



# The HPV FASTER consortium: Searching for the best combinations of vaccination and screening



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## Potential conflict of interest

- Research and educational institutional grants:  
GSK, SPMSD, Merck, Qiagen
- Personal / speaking / travel grants:  
GSK, SPMSD, Merck, Qiagen, RMS

This presentation is the sole responsibility of the author



# Two major stages in vaccine introduction

## Licensing ( Phase I-III)

- Safety
- Efficacy
- Product specific / trial restricted / regulators' agreed
- Defined evaluation criteria & protocols
- *FDA / Advisors / EMA / MoH & National advisory boards...*



## Recommendations

- Uses in a given population
  - Vaccination ages, dosing and schedule
- Adverse events incidence and evaluation
- Cost-effectiveness
- *ACIP / WHO GACVS / National expert bodies & societies*



# Potential new indications for HPV vaccination / screening (before the absence of formal Phase III clinical trials)

## PROPHYLACTIC

(prevent new infections and transmission)

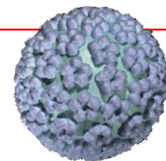
- Adult women
  - To 26, 30, 45+...
- Males
  - To 18, 50+...
- Infants (EPI)



## AS PART OF THERAPY

(interrupt reinfections and prevent transmission)

- HPV + women in screening
- Post treatments in CIN lesions
- RRP
- GW and survivors of HPV related cancers
- Therapeutic / mixed vaccines



## HIGH RISK GROUPS

(selective vaccination & new screening)

- HIV cohorts / MSM
- Transplants & immunosuppressed
- Autoimmune patients
- STI clinics
- Partners of HPV+
- Migrants / marginal
- Abused children

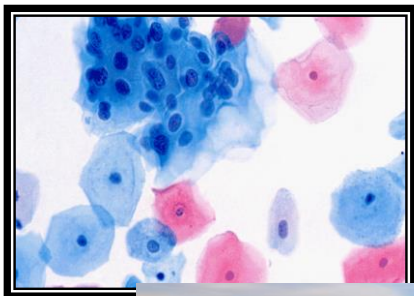


# Cervical Cancer prevention: Social Partners



## screenologists

- Gynecologists
- Pathologists
- GP's
- Treatment
- *HPV screening technologies*



## vaccinologists

- Pediatricians
- GP's
- Vaccine experts
- Infectious diseases
- *Vaccine industry*



## Policy makers

- Centralized public health programs organizers
- Communication & education
- International Phase IV follow up
- *Financing & equity*



# Options to control cervical cancer

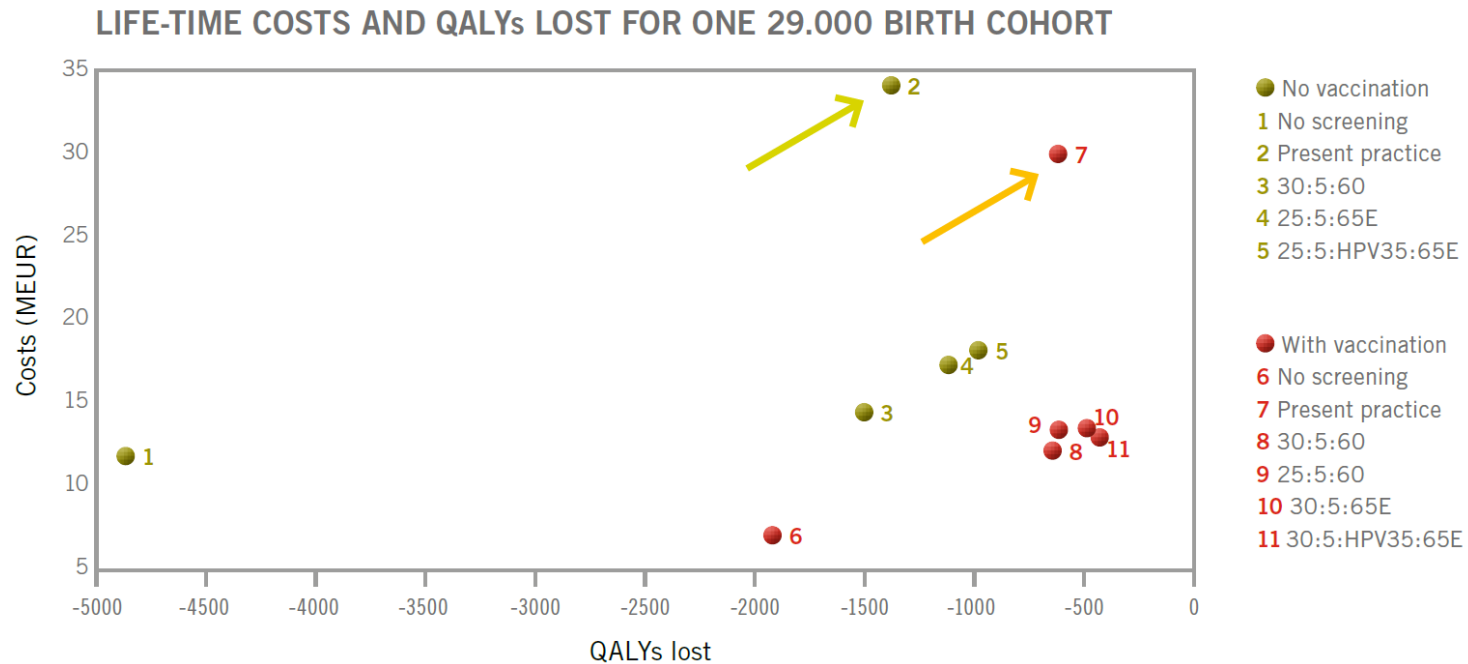


	SCREENING (PAP) <sup>1-3</sup>	SCREENING (HPV)	HPV 16/18 VACCINATION <sup>3-6</sup>
Target	Cervical cancer / pre- cancer		Cervical cancer / pre-cancer <i>HPV infection &amp; Interrupt Transmission</i>
Impact	Participant		Participant + <i>Herd effect</i>
Number of interventions	<b>10...50+ tests lifetime</b>	<b>5+ tests lifetime</b>	3 / 2 doses no booster dose to date
Follow-up	Local diagnostic & treatments network		Phase IV effectiveness & safety studies in selected countries
Side effects	Mild / Obstetrics /over-diagnostics		Local/short-lived
Impact on other cancers	Limited / none		<b>Significant in HPV related cancers</b>

1. Kesic V, et al. *Cancer Epidemiol Biomarkers Prev* 2012; 21:1423–1433; 2. Anttila A, et al. *Eur J Cancer* 2009; 45:2649–2658; 3. Cuzick J, et al. *Vaccine* 2008; 26S:K29–K41; 4. EMA. *Cervarix®*, European Summary of Product Characteristics, 2013; 5. GSK. Clinical Study Register. 2013; 6. Downs LS Jr, et al. *Gynecol Oncol* 2010; 117:486–490.



## Cost and benefits of cervical cancer prevention in Finland



**Figure 2.** Under no vaccination and no screening programs (green dot number 1) the social costs of cervical cancer would be low (i.e. some 11M€) and the quality adjusted years of life lost very high (close to 5,000). Vaccination programs with a range of screening options (red dots 8,9,10 or 11) would have a similar cost but the number of QALYs lost would be reduced to around 500.

# Accuracy of HPV screening vs. cytology

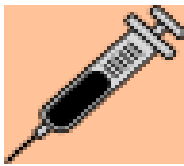


Screening test	N	Sensitivity (95% CI)	Specificity (95% CI)
<b>Detection of CIN2+</b>			
Cytology (ASC-US+)	25	70.0% (62.5–77.6%)	91.9% (90.3–93.6%)
HC2	31	<b>90.4% (88.0–92.8%)</b>	<b>88.5% (87.0–90.0%)</b>
Co-testing*	13	94.2% (90.8–97.6%)	87.7% (85.0–90.3%)
<b>Detection of CIN3+</b>			
Cytology (ASC-US+)	21	74.6% (65.6–83.6%)	91.8% (90.0–93.7%)
HC2	<b>22</b>	<b>95.3% (93.3–97.3%)</b>	<b>89.0% (87.2–90.8%)</b>
Co-testing*	12	96.7% (93.7–99.7%)	82.9% (77.1–88.6%)

\*Cytology (ASC-US+) and HC2

Updated meta-analysis data from Arbyn et al.<sup>21,22</sup>  
 In Bosch FX et al. Nature reviews Clinical oncology 2015

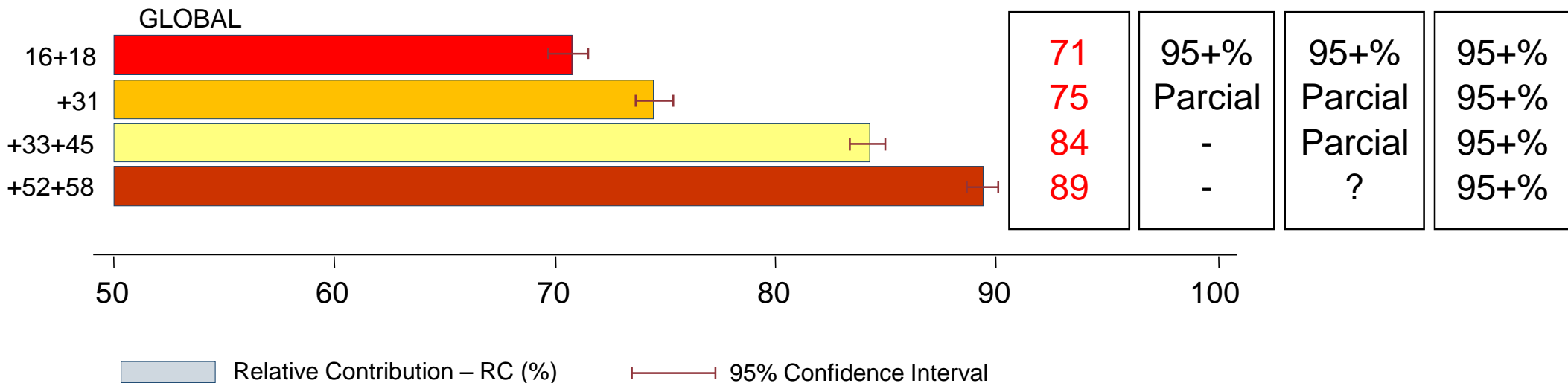




# HPV type-specific contribution to cervical cancer and potential for prevention of existing vaccines

Type specific Vaccine efficacy

RC %      **Gardasil**      **Cervarix**      **Gardasil9**



de Sanjosé S et al. Lancet Oncol, 2010  
 Serrano B et al. Infect Ag Cancer, 2012  
 Schiller J et al Vaccine 30 S 5 2012  
 Lehtinen M et al. Nat Rev Clin Oncol. 10 2013

# HPV FASTER: Master concept

HPV  
FASTER

Women in middle age groups, found HPV negative and receiving a broad spectrum HPV vaccine (expected 90% protection against oncogenic HPV types) has a **subsequent risk of cervical cancer** extremely low

Under these risk estimates, the requirements for **further screening** are likely to be **minimal** ( one / two lifetime), necessarily **HPV based**



A choice

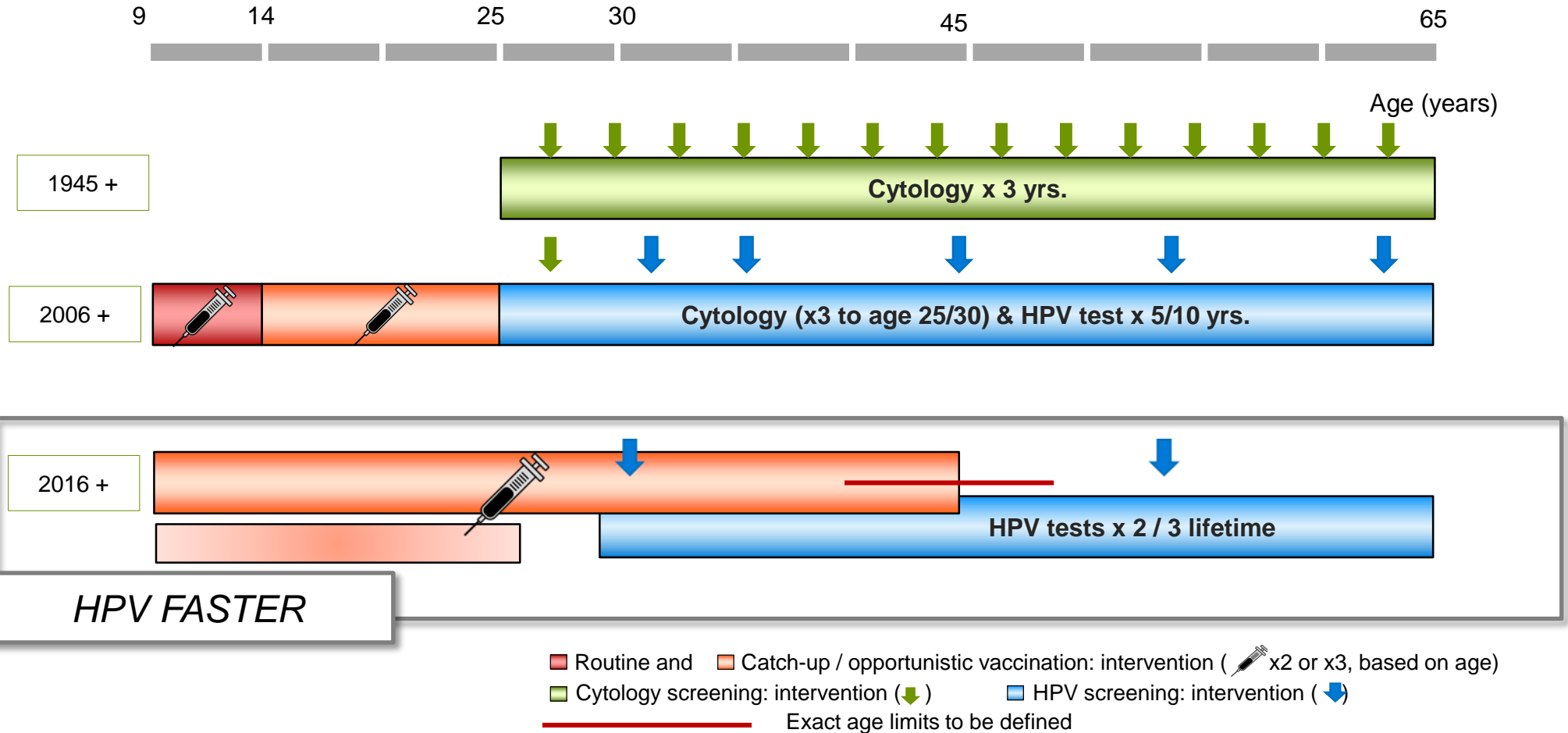
## NOVEL OPTIONS

self sampling,  
urine HPV test  
point of care tests  
screen and treat  
HPV therapeutics...

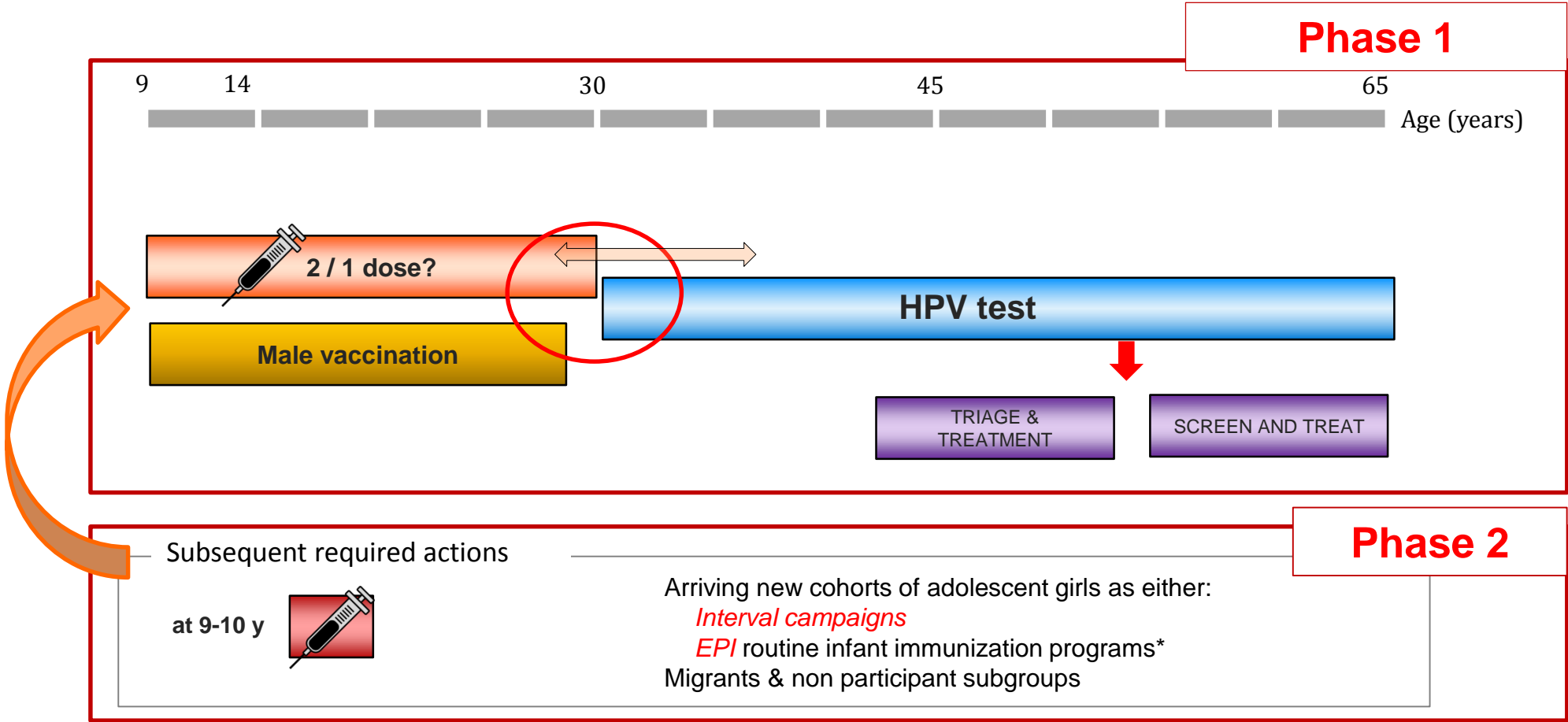


A unique chance

# Current cervical cancer preventive strategies (simplified) and proposed HPV FASTER initiative



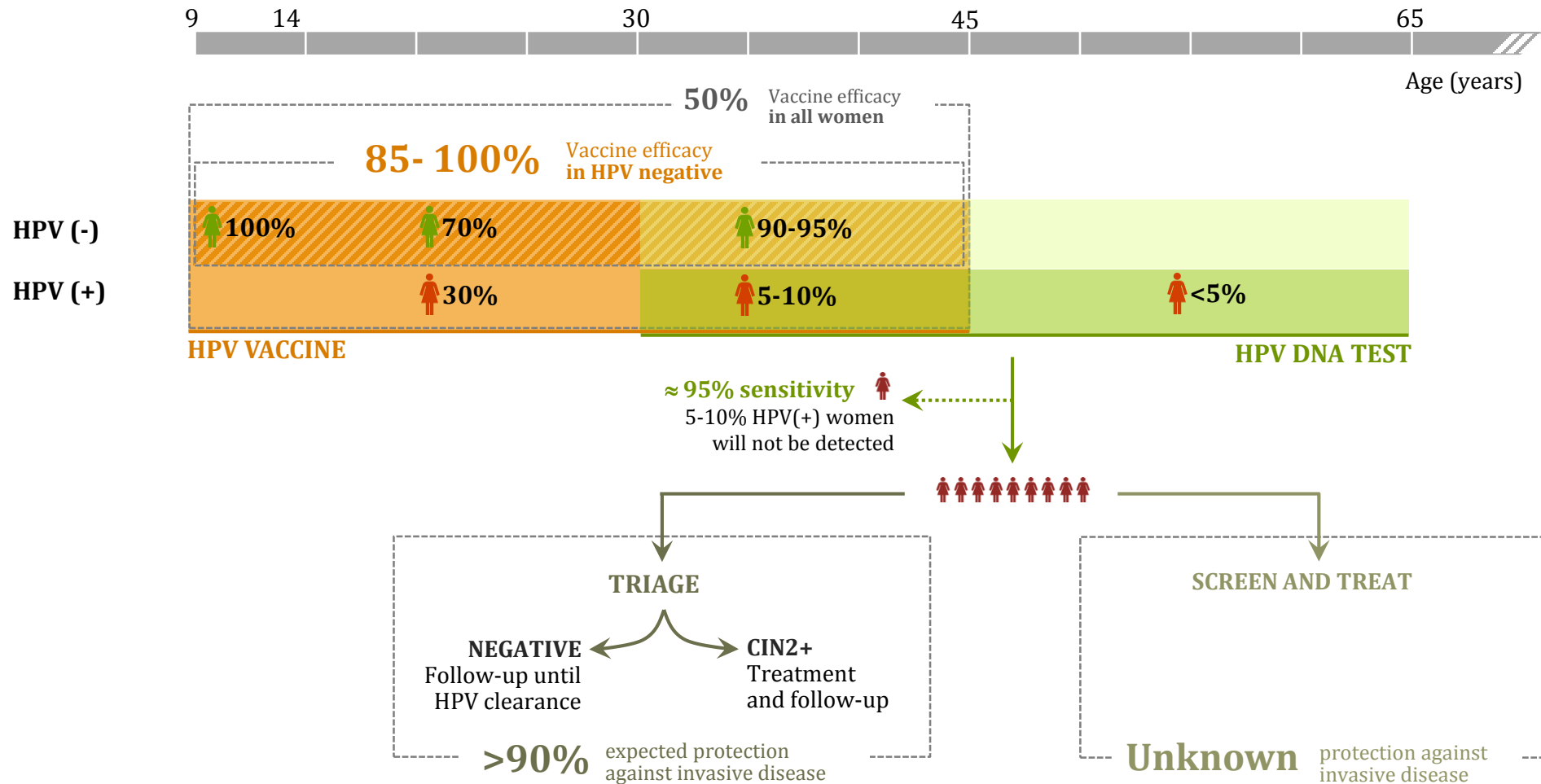
# HPV-FASTER deployment: potential for minimum cross sectional interventions across all age groups



- Routine vaccination
  - HPV screening
  - Catch-up / opportunistic vaccination
  - Male vaccination
- \*EPI: Expanded Program of immunization



# HPV-FASTER strategy: Core concept and expected impact



†Triage: HPV typing, cytology, other biomarkers, colposcopy or biopsy paired with management algorithms

# HPV FASTER: Master impact expected

HPV  
FASTER

One HPV testing / treatment round at a sensitivity of 90-95% would reduce the incidence of cervical cancer *within years*

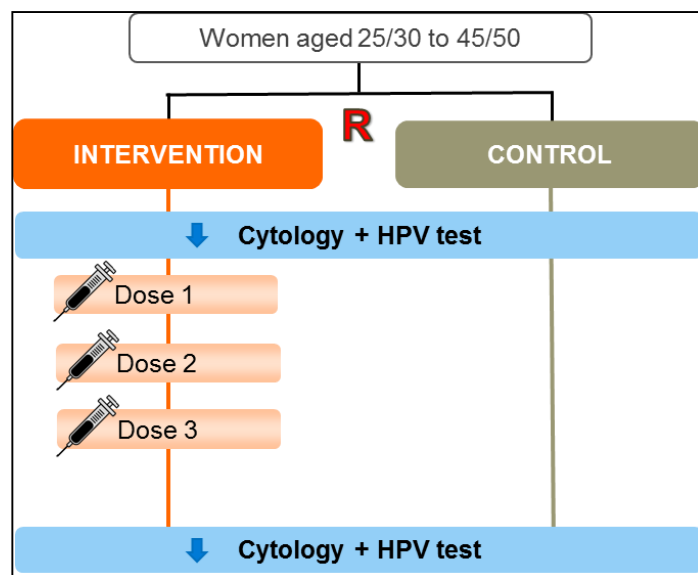
Generalized vaccination over a wider age range would ensure medium & *long term reduction* of viral infections, pre-cancer and cancer

The strong herd protection effect of HPV vaccines suggests that male vaccination will *further accelerate* the reduction of HPV infections



# HPV FASTER: formats & research issues

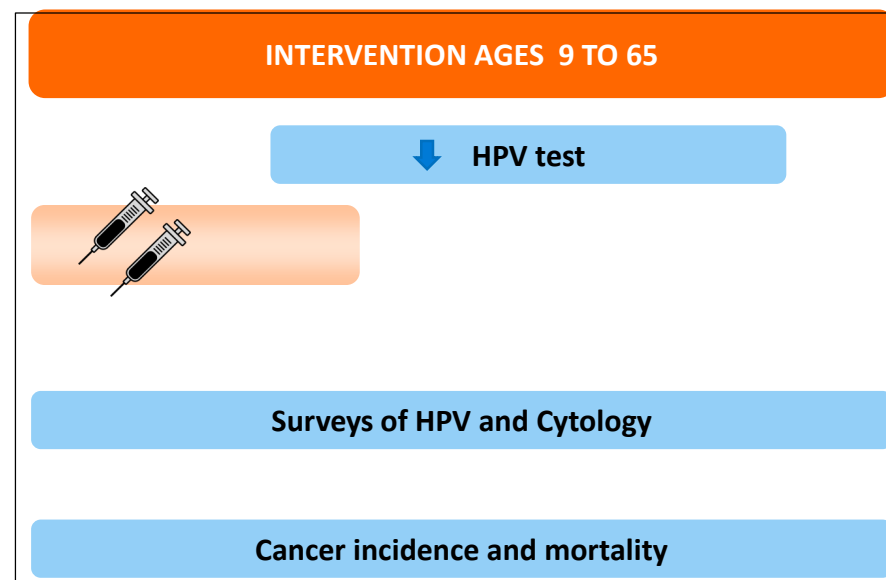
## Trials



Self sampling  
Urine tests  
Point of care  
testing systems

Triage technology  
Treatment  
Vaccine dosing  
New vaccines

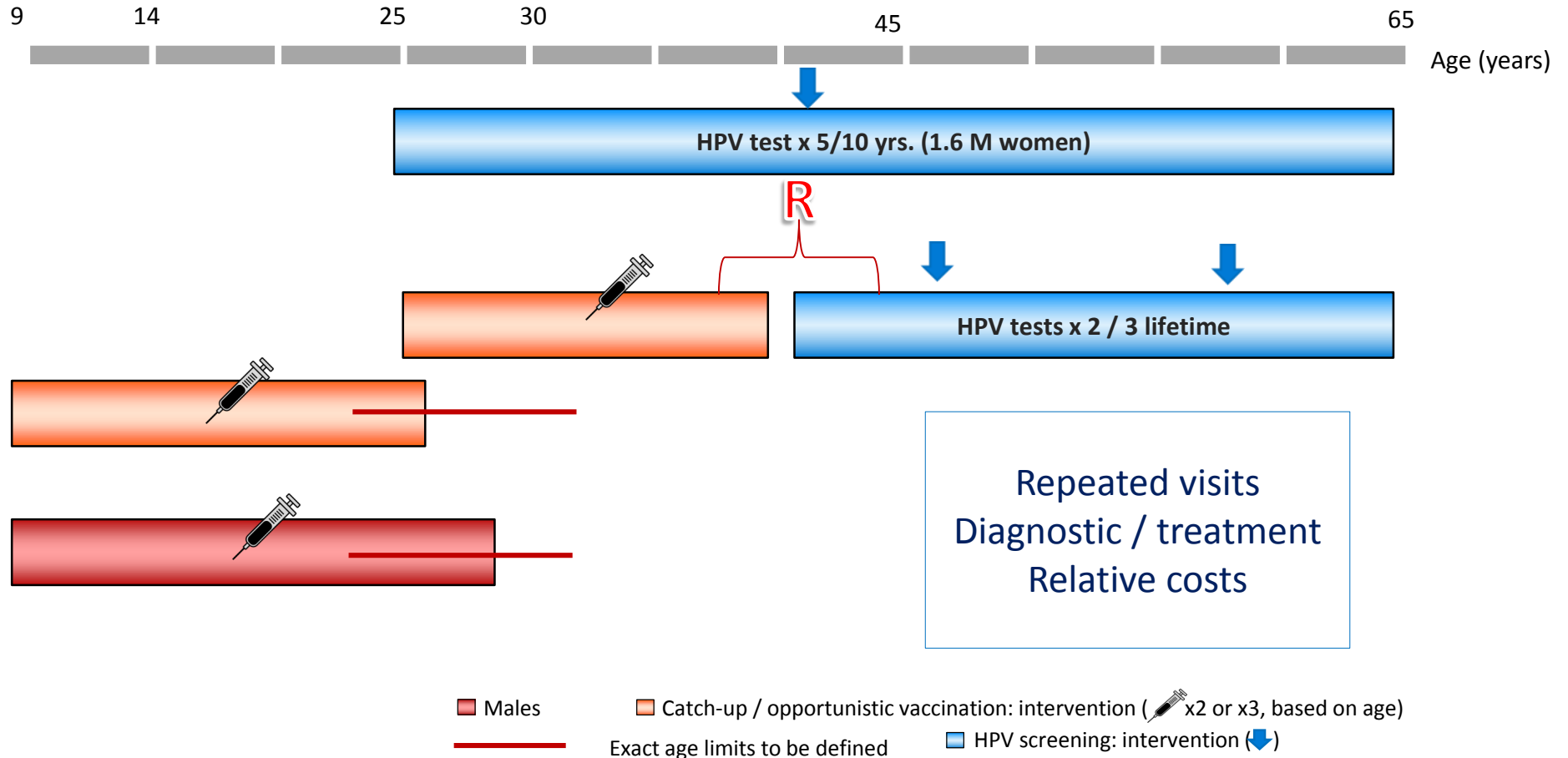
## Demonstration projects



Input data for models  
Population impact  
Time to impact  
Acceptability, coverage & compliance



# Example : Enter HPV vaccination into the HPV screening program in Turkey





# The proposal for a consortium



M. Steben

X. Bosch

S. de Sanjose

K Canfell  
S Garland

J Salmeron

M. Stanley

Inuit & migrants

CoheaHr: Vaccine acceptability & logistics

FRIDA2 Unscreened semi-rural areas



Amazonian Favelas in BA

Aborigine & marginal populations

★ Studies Under evaluation

F. Carozzi

S. Tatti

C. Wiesner

Oswaldo Cruz Fnd.

YLQiao.

B&M Gates Fund. / GAVI / H2020 / ERC / Local funds

## HPV FASTER: Public health message

HPV  
FASTER

- Attempt to get the best from two *complementary* technologies for cervical cancer prevention
- *Comprehensive* and coherent preventive plan for women *9 to 65*
- Potential for prevention of cervical cancer in the range of a reduction of *70-80% with 2/3 visits lifetime*
- *Accelerate* cancer reduction as compared to current vaccine indications
- The costs that will make the program cost-effective and sustainable are at reach



# Reasonable objectives for the next generation



<b>Disease Control</b>	Reduction to acceptable limits. Requires continuous intervention	<b>Increase the number of populations</b>
<b>Disease elimination</b>	Reduction of disease to zero in a given population. Requires continuous intervention	<b>Cervical Cancer in some developed populations</b>
<b>Infection elimination</b>	Reduction of infection to zero in a given population. Requires continuous intervention	Polio, measles
<b>Eradication</b>	<b>Permanent reduction to zero worldwide. Does not require continuous intervention</b>	<b>Small pox</b>
<b>Extinction</b>	Infectious agent does not exist, naturally or in labs.	None