

## **Disclosures**

- Pfizer Grants for Independent Learning and Change CoVER
- Pfizer and Sanofi- non-branded speaker
- Sequirus, Pfizer and Sanofi advisory board
- GSK, Alere, Clinical trials
- CDC, NIH



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## **Objectives**

- Recognize the range of parental attitudes on immunization
- Identify effective approaches to discuss immunizations with specific parents
- Apply above mentioned approaches to increase HPV acceptance



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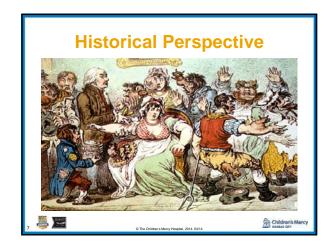
## What do parents know?

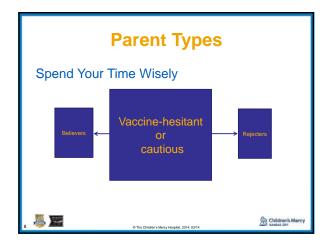
- Belief that vitamin K is a vaccine
- Belief that their 3-6 month old infant had received vaccines against chickenpox, smallpox, or measles, mumps, and rubella
- Belief that they themselves had received a vaccination against chickenpox as a child
- Belief that their infant could become infected with HIV from vaccines
- · Belief that infants develop influenza from the vaccine



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## **Know Your Audience**

- Tailor your dialogue to match the needs of your patient/parent
- Hesitancy: 34% of parents with up-todate children had major concerns regarding vaccines

















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## Make a "CASE" for Vaccines

- Corroborate
  - Acknowledge the parent's concern
  - Find some point of agreement between you and the parent
  - Set the tone for a respectful conversation
- · About me
  - Talk about what you've done to enhance your knowledge and expertise (eg, attended a conference)
- Science\*
  - Describe what science has to say about the topic in question
- Explain and advise
  - Offer your recommendation, based on the science
  - Personal recommendation



Singer A. http://www.vicnetwork.org/wp-content/uploads/VICNetworkWebin



## Case 1



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Singer A. http://www.vicnetwork.org/wp-content/uploads/VICNetworkWel

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## A Touch of Humanity

- Resist the righting reflex
  - Otherwise you run the risk of increasing a vaccine-hesitant parent's commitment to the status quo
- Understand motivations
  - Ask questions that elicit values and concerns
- Listen
  - Realize that simply providing the vaccine-hesitant parent with information doesn't automatically bring about change
- Empower
  - Remember: you are guiding the parent through the process of thinking aloud and deciding whether to change



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nature human behaviour LETTERS

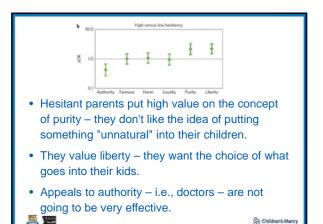
Association of moral values with vaccine hesitancy

- When faced with parents who are hesitant with regards to vaccinating their children, physicians often trot out the same aphorisms:
  - "vaccines protect your children from harm"
  - "vaccines protect society"
- New research shows that, far from being persuasive, individuals who are hesitant with vaccination to begin with may become <u>more entrenched</u> in their beliefs when they are confronted with these types of arguments.

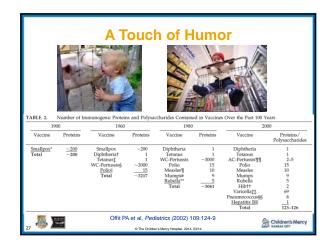


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# Tips • Appeal to concepts like purity and liberty. Instead of saying "vaccines protect your children" Say "Keep your child pure of infections — Vaccinate!"



# A Touch of Reality

What We're Afraid Of	What The Real Risk Is
Shark attacks (28)	Dog bites (4.5 million)
Murder (14,180)	Suicide (33,289)
Death by peanut allergy (50)	Death by poisoning (27,531)
Death by plane crash (321)	Death by car crash (34,017)

Figures shown in parentheses are annual averages



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## Case 2



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# A touch of – just tell them what to do!

- Use a presumptive format (eg, "Well, we have some shots to give today")
  - Presupposes patient will be immunized, increasing the likelihood of vaccine acceptance
- Avoid a participatory format (eg, "What do you want to do about shots?")
  - Implies that choosing not to vaccinate is medically acceptable
- Be persistent in cases of initial resistance (eg, "He really needs these shots" or "If she were my child, I'd definitely go ahead")

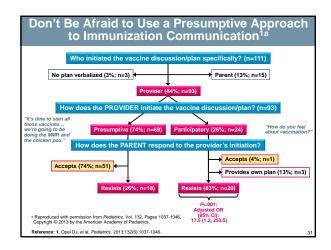


Opel DJ, et al. *Pediatrics*. 2013;132(6):1037-1046. 2. Opel DJ, et al. *Am J Public Health*. 2015;105(10):1998-2004.

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From: Effect of a Health Care Professional Communication Training Intervention on Adolescent Human Papillomavirus Vaccination: A Cluster Randomized Clinical Trial

5 Interventions:

HPV fact sheet library to create customized information sheets relevant to each practice's patient population

Tailored parent education website

A set of HPV-related disease images

An HPV vaccine decision aid

2½ hours of communication training on using a presumptive vaccine recommendation, followed by motivational interviewing if parents were resistant to vaccination.

self-guided, 30-minute webinar, plus 2 in-person, group training sessions that lasted 1 hour each

## Did it work?

- Adolescents in the intervention practices had significantly higher odds of HPV vaccine series initiation (adjusted odds ratio [aOR], 1.46; 95% CI, 1.31-1.62) and completion (aOR, 1.56; 95% CI, 1.27-1.92) than those in the control practices (a 9.5-absolute percentage point increase in HPV vaccine series initiation and a 4.4-absolute percentage point increase in HPV vaccine series completion in intervention practices).
- The intervention had a greater effect in pediatric practices compared with family medicine practices and in private practices compared with public ones.



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## What can I do?

 Health care professionals reported that communication training and the fact sheets were the most used and useful intervention components.



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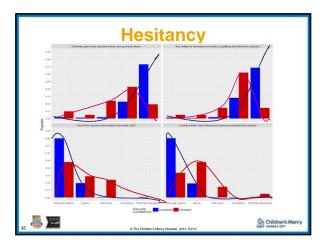
Of 1447 residents invited, 746 completed the survey (52% response rate). Among participants, 12 were excluded due to inability to determine residency type and or year. The final cohort consisted of 734 residents.

- Knowledge: The proportion of correct answers increased with residency year from PGY1 to PGY4 (49%, I95% CI 47-51]; 64% [95% CI 58-70]; test for trend p=.001).
   Compared to Family Medicine residents, Pediatric residents were more likely to answer knowledge questions correctly (56%; 49%; p=.001).
- Attitudes: Confidence in communicating with parents increased with training year (p <.001), but confidence in vaccination did not.
- Hesitancy: Three percent of residents (n=21) self-reported as vaccine hesitant. They were more likely to be FM (75%, p<.001). Residents were more likely to delay a vaccine in a vaccine eligible patient (i.e., someone without a medical contraindication) with increased year of training (p<0.001).



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Understanding the Burden

## **HPV INFECTION & DISEASE**



## **HPV Infection**

- Almost all females and males will be infected with at least one type of HPV at some point in their lives
  - Estimated 79 million Americans currently infected
  - 14 million new infections/year in the US
  - HPV infection is most common in people in their teens and early 20s
- Most people will never know that they have been infected

emal A et al. J Natl Cancer Inst 2013;105:175-201



## **HPV Transmission**

- HPV exposure can occur with any type of intimate sexual contact
- ■Intercourse is not necessary to become infected
- Nearly 50% of high school students have already engaged in sexual (vaginal-penile) intercourse
  - 1/3 of 9th graders and 2/3 of 12th graders have engaged in sexual intercourse
  - 24% of high school seniors have had sexual intercourse with **4 or more partners**

Iemal A et al. I Natl Cancer Inst 2013:105:175-201



## **HPV** is found in virgins

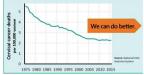
- Study examined the frequency of vaginal HPV and the association with non-coital sexual behavior in longitudinally followed cohort of adolescent women without prior vaginal intercourse
- ►HPV was detected in 46% of women prior to first vaginal sex
- ■70% of these women reported non-coital behaviors that may in part explain genital transmission

Shew, J Infect Dis. 2012



## **Cervical Cancer**

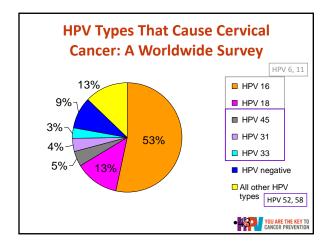
- Cervical cancer is the most common HPV-associated cancer among women
  - 528,00 new cases and 266,000 deaths world-wide in 2012
  - 12,000 new cases and **4,000 deaths** in the U.S. in 2013



- ► Half of cervical cancers occur in women <50 years
  - A quarter of cervical cancers occur in women 25-39 years

ttps://nccd.cdc.gov/uscs/ and http://gco.larc.fr/today/home





## The Pap smear in the 21st Century

- **■** Sensitivity of pap smear is problematic
- ■50% of women diagnosed with cervical cancer never had cytology screening
- HPV testing is extremely sensitive, but less specific than Pap
  - ►All cervical cancers are due to HPV
  - ■But most HPV resolves without clinical disease
- Combinations of tests may emphasize strengths and decrease weaknesses



# Without vaccination, annual burden of genital HPV-related disease in U.S. females: 4,000 cervical cancer deaths 10,846 new cases of cervical cancer 330,000 new cases of HSIL: CIN2/3 (high grade cervical dysplasia) 1 million new cases of genital warts 1.4 million new cases of LSIL: CIN1 (low grade cervical dysplasia) Nearly 3 million cases and \$7 billion American Cancer Society, 2008; Schiffman Arch Pathol Lab Med. 2003; Koshiol Sex Transin Dis. 2004; YOU ARE THE KEY TO CANCER PREVENTION

# Average Number of New HPV-Associated Cancers by Sex, in the United States, 2015 Men N = 15, 346 Women N = 23, 875 8% 14% 9% Cervix Vagina & Vulva Anus Penis 19% See Pahud & Ault 2015 and Saraiya et al 2015

# HPV-Associated Oropharyngeal Cancers

- Prevalence increased from 16.3% (1984-89) to 71.7% (2000-04)
- ■Population-level incidence of HPVpositive cancers increased by 225% while HPV-negative cancers declined by 50%



If trends continue, the annual number of HPV-positive oropharyngeal cancers is expected to surpass the annual number of cervical cancers by the year 2020

Chaturvedi, 2011, J Clin Oncol- data from SEER



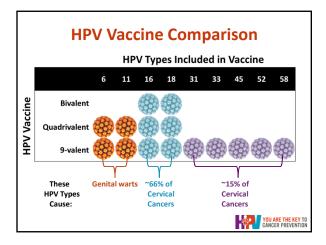
## **HPV Prophylactic Vaccines**

- Recombinant L1 capsid proteins that form "virus-like" particles (VLP)
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection



**HPV Virus-Like Particle** 





## **HPV Vaccine Recommendation**

CDC recommends routine vaccination at age 11 or 12 years to prevent HPV cancers

- ■The vaccination series can be started at age 9 years
- ■Two doses of vaccine are recommended
- ■The second dose of the vaccine should be administered 6 to 12 months after the first dose.

eites et al. MMWR. 201



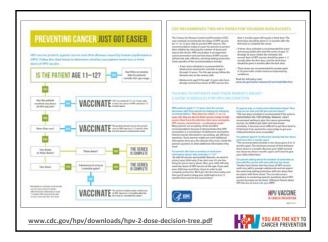
# HPV Vaccine Recommendations: Catch Up/Late

- Cat B: Vaccination for females through age 26 years and for males through age 21 years who were not previously adequately vaccinated. Males aged 22 through 26 years may be vaccinated.
- Vaccination is also recommended through age 26 for gay, bisexual, and other men who have sex with men (MSM), transgender people, and people with certain immunocompromising conditions (including HIV infection).

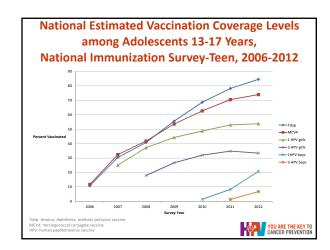
feites et al. MMWR. 20

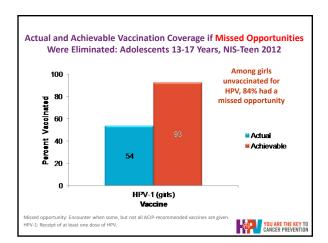


# Before 15th birthday Before 15th birthday OR Immunocompromised 9-26 years Recommended schedule is 2 doses of HPV vaccine 2nd dose: 6-12 months after 1st 1st (0, 6-12 month schedule) On or after 15th birthday OR Immunocompromised 9-26 years Recommended schedule is 3 doses of HPV vaccine 2nd dose: 1-2 months after 1st 3rd dose: 6 months after 1st (0, 1-2, 6 month schedule)



# HPV Vaccination Is Safe, Effective, and Provides Lasting Protection HPV Vaccine is SAFE Benefits of HPV vaccination far outweigh any potential risks Safety studies findings for HPV vaccination similar to safety reviews of MCV4 and Tdap vaccination HPV Vaccine WORKS Population impact against early and mid outcomes have been reported in multiple countries HPV Vaccine LASTS Studies suggest that vaccine protection is long-lasting No evidence of waning protection

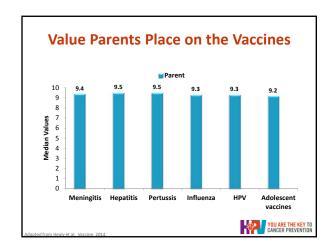




Talking about HPV vaccine

FRAMING THE CONVERSATION

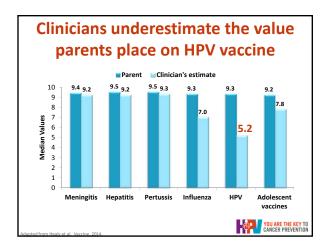
YOU ARE THE KEY TO CANCER PREVENTION







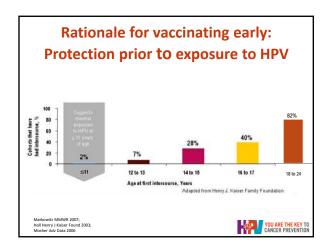


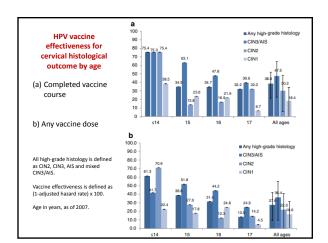


## Why at 11 or 12 years old?

- Parents want a concrete reason why 11-12 year olds should receive HPV vaccine
  - ■In audience research with moms, almost all respondents were unaware of the correct age range the vaccine was recommended
  - Respondents also missed the concept of vaccinating before sexual activity







# When do we put our seat belts on? A. Before turning on car B. When leaving driveway C. After a near accident

YOU ARE THE KEY TO CANCER PREVENTION

# Give a Strong Recommendation to Receive HPV Vaccine at Ages 11 or 12 Not sexually active Not recommended Safety concern/Side effects Not needed or necessary Lack of knowledge 0 5 10 15 20 Percent A strong recommendation from you is the main reason parents decide to vaccinate Many moms in focus groups stated that they trust their child's doctor and would get the vaccine for their child as long as they received a recommendation from the doctor

"The perceived and real concerns of parents influence how the clinician recommends and administers HPV vaccine."

YOU ARE THE KEY TO CANCER PREVENTION

## **Some Parents Need Reassurance**

- Many parents simply accept of this bundled recommendation
- Some parents may be interested in vaccinating, yet still have questions. Interpret a question as they need additional reassurance from YOU, the clinician they trust with their child's health care
- Ask parents about their main concern (be sure you are addressing their real concern)

Inpublished CDC data, 2013



## An anti-cancer vaccine

- ■The "HPV vaccine is cancer prevention" message resonates strongly with parents
  - In focus groups and online panels, mothers wanted more information on the types of HPV cancers
  - In focus groups mothers stated they were influenced to vaccinate their child because HPV vaccine prevents cancer, they had a family history of cervical cancers, and/or because they had a personal experience with cervical cancer





## **Make an Effective Recommendation**

- Same way: Effective recommendations group all of the adolescent vaccines
  - Recommend HPV vaccination the *same way* you recommend Tdap & meningococcal vaccines.
- Same day: Recommend HPV vaccine today
  Recommend HPV vaccination the same day you
  recommend Tdap & meningococcal vaccines or at
  any visit.

Jnpublished CDC data, 2013



## Is it safe?

Frequently Asked Questions about HPV Vaccine Safety



- Which HPV-vaccine is available in the United States?
  Are there known side effects from petting HPV vaccine?
  Is there arrone into should not set HPV-vaccine/Gardisal 91?
  How are HPV-vaccines monitored for obsible safety problems?
- . Have serious adverse events been reported after people receive HPV vaccines?

- Can HPV vaccines users better beautiful and except members
  Are HPV vaccines safe for occeptant earners?

  Here HPV vaccines been linked to Guillain Barré syndrome? IGBS!
- Can HPV\_vaccines cause contural orthostatic tachycantila syndrome./POTSP
- . Do HPV vaccioes cause chronic regional pain syndrome (CRPS)?
- Do HPV vaccines cause chronic fatinue syndrome?
   Has anyone died after receiving HPV vaccines?
   Havs FDA and CDC changed and HPV vaccine record
- . What if someone has a serious reaction after pettine an HPV vaccine?
- . Where can lifet more information about HPV vaccines?



## **HPV Vaccine Safety Data Sources**

- Over 60 million doses of HPV vaccine distributed in US since 2006
- Over 200 million doses of the quadrivalent and 80 million doses of the bivalent vaccines have been administered globally (2015)
- ■The vaccine surveillance systems in countries regularly monitor and report the serious and the non-serious adverse events after HPV vaccination



## **Over 10 Years of HPV Vaccine Safety Data**

- HPV vaccine is safe
- Reactions after vaccination may include
  - Injection site reactions: pain, redness, and/or swelling in the arm where the shot was given
  - Systemic: fever, headaches
- Brief fainting spells (syncope) and related symptoms (such as jerking movements) can happen soon after any injection, including HPV vaccine
- Patients should be seated (or lay down) during vaccination and remain in that position for 15 minutes



# Evaluating and Monitoring 9-valent HPV Vaccine Safety in the United States

## **Monitoring of VAERS Reports**

- Clinical review of deaths and other pre-specified adverse events
- Data mining to identify disproportional reporting

### Vaccine Safety Datalink

- Near real time monitoring of 10 pre-specified outcomes
- Evaluation of spontaneous abortion

## Manufacturer post-marketing commitments

- Two, 10-year studies to assess long term safety
- Observational study to further characterize the safety profile in 10,000 persons
- Pregnancy registry





Monitoring Impact of HPV Vaccine Programs on HPV-Associated Outcomes

## **HPV VACCINE IMPACT**



## **HPV vaccine impact monitoring**

- Post licensure evaluations are important to evaluate real world effectiveness of vaccines
- Population impact against early and mid outcomes have been reported:

## **Genital warts**

■Australia, New Zealand, Denmark, Sweden, Germany, Quebec, US

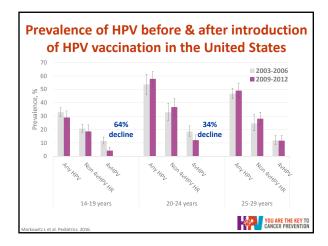
## **HPV** prevalence

■Australia, Norway, Denmark, Sweden, UK, US

## **Cervical lesions**

Australia, British Columbia, Denmark, Sweden, US





# HPV Vaccine Impact: High HPV Vaccine Coverage in Australia

- ■80% of school-age girls in Australia are fully vaccinated
- ► High-grade cervical lesions have declined in women less than 18 years of age
- ■For vaccine-eligible females, the proportion of genital warts cases declined dramatically by 93%
- Genital warts have declined by 82% among males of the same age, indicating herd immunity

Garland et al, Prev Med 2011 Ali et al, BMJ 2013



## Impact of HPV vaccination in Australia Proportion of Australian born females and males diagnosed as having genital warts at first visit, by age group, 2004-11 20 — <21 years --- 21-30 years --- 21-30 years - >30 years 2004 2005 2006 2007 2008 2009 2010 2011 Females Year Males YOU ARE THE KEY TO CANCER PREVENTION et al. BMJ 2013

# Systematic Review and Meta-Analysis: Population-Level Impact of HPV Vaccination

- Review of 20 studies in 9 high income countries
- ■In countries with >50% coverage, among 13-19 year olds
  - ► HPV 16/18 prevalence decreased at least 68%
  - ► Anogenital warts decreased by ~61%
- **■** Evidence of herd effects
- Some evidence of cross protection against other types

Project et al. Lancet Infact Dic. 2011



# HPV Vaccine Duration of Protection

- Studies suggest that vaccine protection is long-lasting
- No evidence of waning protection
  - Available evidence indicates protection for at least 10 years
  - Multiple studies are in progress to monitor

ACIP. Summary Report. June 22-23, 2016



# Why We Need to Do Better in HPV Vaccination of 12 year olds

- Currently 26 million girls <13 yo in the US; If none of these girls are vaccinated then:
  - ■168,400 will develop cervical cancer and
  - ■54,100 will die from it
- Vaccinating 30% would prevent 45,500 of these cases and 14,600 deaths
- Vaccinating 80% would prevent 98,800 cases and 31,700 deaths

For each year we stay at 30% coverage instead of achieving 80%, 4,400 future cervical cancer cases and 1400 cervical cancer deaths will occur.



## **Avoid Missed Opportunities**

- ►HPV vaccine can safely be given at the same time as the other recommended adolescent vaccines
- Provide HPV vaccine during routine sports, or camp physicals
- Review immunization record even at acute care visits
- Systems interventions depend on clinician commitment- determine what would work best for YOUR practice



## A green light for sexual activity?

- Parents may be concerned that vaccinating may be perceived by the child as permission to have
  - In focus groups, some parents expressed concern that in getting HPV vaccine for their child, they would be giving their child permission to have sex
  - This was one of the top four reasons respondednts gave when asked why they would not vaccinate their daughter
  - A few parents expressed that while they wanted their child to "wait to have sex" they understood that might not be the case



# Receipt of HPV vaccine does not increase sexual activity or decrease age of sexual debut

- ► Kaiser Permanente Center for Health Research
- ■1,398 girls who were 11 or 12 in 2006, 30% of whom were vaccinated, followed through 2010
- No difference in markers of sexual activity, including
  - Pregnancies
  - Counseling on contraceptives
  - Testing for, or diagnoses of, sexually transmitted infections

ednarczyk Pediatrics Oct 201



"How long can we wait and still give just two doses?"





The two-dose schedule is recommended if the series is started before the 15th birthday.

However, I don't recommend waiting to give this cancer-preventing vaccine. As children get older and have busier schedules, it becomes more difficult to get them back in.

I'd feel best if we started the series today to get your child protected as soon as possible.



## **How Can Clinicians Help?**

- 1. Give a STRONG recommendation
- Ask yourself, how often do you get a chance to prevent cancer?
- 2. Start conversation early and focus on cancer prevention
  - ► Vaccination given well before sexual experimentation begins
  - Better antibody response in preteens
- 3. Offer a personal story
  - Own children/Grandchildren/Close friends' children
  - HPV-related cancer case
- 4. Welcome questions from parents, especially about safety
  - Remind parents that the HPV vaccine is safe and not associated with increased sexual activity





# References Advices/Committee on immunistation Practices. Summany Report. Jane 22-23, 2016. Available at <a href="https://www.cdc.gov/vaccines/pcis/meetings/downloads/dides-2016-06/june-22-32-3016-en.pdf">https://www.cdc.gov/vaccines/pcis/meetings/downloads/dides-2016-06/june-22-32-3016-en.pdf</a> All K et al. Gental work in project for years into national human papillomavirus vaccination programme nation durables and 814 30 2013 445-78022. Baldur Fellow or I. Treds in the Nucleose of enviol cancer and enview presentenous lessons to hermats, 1997-3012. Cancer Causes Control 2015 Aug-26/96/1105-16. Beanar MV, Casler Ri, Jenico SA, et al. Population-Based loadness faites of Convoid intraeptibeal Recipions in the Human Papillomavirus Vaccine to Beanary of the Section of the S

