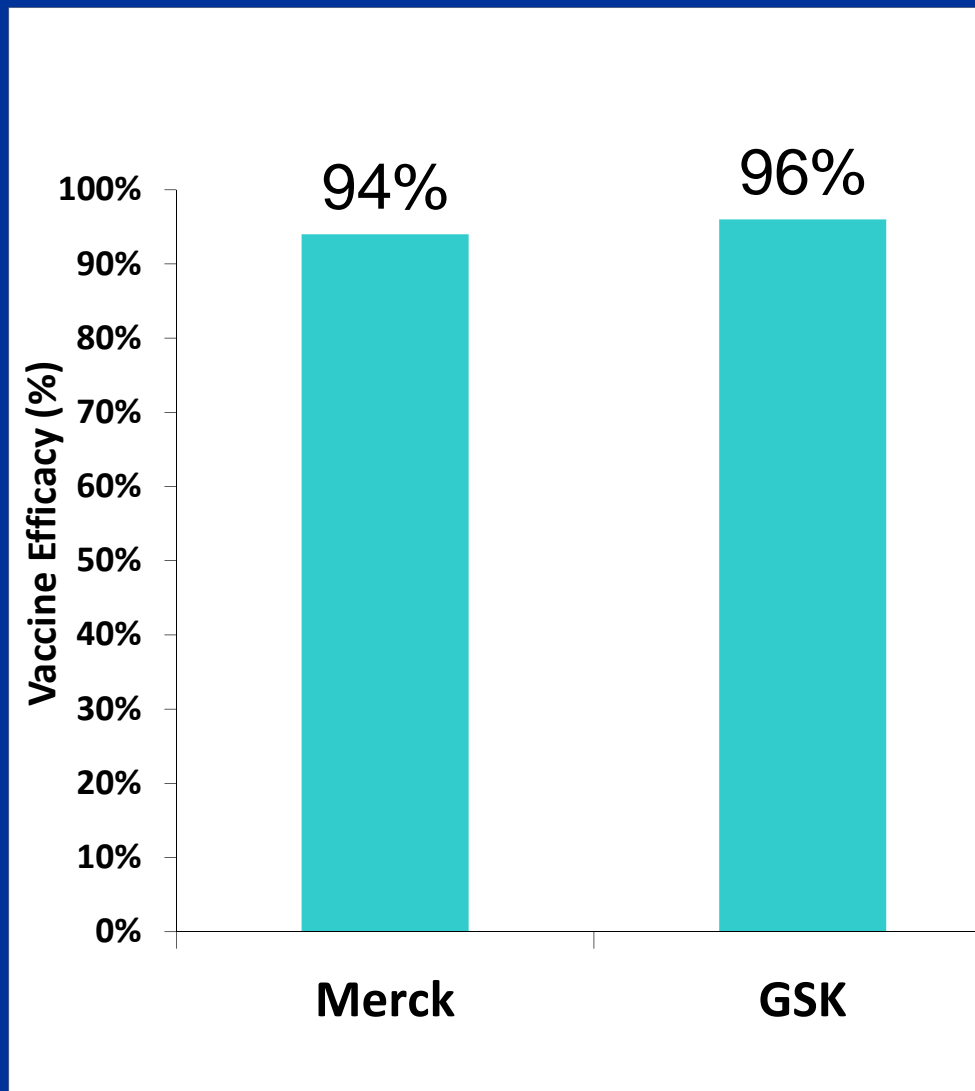
Two prophylactic HPV Vaccines

Manufacturer	HPV Types Included in Vaccine	US FDA Licensure
Glaxo Smith Kline Cervarix	HPV 16 } HPV 18 } 70% of Cervical Cancer	Females ages 10-25 for the prevention of cervical disease
Merck Gardasil	HPV 16 } HPV 18 } HPV 6 } 90% of HPV 11 } Genital Warts	Females ages 9-26 for the prevention of cervical, vulvar, vaginal, and anal disease Males ages 9-26 for the prevention of genital warts and anal disease

Use of the vaccine

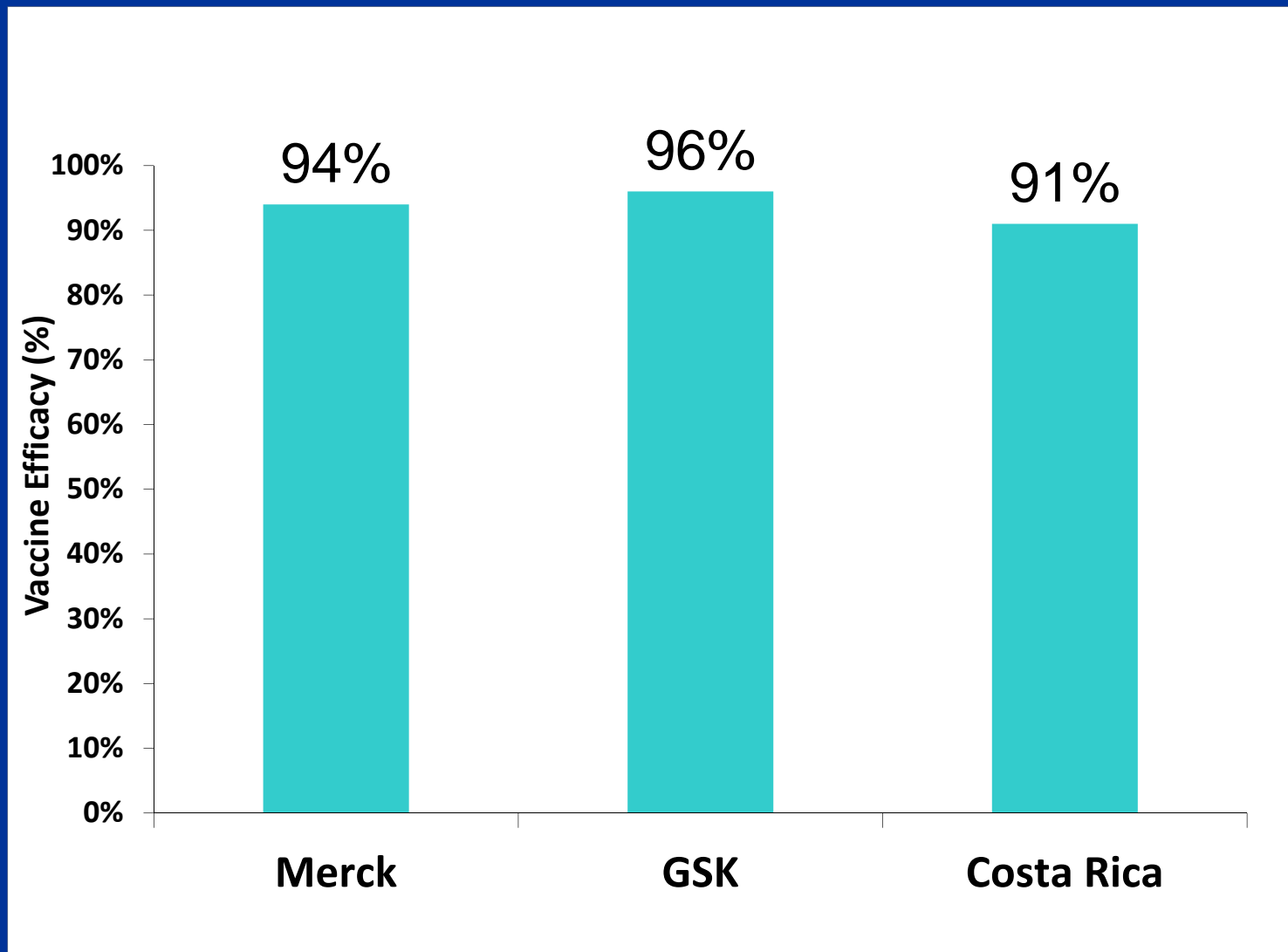
- Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention
- HPV vaccine recommended for:
 - Females- ages 11-12; range: 9 to 26 years
 - Males- ages 11-12 with the quadrivalent vaccine;
 - Recommended range: 9 to 21 years
 - Permissive range: 22 to 26 years

Both HPV vaccines prevent cervical HPV infections among uninfected young women



Villa LL et al. BMJ 2006; Paavonen J et al. Lancet 2009

Findings from our vaccine trial confirm reports from commercial trials



Villa LL et al. BMJ 2006; Paavonen J et al Lancet 2009; Herrero R et al Cancer Discovery 2011

NCI findings from the Costa Rica Vaccine Trial

1. No therapeutic efficacy of the prophylactic HPV vaccine
2. Vaccine safety profile is comparable to other licensed vaccines
 - Not recommended during pregnancy
3. High vaccine efficacy for HPV16/18 as well as non-vaccine HPV types
 - Vaccine impact highest when vaccination is given at younger ages, prior to sexual initiation

1) Hildesheim A. et al. JAMA 2007 2) Wacholder S. BMJ 2009 3) Herrero R. Cancer Discovery 2011

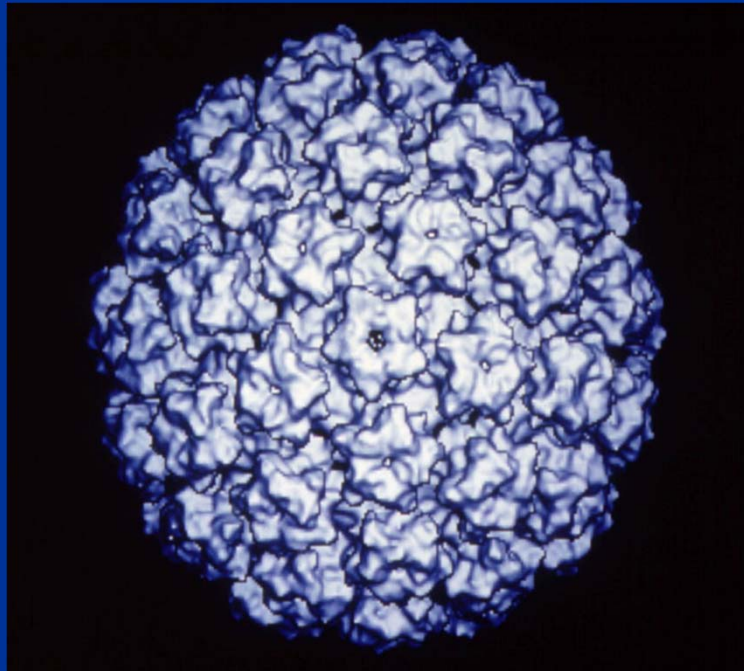
Recent Findings from NCI

1. Vaccine efficacy of fewer than 3 doses
2. Vaccine efficacy at other anatomic sites



Costa Rica Vaccine Trial

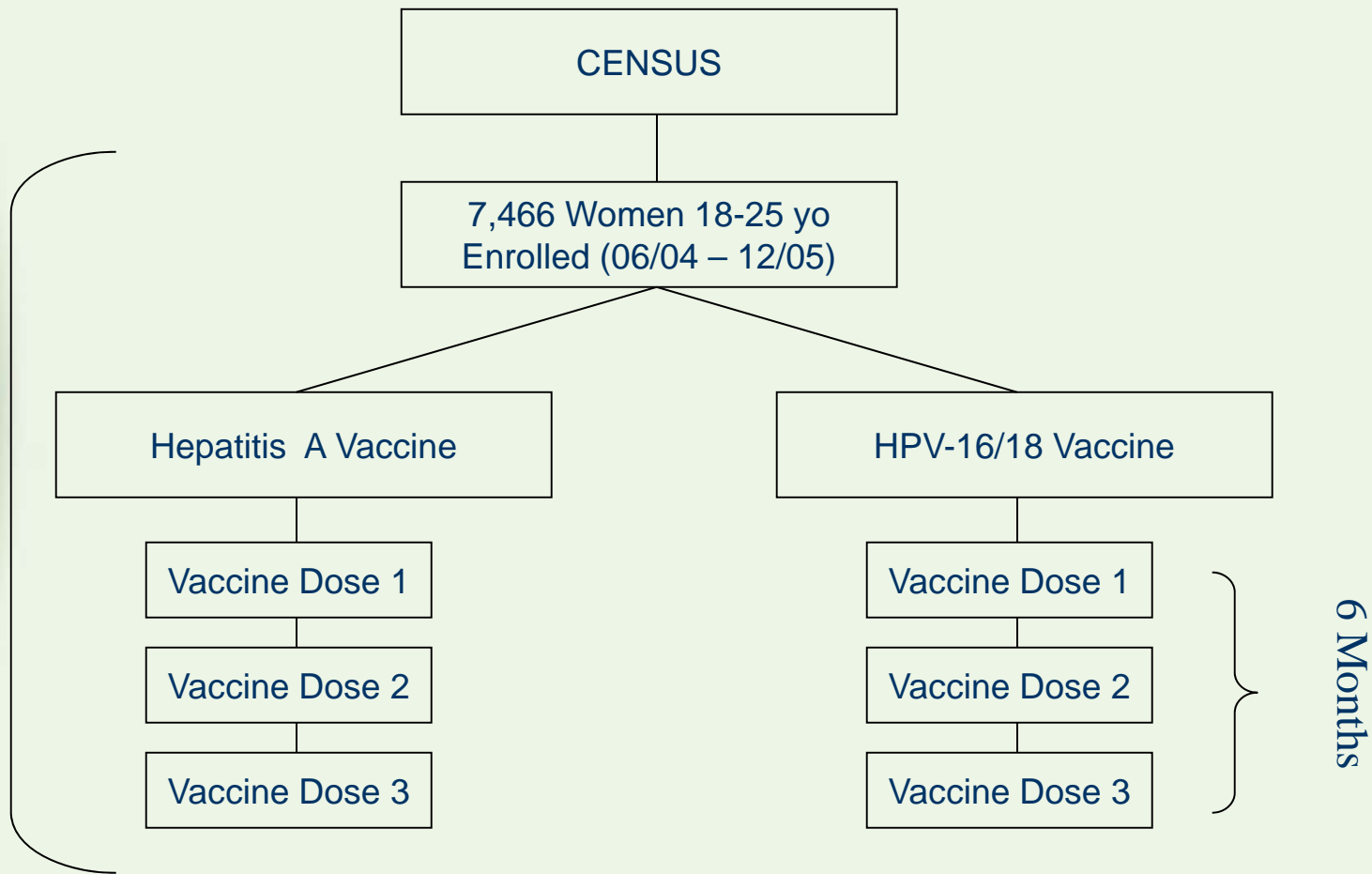
Design of the Trial



HPV Vaccine: Virus-like particle

Costa Rica Vaccine Trial

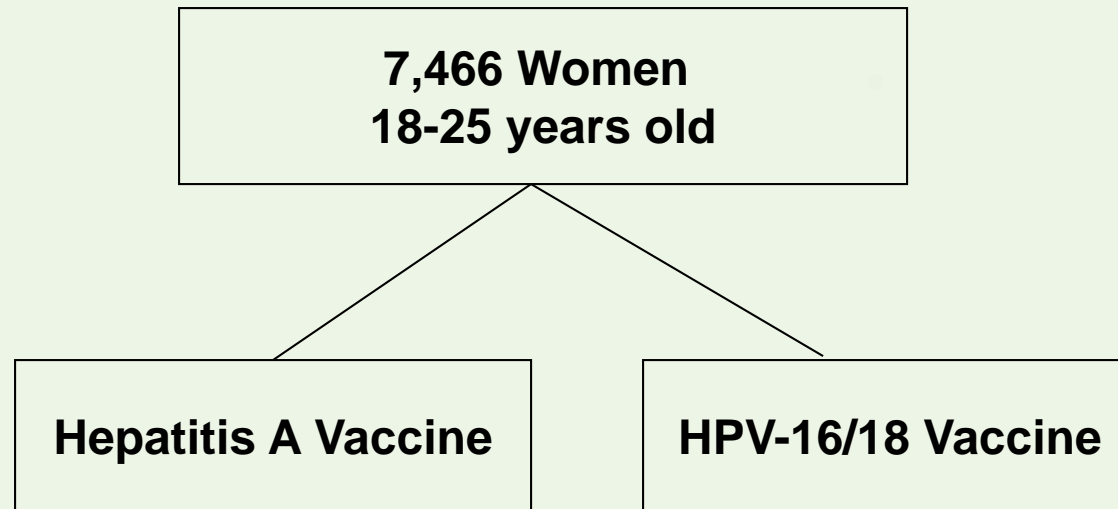
A community-based, randomized trial



COMPLETED

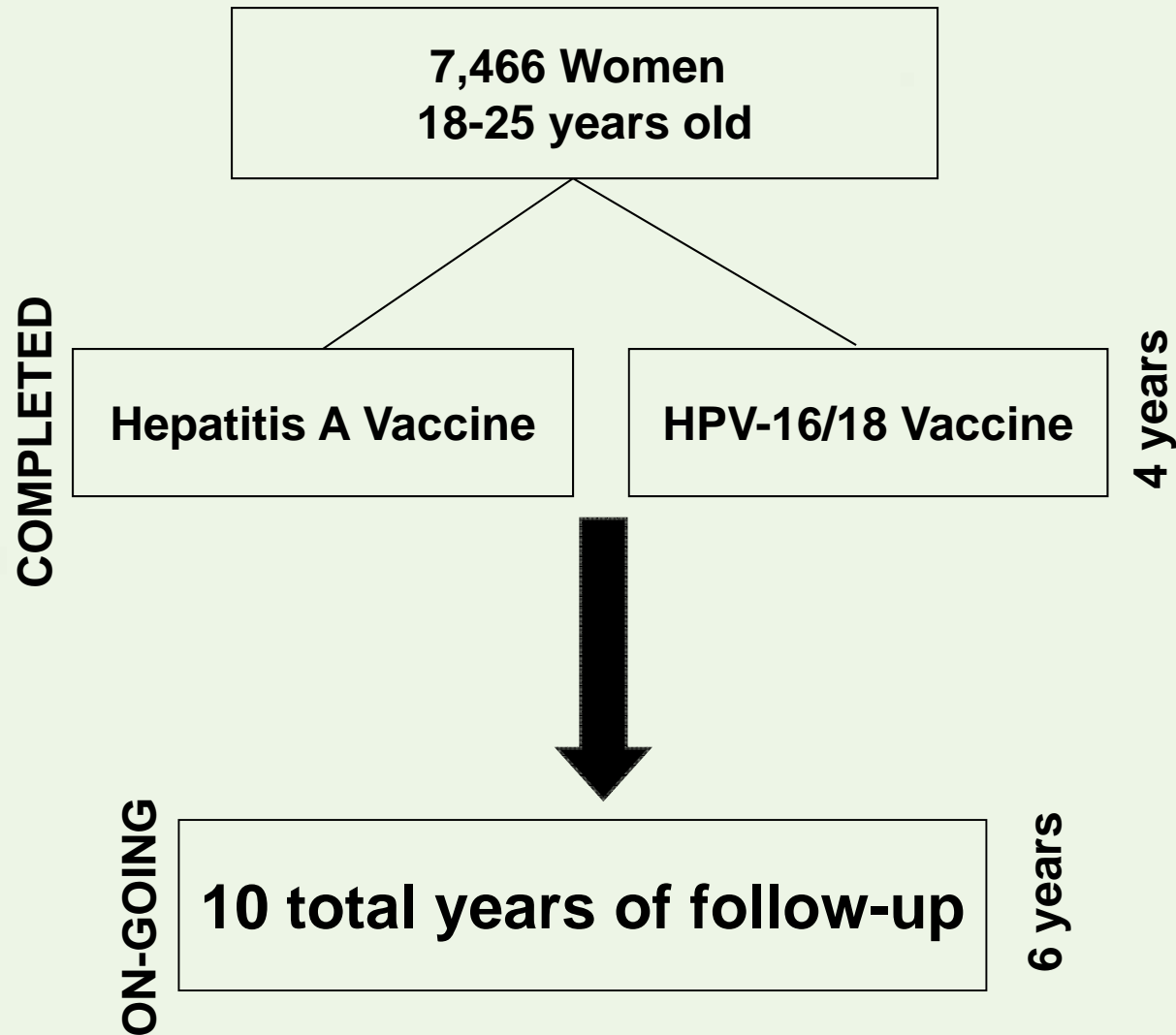
6 Months

Costa Rica Vaccine Trial



- Annual follow-up visits for 4 years
- Cervical samples collected at all visits
- Anal and oral specimens collected at 4 year visit

Long-term follow-up of the Costa Rica Vaccine Trial

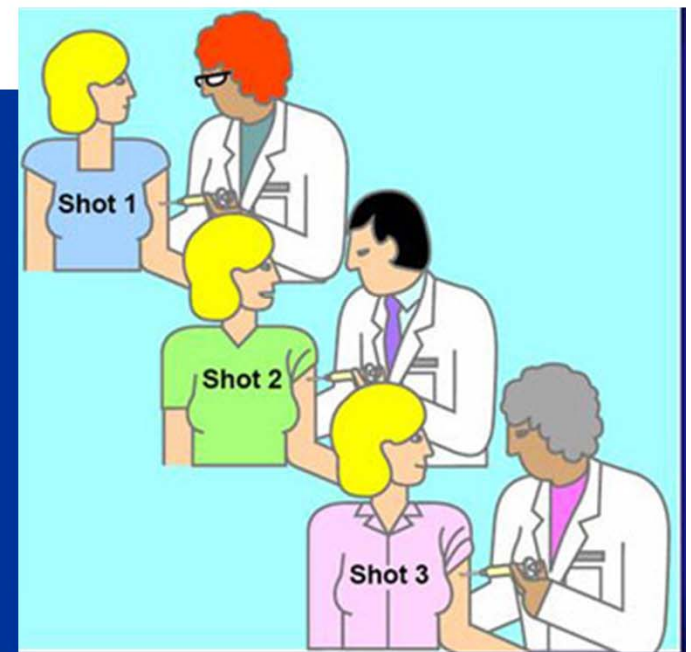


Proof-of-Principle Evaluation of the Efficacy of Fewer Than Three Doses of a Bivalent HPV16/18 Vaccine

Aimée R. Kreimer, Ana Cecilia Rodriguez, Allan Hildesheim, Rolando Herrero, Carolina Porras, Mark Schiffman, Paula González, Diane Solomon, Silvia Jiménez, John T. Schiller, Douglas R. Lowy, Wim Quint, Mark E. Sherman, John Schussler, Sholom Wacholder; for the CVT Vaccine Group

Conclusion Four years after vaccination of women who appeared to be uninfected, this nonrandomized analysis suggests that two doses of the HPV16/18 vaccine, and maybe even one dose, are as protective as three doses.

J Natl Cancer Inst 2011;103:1-8



Vaccine efficacy by doses received

# of Doses	Arm	# of Women	# of persistent HPV16/18 infections	HPV16/18 VE (95%CI)
3	Control	3010	133	80.9% (71.1% to 87.7%)
	HPV	2957	25	

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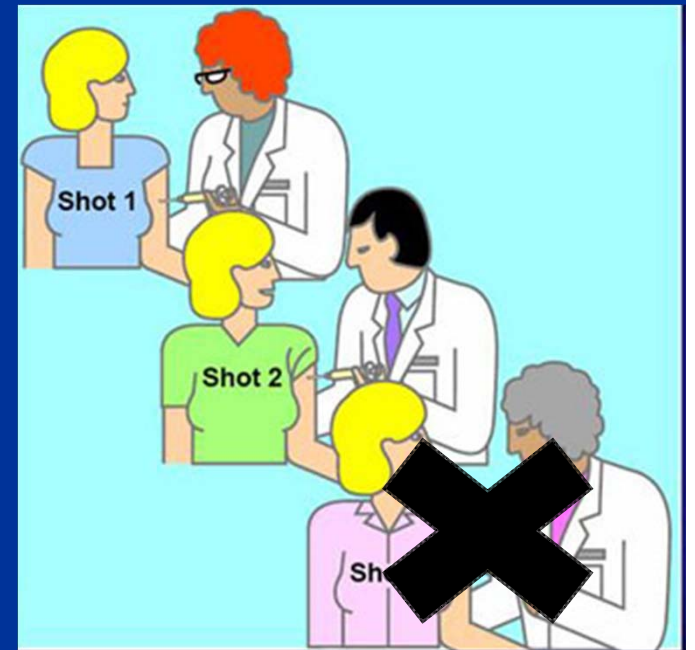
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2	Control	380	17	84.1% (50.2% to 96.3%)
	HPV	422	3	

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2	Control	380	17	84.1% (50.2% to 96.3%)
	HPV	422	3	
1	Control	188	10	100% (66.5% to 100%)
	HPV	196	0	

Conclusions

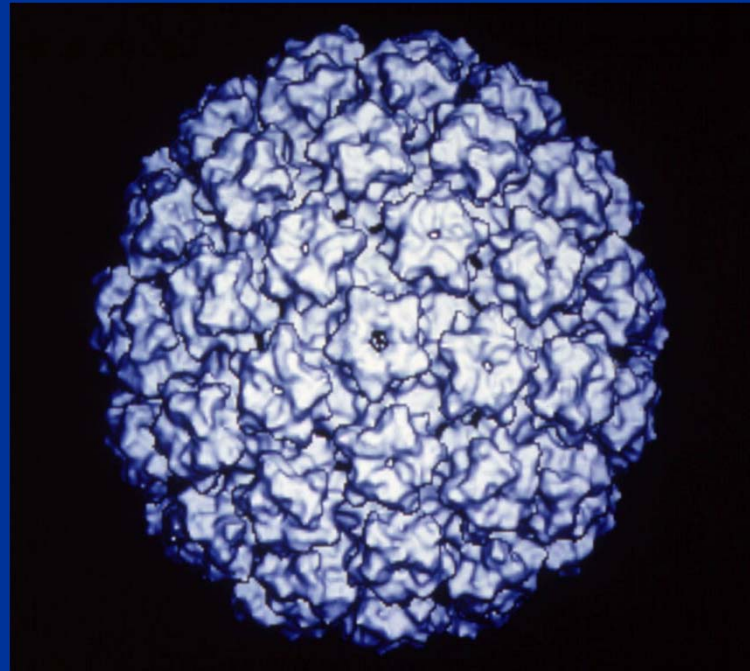
- After 4 years, the HPV vaccine provides high efficacy regardless of the number of doses received
- A simpler, more affordable vaccination schedule might be feasible



Important Questions Remain

- Will these results apply to other populations?
- Will these results apply to other vaccine formulations?
- What is the minimum antibody level required for protection?
- **What is the duration of protection for <3 doses?**

Vaccine efficacy at other anatomic sites



HPV Vaccine: Virus-like particle



Efficacy of a bivalent HPV 16/18 vaccine against anal HPV 16/18 infection among young women: a nested analysis within the Costa Rica Vaccine Trial

Aimée R Kreimer, Paula González, Hormuzd A Katki, Carolina Porras, Mark Schiffman, Ana Cecilia Rodriguez, Diane Solomon, Silvia Jiménez, John T Schiller, Douglas R Lowy, Leen-Jan van Doorn, Linda Struijk, Wim Quint, Sabrina Chen, Sholom Wacholder, Allan Hildesheim, Rolando Herrero, for the CVT Vaccine Group

Interpretation The AS04-adjuvanted vaccine affords strong protection against anal HPV infection, particularly among women more likely to be HPV naive at enrolment.

Vaccine efficacy among women without HPV

Site	Arm	# Women	# HPV16/18 Infections	HPV16/18 VE (95%CI)
Anus	HPV	1003	8	83.6% (66.7% to 92.8%)
	Control	986	48	

Vaccine efficacy among women without HPV

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Anus	HPV	1003	8	83.6% (66.7% to 92.8%)
	Control	986	48	
Cervix	HPV	1003	10	87.9% (77.4% to 94.0%)
	Control	986	81	

Conclusions

- HPV vaccine strongly protects against anal HPV16/18 infections in women
- Protection is comparable to that observed at the cervix
- Women who receive the HPV vaccine will have less anal HPV infection

Upcoming research and future directions

1. Oral HPV16/18 vaccine efficacy
2. Long-term impact of vaccination
 - Duration of protection
 - Screening
 - Safety
3. Immunological markers of protection
4. Natural history of HPV infection in a vaccinated cohort

Summary of recent findings

1. Confirmed that the bivalent HPV vaccine is highly effective in the prevention of cervical HPV infection
2. Raised the possibility that only two, or maybe even a single dose, of the HPV vaccine may be necessary
3. Demonstrated the vaccine protects at an additional anatomic site where HPV is known to cause cancer

Acknowledgements

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- Allan Hildesheim (IIB)
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- John Schiller (CCR)
- Mark Sherman (HREB)
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- Sholom Wacholder (BB)

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- Ana Cecilia Rodriguez

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- LJ van Doorn (DDL)