

# Single-dose HPV vaccination

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Nothing to disclose

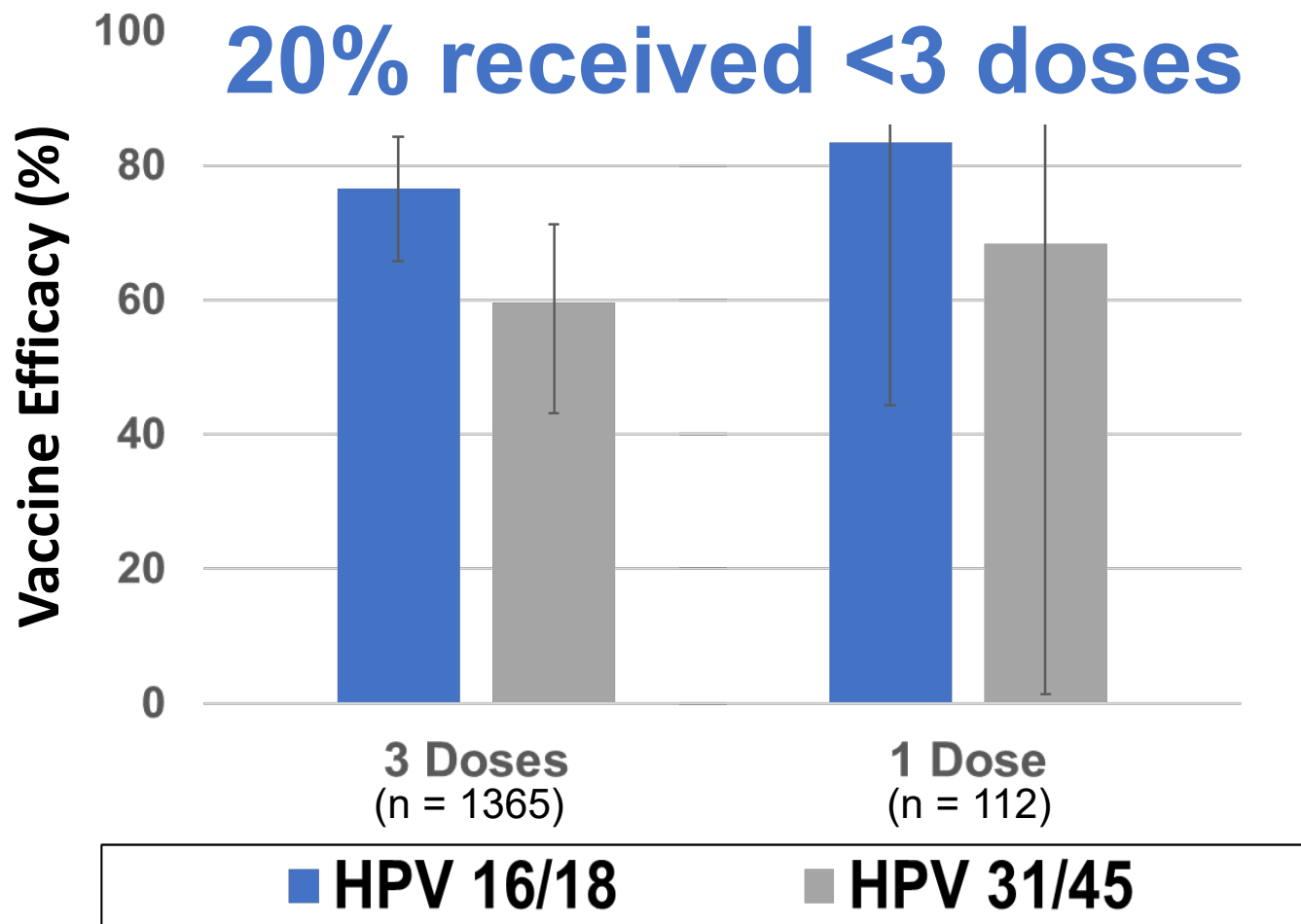
# Single-dose HPV vaccination- current status and findings

## Presentation outline

1. Post-hoc analyses of RCTs
  - Bivalent HPV Vaccine- Costa Rica HPV Vaccine Trial
  - Quadrivalent HPV Vaccine- India HPV Vaccine Trial
2. Vaccine registry/phase 4 studies
3. Trials that aim to investigate single-dose efficacy

# NCI Costa Rica HPV Vaccine Trial: RCT to evaluate safety and efficacy of 3 doses the bivalent HPV vaccine among women aged 18 to 25

Vaccine efficacy >10 years since bivalent HPV vaccine, by dose

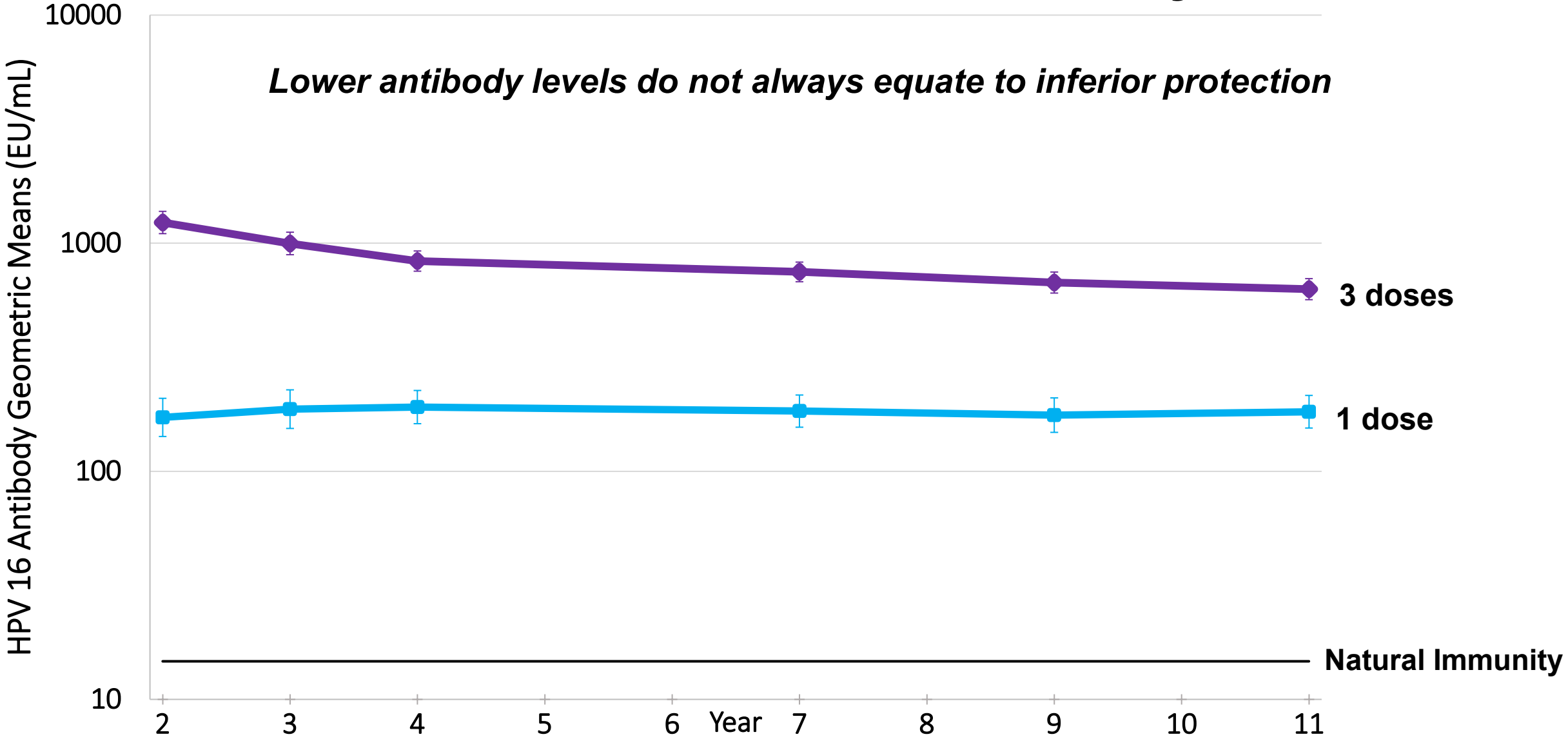


*\*Lower efficacy with 3 doses because the endpoint was prevalent HPV infection assessed in a total vaccinated cohort*

Kreimer AR et al, JNCI 2020

Tsang SH et al, JNCI 2020

# One dose of bivalent HPV vaccination induces stable HPV16 serum antibodies for >10 years



*Lower antibody levels do not always equate to inferior protection*

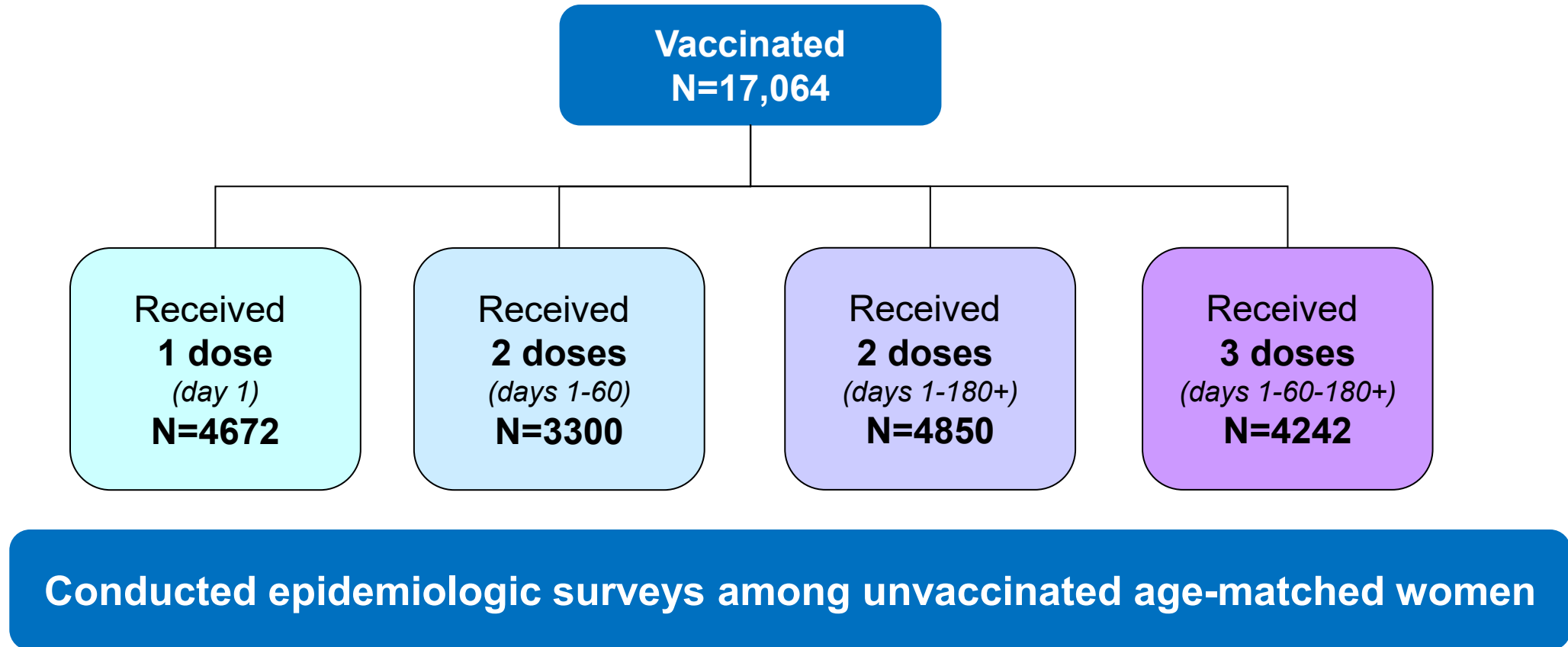
**3 doses**

**1 dose**

**Natural Immunity**

# IARC 2- vs 3- dose 4v HPV Vaccine randomized clinical trial

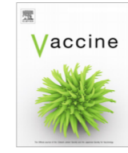
- Recruitment initiated in 2009
- Aimed to recruit 20,000 unmarried girls aged 10-18 years
- 17,729 girls enrolled when recruitment and vaccination phase suspended



**Table 6**  
 Persistent\* HPV infections in women vaccinated with quadrivalent HPV vaccine over a 7-year follow-up period and in the unvaccinated women.

Group	Persistent HPV 16/18 infection	Persistent HPV 31/33/45 infection	Persistent non-vaccine targeted HPV infection excluding 31, 33, and 45
<i>Three doses (Days 1, 60 and 180+)</i>			
N positive/Total	1/604	1/604	16/604
%	0.2	0.2	2.6
95% CI	(0.0–0.9)	(0.0–0.9)	(1.5–4.3)
<i>One dose (Day 1)</i>			
N positive/Total	0/959	7/959	16/959
%		0.7	1.7
95% CI		(0.3–1.5)	(1.1–2.7)
<i>Unvaccinated</i>			
N positive/Total	14/1141	6/1141	27/1141
%	1.2	0.5	2.3
95% CI	(0.7–2.1)	(0.2–1.1)	(1.5–3.3)

\* Persistent infections defined as incident infections that persisted for 12+ months without an HPV negative test (for HPV type in question) between positive tests.



Can a single dose of human papillomavirus (HPV) vaccine prevent cervical cancer? Early findings from an Indian study



Rengaswamy Sankaranarayanan<sup>a,\*</sup>, Smita Joshi<sup>b</sup>, Richard Muwonge<sup>a</sup>, Pulikottil Okkuru Esmey<sup>c</sup>, Partha Basu<sup>a</sup>, Priya Prabhu<sup>d</sup>, Neerja Bhatla<sup>e</sup>, Bhagwan M. Nene<sup>f</sup>, Janmesh Shaw<sup>g</sup>, Usha Rani Reddy Poli<sup>h</sup>, Yogesh Verma<sup>i</sup>, Eric Zomawia<sup>j</sup>, Sharmila Pimple<sup>k</sup>, Massimo Tommasino<sup>l</sup>, Michael Pawlita<sup>m</sup>, Tarik Gheit<sup>l</sup>, Tim Waterboer<sup>m</sup>, Peter Sehr<sup>n</sup>, Madhavan Radhakrishna Pillai<sup>d</sup>, for the Indian HPV vaccine study group<sup>1</sup>

# Post-hoc analysis of RCTs provides compelling evidence of single-dose protection

1. Reasons for missing doses are known and usually unrelated to randomization and subsequent risk of HPV acquisition
2. Trials have pre-vaccination information (i.e.: HPV status at time of HPV vaccination, important for vax of older girls) and in-depth information on covariates

**\*\*Robust comparisons between vaccinated and unvaccinated\*\***

3. Data available for both alum- and AS04-adjuvanted vaccines

# Dose-specific vaccine effective in phase 4 registry studies

- Registry studies provide important information on programmatic effectiveness
  - Vaccine linkage studies have been used to reduced-dose schedules of HPV vaccines
- Initial studies included women vaccinated outside of routine program (i.e.: catchup vaccination) resulting if differences in characteristics of women by number of doses received
- Older women have more HPV infection at time of vaccination and thus more likely to appear as vaccine failures
- Hypothesized these earlier studies would be biased and suggest 1 dose was less effective than 3 doses



# Example of older age at vaccination having lower vaccine effectiveness

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## HPV Vaccination and the Risk of Invasive Cervical Cancer

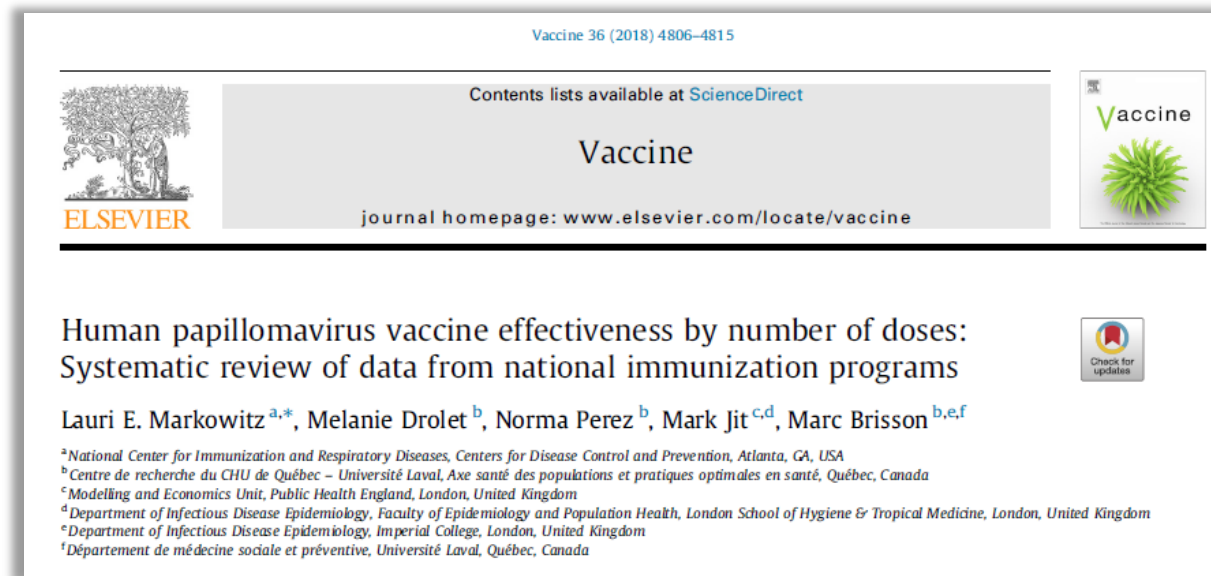
Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D.,  
Jiangrong Wang, Ph.D., Adam Roth, M.D., Ph.D., Fang Fang, M.D., Ph.D.,  
Karin Sundström, M.D., Ph.D., Joakim Dillner, M.D., Ph.D.,  
and Pär Sparén, Ph.D.

- Sweden started 3 dose vaccination program with 4vHPV in 2007
- Linked vaccine information to health registries
- Overall adj. IRR = .37 (.21-.57)
  - Vaccinated <17yr IRR = .12 (.00-.34)
  - Vaccinated 17-30 IRR = .47 (.27-.75)

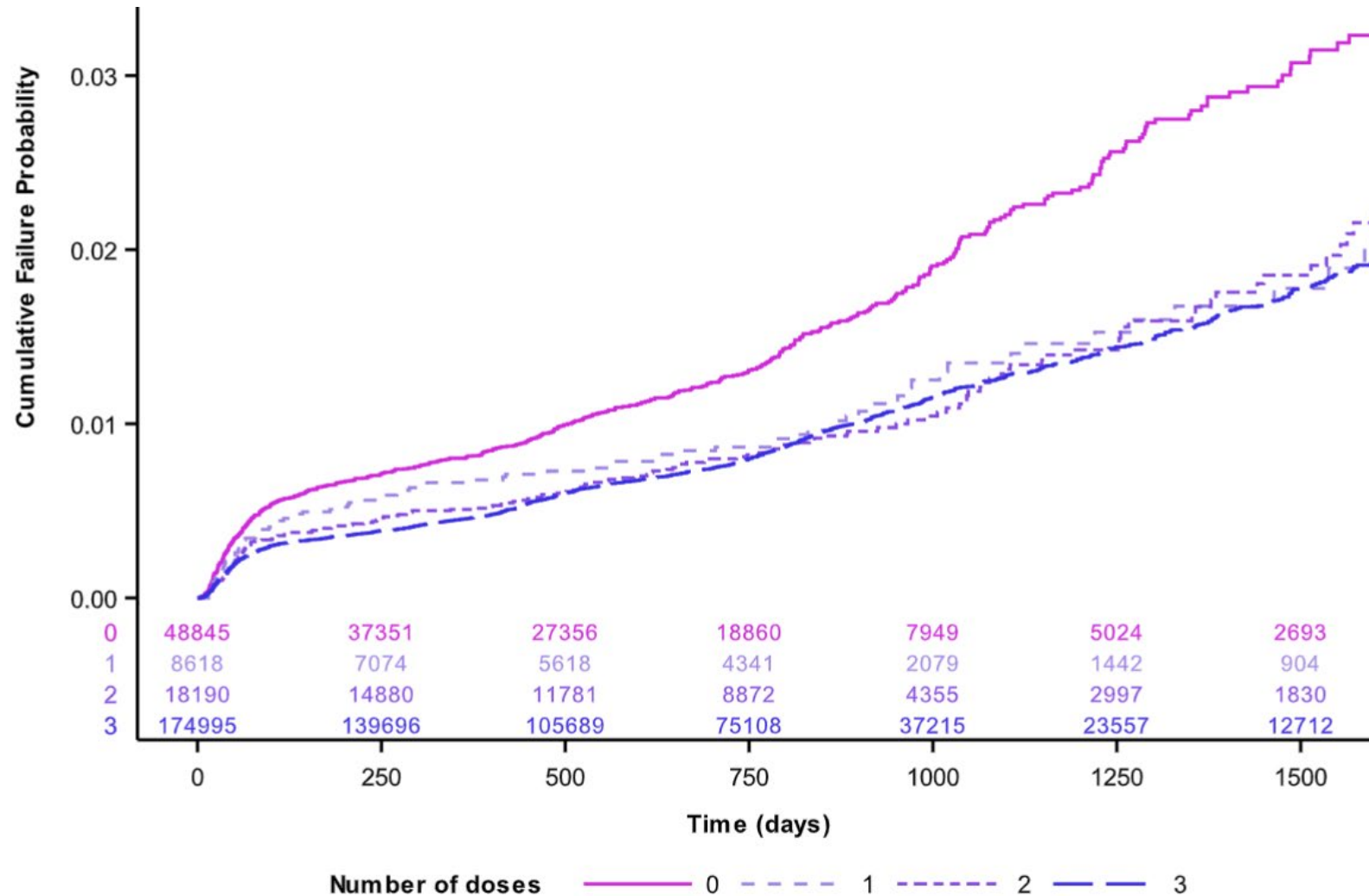
***If older women are more likely to receive 1 dose, we will falsely conclude that 1 dose is less effective***

# 2018 systematic review of dose-specific vaccine effective in phase 4 registry studies

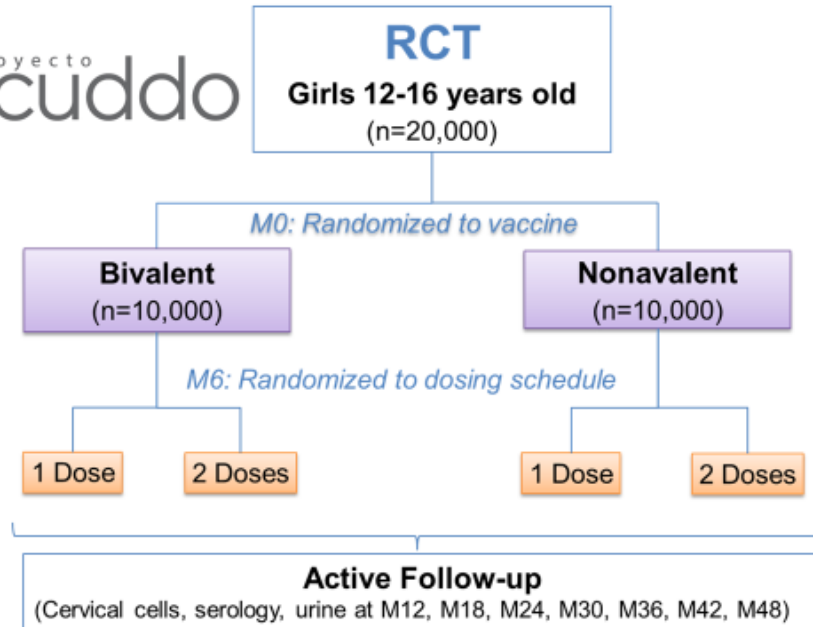
- 14 studies includes, from many world regions
- Most studies found number of doses impacted effectiveness estimates
  - Greater effectiveness with 3 doses, followed by 2 doses and 1 dose
  - Some effectiveness for 1 dose found in main or sub-analyses in 9 studies
  - More recent studies and studies that stratified by age at vaccination - less difference by dose



# A national cohort analysis of dose-specific HPV protection against CIN2/AIS+ in Australia

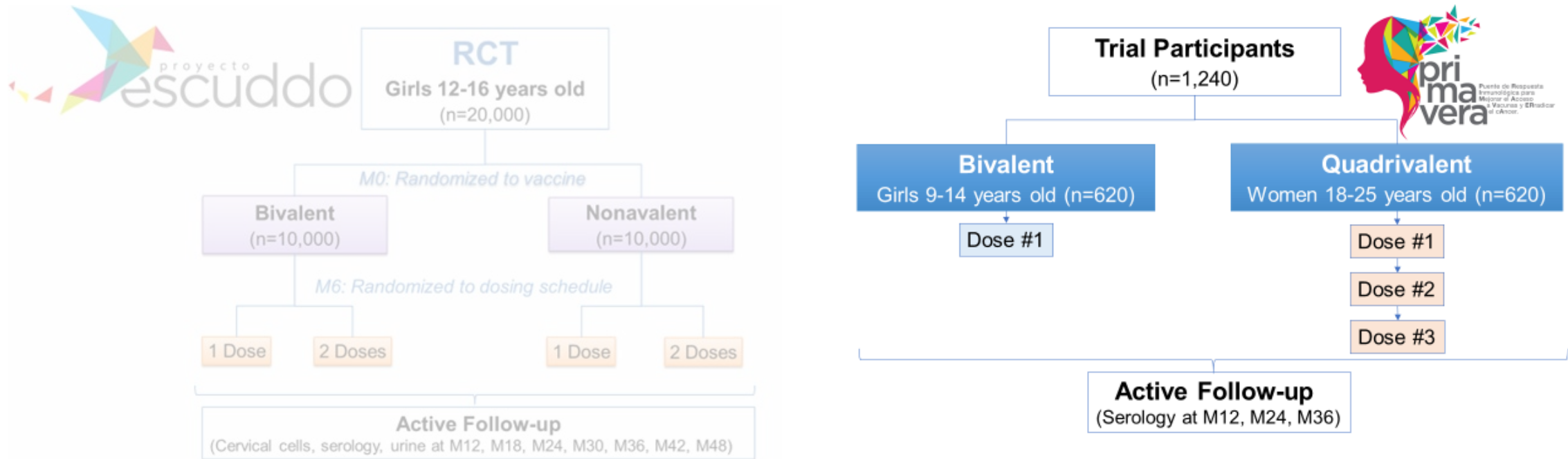


# Ongoing trials investigating single-dose HPV vaccine protection



*Is 1 dose non-inferior to 2 doses?*

# Ongoing trials investigating single-dose HPV vaccine protection



*Are antibody levels induced by 1 dose of the ASO4-adjuvanted HPV vaccine non-inferior to levels observed in an efficacy population?*





World Health  
Organization

Organisation mondiale de la Santé

# Weekly epidemiological record Relevé épidémiologique hebdomadaire

22 NOVEMBER 2019, 94th YEAR / 22 NOVEMBRE 2019, 94<sup>e</sup> ANNÉE

No 47, 2019, 94, 541–560

<http://www.who.int/wer>

*“Countries could adopt an extended interval of 3-5 years between the 2 doses, with the first dose being given to younger girls, such as those aged 9 or 10 years or in the equivalent lower school grade, and the second dose to 13–14-year-old girls or in the equivalent higher school grade....”*

# Summary

- Continuing post-hoc analyses of two RCTs suggest that HPV vaccines may generate long-term protection after a single dose
- Vaccine registry studies support the possibility of substantial single-dose protection in national immunization programs, but controlling for potential bias is critical
- A series of ongoing efficacy, immunobridging and demonstration trials will provide increasingly robust data over the next 4 years
  - Several important studies generating data in 2021

**Thank you!**