

HPV vaccine perspectives

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Disclosure statement

- The presenter has received honoraria from Novartis and GlaxoSmithKline (GSK) as an investigator in vaccine clinical trials, from GSK, Schering Plough and Aventis as an investigator in clinical antibiotics trials, from GSK as member of advisory boards and from Novartis and GSK as lecturer



- Overview of HPV
- HPV vaccines
- Why vaccinate at age 11 or 12 years?
- Safety of vaccines
- Strategies for increasing uptake
- Conclusions



- **Overview of HPV**

- HPV vaccines

- Why vaccinate at age 11 or 12 years?

- Safety of vaccines

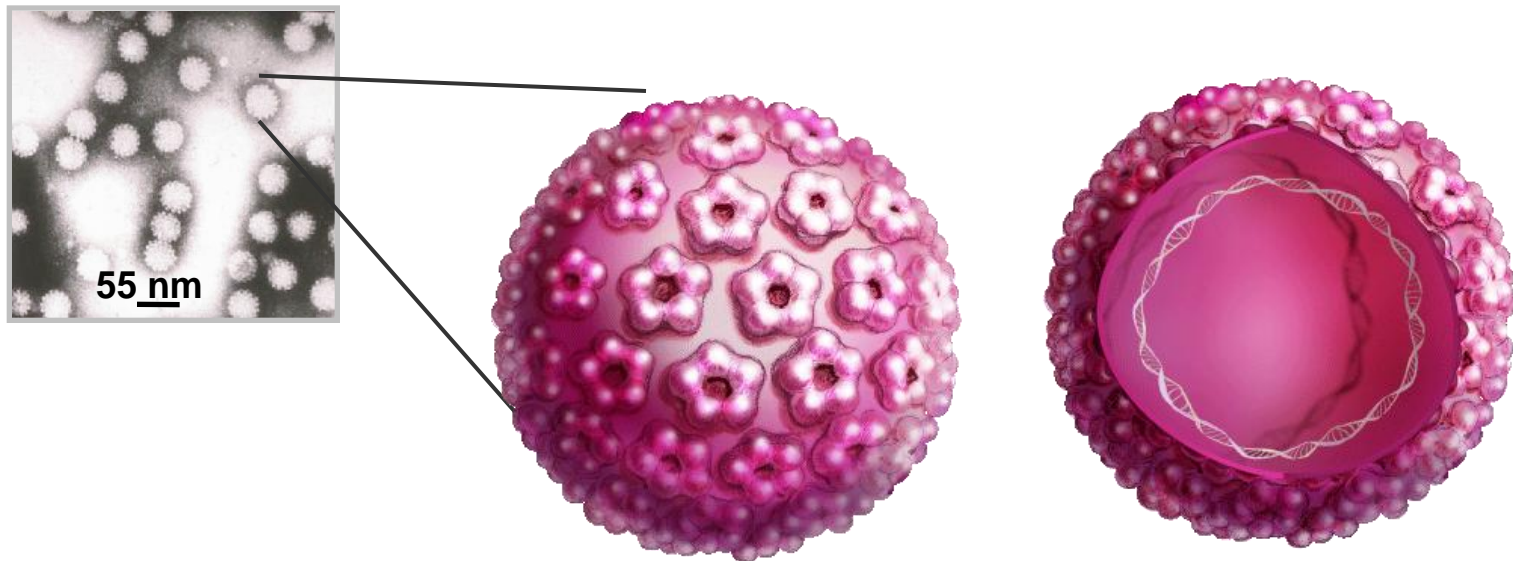
- Strategies for increasing uptake

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Human papillomavirus

- HPV is a small virus containing circular double-stranded DNA within a spherical shell (capsid)



HPV is the most
frequent sexually
transmitted disease



- The cumulative risk of acquiring cervical HPV infection in women with only one sexual partner is **46%** (3 years after first sexual encounter)
- HPV infections are very common: up to 80% of women will acquire an HPV infection in their lifetime

HPV is the necessary cause of cervical cancer

Second human carcinogen (after tobacco)



→ 5% of cancer in humans



→ 10% of cancer in women



→ 15% of cancer in women in developing countries



It is also a cause of
disease and death in
developed countries



HPV types

- At least **30** HPV types target the genital mucosa¹
- At least **15** HPV types are classified as **oncogenic** (high risk)¹
- Globally, HPV types **16** and **18** together account for > 70% of cervical cancer cases^{1,2}

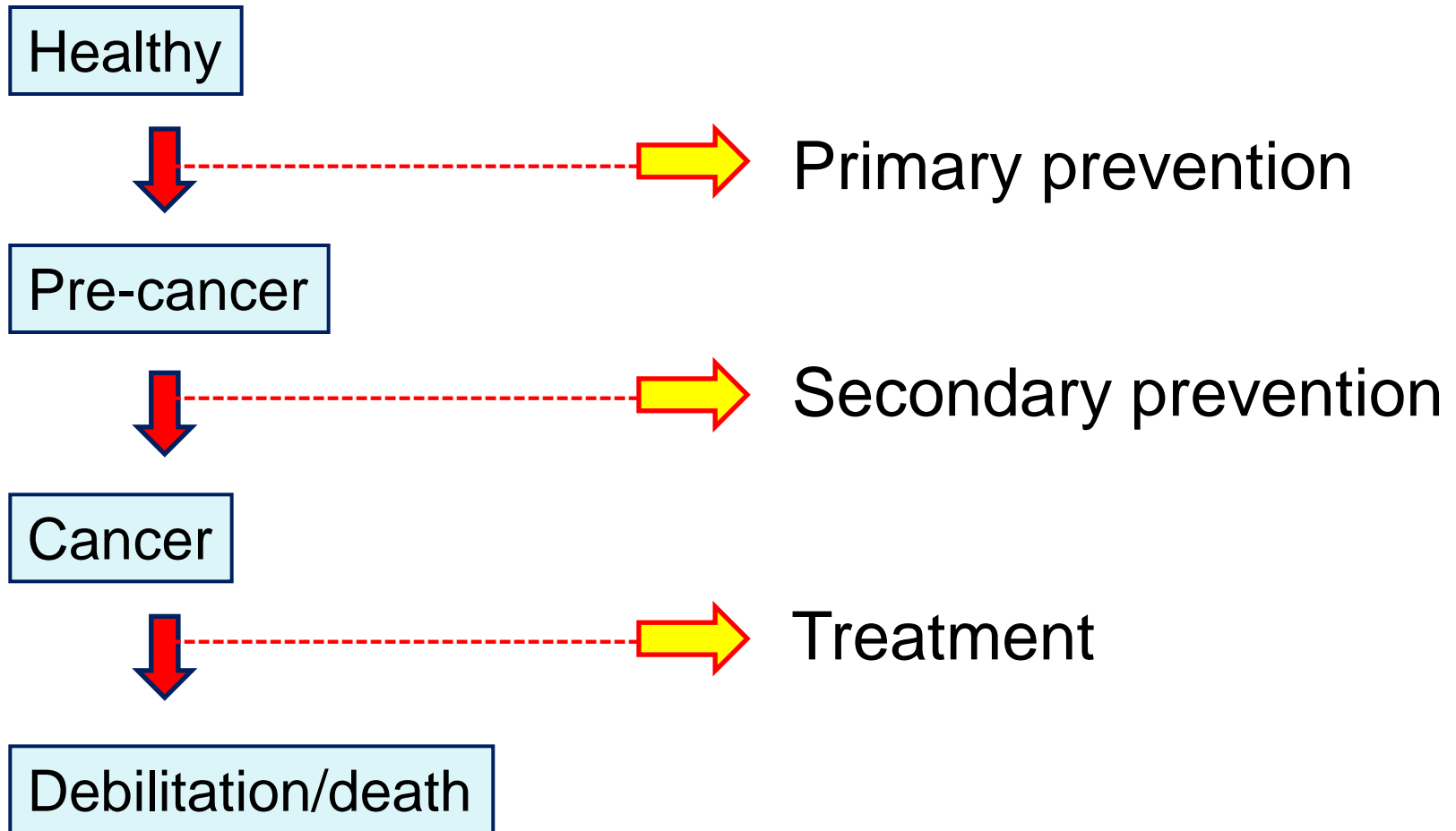
HPV types

- Low-risk (non-oncogenic) types cause benign genital warts/lesions
- HPV type 6 is most commonly detected in genital warts (~90% of warts) followed by HPV type 11 (10–30% of warts)

HPV transmission

- Sexual intercourse and/or genital skin-to-skin contact are the primary routes (condom does not provide complete protection)
- Transmission by non-sexual routes is thought to be uncommon, but possible

Screening identifies existing pre-cancerous lesions
Vaccination prevents them occurring in the first place



- One of the paradoxes of HPV is that clinicians who are largely responsible for vaccinating against cervical cancer, are unlikely to ever see a case of cervical cancer

I think we are blind. Blind people
who can see, but do not see

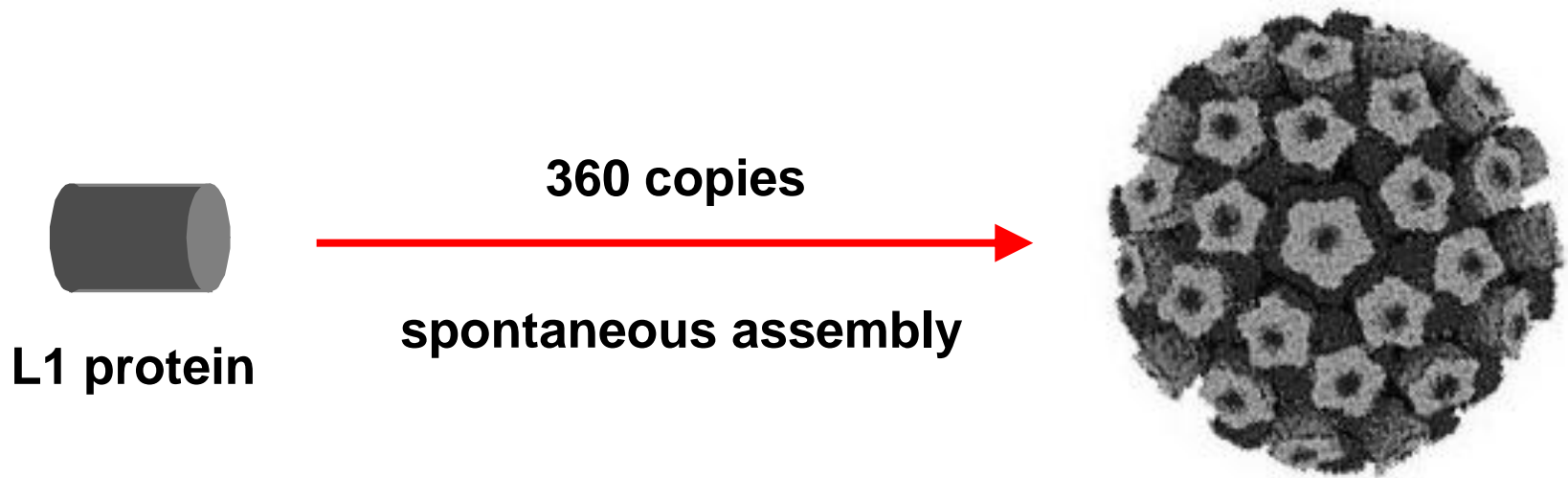
José Saramago



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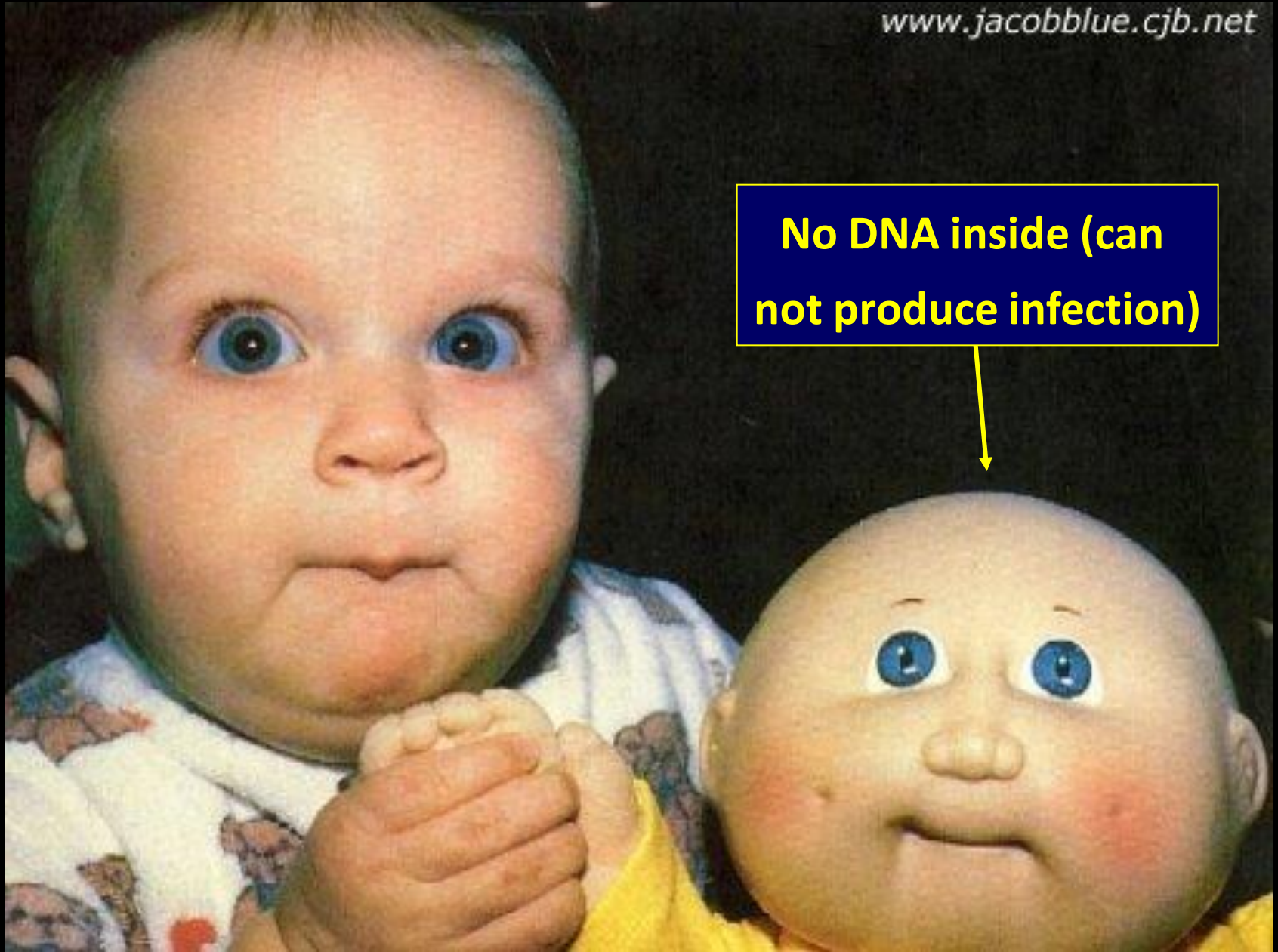
HPV vaccines: virus-like particles (VLP)



- VLPs consist of only one protein (L1)
- VLPs are virus particles without DNA hence are not infectious
- VLPs are immunologically identical to infectious virus



**No DNA inside (can
not produce infection)**



Vaccine



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graph TD; Vaccine[Vaccine] --> Antigen[Antigen]; Vaccine --> Adjuvant[Adjuvant system];
```

Antigen

Specificity of the
immune response

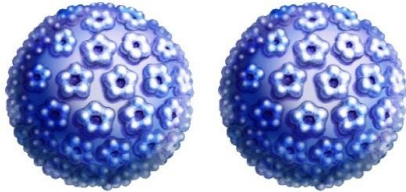
Adjuvant
system

Designed to enhance and modulate
the immune response by combining
the effect of two or more adjuvants

Composition of HPV2 and HPV4

Cervarix[®]

Antigens



HPV 16 VLPs

HPV 18 VLPs

+

AS04 adjuvant

Aluminium
salt
(Al(OH)₃)

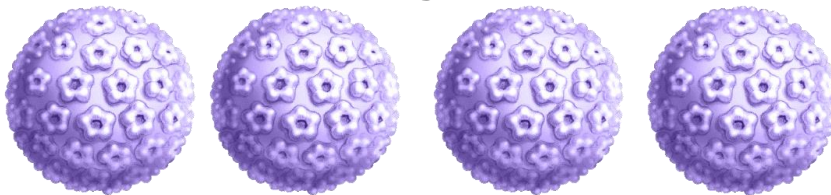
+

MPL
Immunostimulant

AS04-containing vaccine

Gardasil[®]

Antigens



HPV 16 VLPs

HPV 18 VLPs

HPV 6 VLPs

HPV 11 VLPs

+

Adjuvant


Aluminium salt
(amorphous aluminium
hydroxyphosphate
sulphate [AAHS])

AAHS-containing vaccine

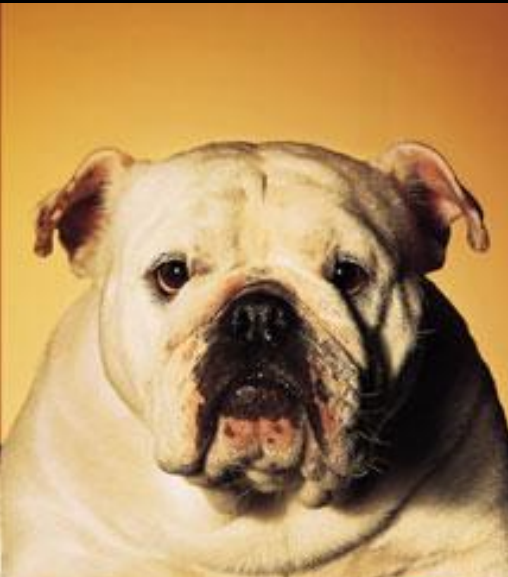
Advantages of Gardasil^R over Cervarix^R

- The Mercks' quadrivalent vaccine also includes HPV **6** and **11** (non oncogenic types)
- Gardasil^R has the advantage of protecting against genital warts
- Gardasil^R is licensed for males

Advantages of Cervarix[®] over Gardasil[®]

- 
- Cervarix[®] offers the advantage of a better cross-protection profile





Likely impact on cervical cancer

- Increased protection by 6 -- 12%
- Estimated protection from cervical cancer:
76 -- 82%

ACIP recommendations

- Females (either HPV 2 or HPV 4)
 - Routine: aged 11 to 12
 - Catch-up: aged 13 through 26 years
- Males (HPV 4)
 - Routine: aged 11 to 12
 - Catch-up: aged 13 through 21 (22 through 26 may be vaccinated)

ACIP recommendations

- Both vaccines are given as a 3-dose series
- The series can be started beginning at age 9 years
- Administer the 2nd dose 1-2 months after the 1st dose
- Administer the 3rd dose 6 months after the 1st dose

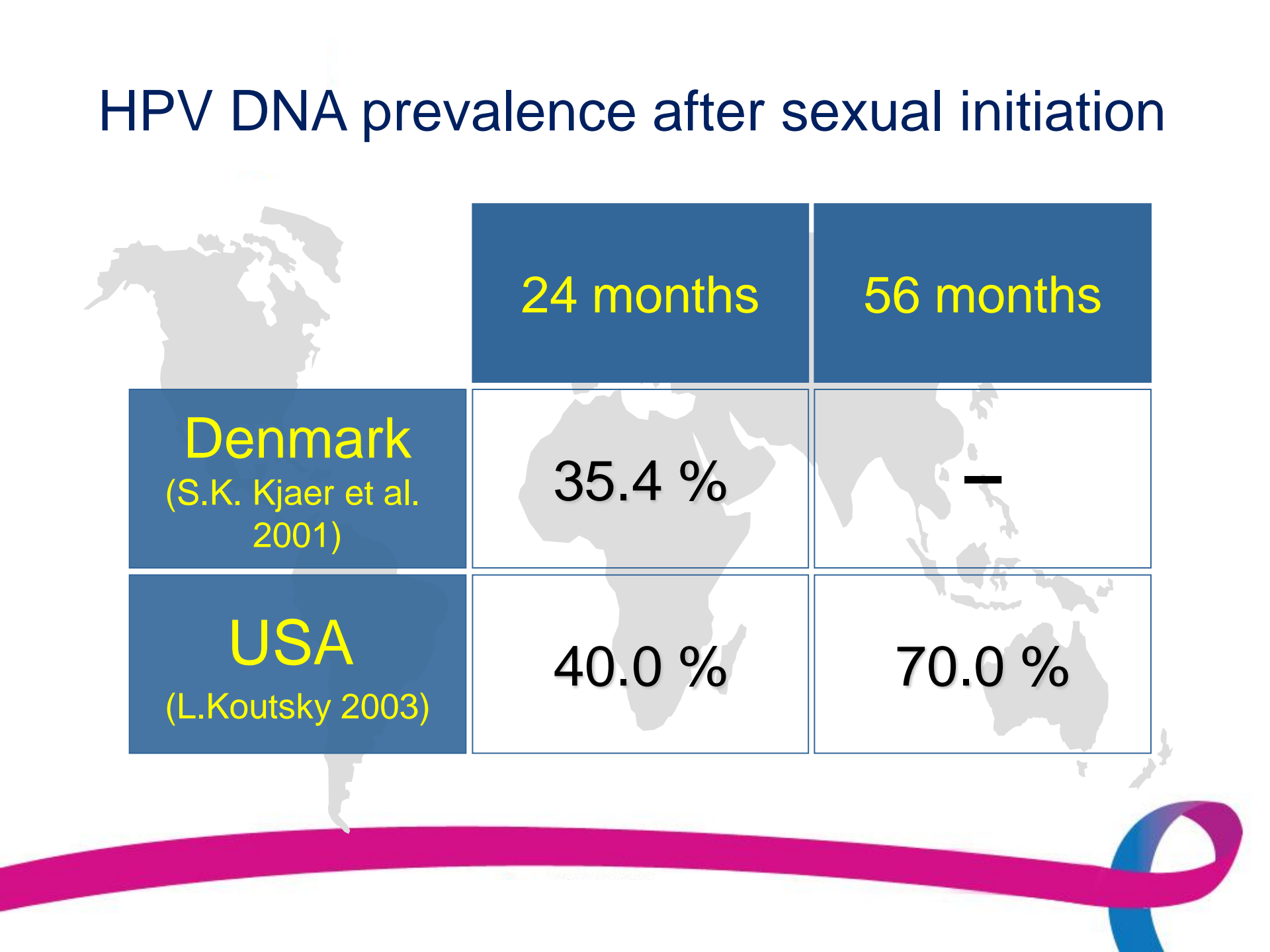
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Initial HPV infection occurs
soon after onset of sexual
activity

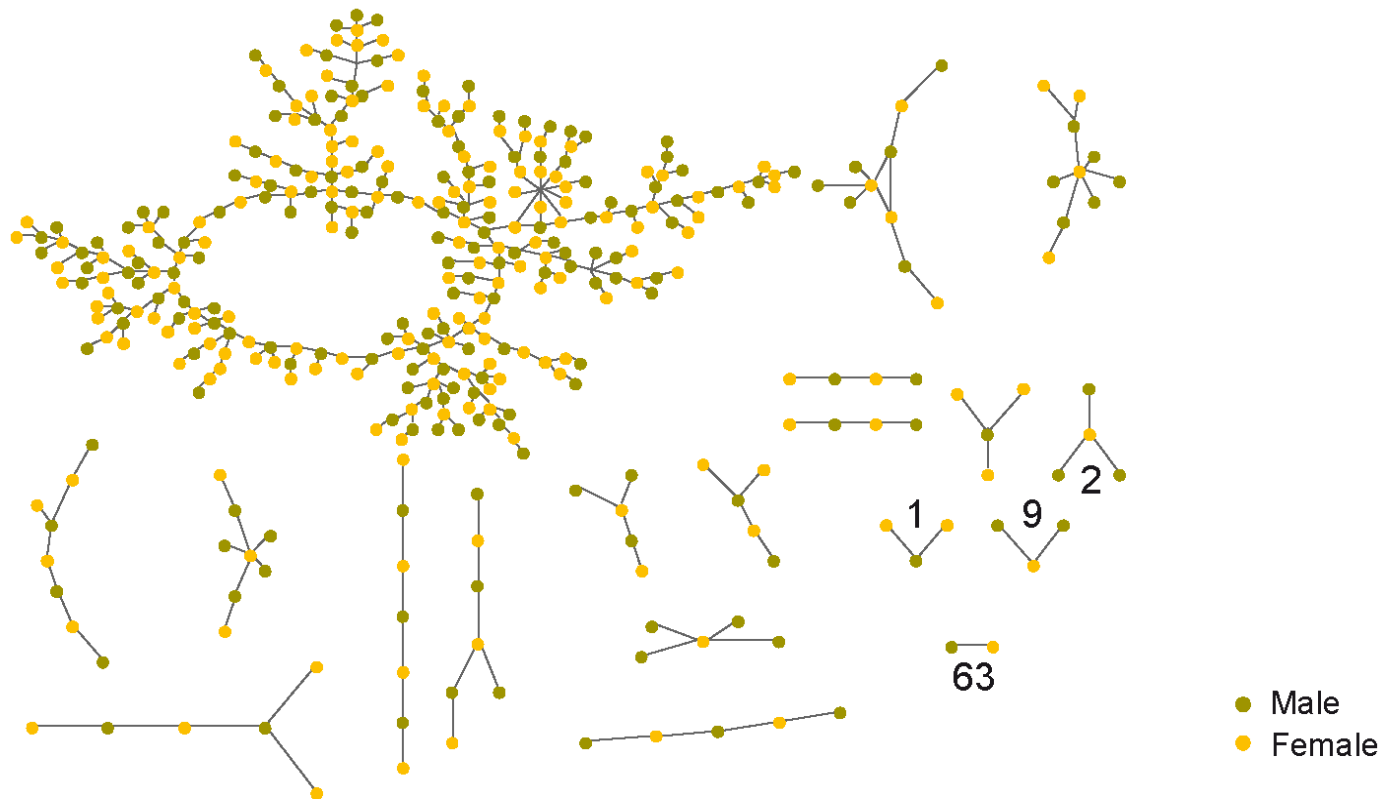


HPV DNA prevalence after sexual initiation



	24 months	56 months
Denmark (S.K. Kjaer et al. 2001)	35.4 %	—
USA (L.Koutsky 2003)	40.0 %	70.0 %

NETWORK STRUCTURE LINKING 573 SECONDARY SCHOOL STUDENTS IN A ROMANTIC OR SEXUAL RELATIONSHIP WITH ANOTHER STUDENT AT "JEFFERSON HIGH", USA



Numbers in the graph represent occasions in which the pattern was observed (i.e., 63 individuals reported monogamous dyadic relationships)

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Infection is not harmless



HPV infection frequently results in dysplasia

- A cohort of 60 adolescent women (aged 14–17 years) was followed over a 2.2-year period
- HPV was detected in **45.3%** of all specimens (**HR types 38.6%, LR 19.6%**)
- During the study period, 49 of 60 subjects tested positive for HPV (cumulative prevalence, **81.7%**).
- **37%** had at least 1 abnormal test (including 2% HGSIL)

Antibody response is optimal



Efficacy of vaccines is ideal



Vaccination does not modify
sexual behavior

Cost-effectiveness is more
favorable

Remember...

Women continue to be at
risk for cervical cancer
throughout their lives



Women might benefit from
vaccination including women
with previous HPV exposure



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How do we know they are safe?

- Large clinical trials
- Over 120 million doses have been distributed globally, no serious safety concerns
- WHO's Global Advisory Committee on Vaccine Safety concluded that both *Cervarix*[®] and *Gardasil*[®] had good safety profiles



- Safety experience in the UK: most reports have related either to the signs and symptoms of recognised, minor side effects listed in the product information, or to the injection process and not the vaccine itself (ie, psychogenic in nature)

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Bachmann claims HPV vaccine might cause ‘mental retardation’

**By [Rachel Weiner](#), Published:
September 13**

Beam me up, Scotty!

There's NO intelligent life down here!

We all have one

USE IT



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Communicating effectively with parents and patients

- Include HPV vaccines in discussion of all vaccines recommended in adolescents
- Use a short, matter-of-fact approach to HPV vaccine recommendation
- Emphasize cancer prevention

Strategies for increasing vaccine uptake

- The strongest predictor of a person being vaccinated is a physician recommendation
- Educate yourself to educate parents and patients about vaccines
- Address parents' questions
- Immunize at every opportunity

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- «HPV vaccines can prevent cancer in an entire generation»
- At least, 70% of cervical cancers could be prevented by HPV vaccines

Cervical cancer prevention: HPV vaccination combined with screening

Vaccination offers an important new management option in the primary prevention of cervical cancer

HPV vaccination combined with screening is the most effective cervical cancer prevention strategy¹

**Vaccines in the time of HPV,
represent a light of hope, so...**



...the races condemned to one hundred years of
solitude will have, at last and forever, a second
opportunity on earth