

Human Papillomavirus:  
What Every Pharmacist Should Know

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Objectives

- Summarize the epidemiological consequences of human papillomavirus (HPV) infections
- Describe the pathophysiology of HPV
- Identify key points regarding the mechanism of action of bivalent and quadrivalent HPV vaccines

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Objectives cont.

- Recommend the clinical use of the HPV vaccine based on documented evidence
- Counsel patients and family members on the importance of vaccination with the HPV vaccine

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### HPV Vaccine Review

Question: HPV vaccines have been studied in which of one the following situations?

- A. Prevention of head and neck carcinoma
- B. Prevention of genital warts in women >26 years of age
- C. Prevention of genital warts in men
- D. All of the above (correct choice)
- E. None of the above

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### Pharmacist Delivered Patient Care

- Pharmacist-run vaccination clinics
- Medication Therapy Management
- Pharmacists as prescribers:
  - Florida
  - Kentucky
  - England

<http://www.rpsgb.org.uk/worldofpharmacy/currentdevelopmentsinpharmacy/pharmacistprescribing/index.html>  
State of Florida 2007 Statute 465.185  
Kentucky Bill HB 673 (BR 1959)

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### Vaccinations in the Community

- By law, who can provide vaccinations?
- What opportunities exist for pharmacists?
- How can we obtain this ability?
- What restrictions apply?

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### Who currently can vaccinate?

- Physicians and their staff:
  - Can administer any vaccination(s) available
- Pharmacists:
  - Can administer influenza vaccinations in MA
    - Injectable and intra-nasal
  - All other vaccines
    - No defined rules or regulations, but possibility for expansion exists

[http://www.mass.gov/Eeoehs2/docs/dph/quality/boards/pharmacy\\_influenza\\_vaccine04.pdf](http://www.mass.gov/Eeoehs2/docs/dph/quality/boards/pharmacy_influenza_vaccine04.pdf)  
Massachusetts Board of Pharmacy 105 CMR 700.004(B)(6)

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### Pharmacist Run Vaccination Clinics

- MA Board of Pharmacy 105 CMR 700.004(B)(6) States that:
  - “Department of Public Health is making influenza vaccination more accessible and easier to obtain by allowing pharmacists, who have completed duly accredited training, to administer injectable influenza vaccine as well as FluMist™, intranasal influenza vaccine”

[http://www.mass.gov/Eeoehs2/docs/dph/quality/boards/pharmacy\\_influenza\\_vaccine04.pdf](http://www.mass.gov/Eeoehs2/docs/dph/quality/boards/pharmacy_influenza_vaccine04.pdf)  
Massachusetts Board of Pharmacy 105 CMR 700.004(B)(6)

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### Obtaining Accreditation

- ACPE accredited continuing education programs are available
  - <http://www.rxce.neu.edu/>
    - Live program held in September of each year
  - [www.aphanet.org](http://www.aphanet.org)
    - Membership required, at-home online study program
  - Many others exist

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## Requirements and Restrictions

Requirements:	Injectable influenza	Intra-nasal influenza
ACPE accredited certification	Required, must keep proof in the pharmacy	Required, must keep proof in the pharmacy
Report to DPH total doses administered	Suggested, not required	Suggested, not required
CPR certification	Recommended, not required	Recommended, not required
Age restrictions	≥18 years of age	Ages 18-49
Required to administer vaccination	Prescription, physician directive, or standing order	Prescription, physician directive, or standing order

[http://www.mass.gov/EcoHHS2/docs/dph/quality/boards/pharmacy\\_influenza\\_vaccine04.pdf](http://www.mass.gov/EcoHHS2/docs/dph/quality/boards/pharmacy_influenza_vaccine04.pdf)  
Massachusetts Board of Pharmacy 105 CMR 700.004(B)(6)144

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## What other opportunities exist?

- Varicella vaccination clinics:
  - Brigham and Women's Hospital
- Oregon:
  - Pharmacists may administer any of 15 different immunizations
  - Among them, HPV is included

<http://oregon.gov/DHS/phi/imm/provider/pharmpro.shtml>

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## Why the focus on HPV?

- In the United States:
  - ≥50% of all adults will develop an STD by age 35
    - ≥25% of all teenage girls estimated to have an STD
  - 12 million estimated new cases/yr
    - Human Papillomavirus (6.2 million new cases)
  - In 2000, \$600 million dollars were spent to treat non-HIV STDs

CDC. MMRW 2006  
Harrell W, et al. 2004

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**Human Papillomavirus (HPV)**

- **Causative virus:**
  - >100 types of HPV exist
    - Types 6 and 11 associated with genital warts
    - Types 16, 18, 31, 33 and 35 associated with neoplasia
- **Transmission:**
  - Skin-to-skin contact with someone infected with HPV

NIAID: Human Papillomavirus and Genital Warts, 2007

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**Clinical Presentation**

- **Symptoms:**
  - Soft, flesh colored genital warts may appear
    - Appear in “Cauliflower”-like clusters
  - Appear within 1-3 months post-infection
  - ~2/3 of all exposed persons develop genital warts

NIAID: Human Papillomavirus and Genital Warts, 2007

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**Impact of HPV**

- **Genital warts:**
  - Non-curable
  - Symptomatic treatment only
- **Cervical neoplasia:**
  - 5-year survival rates from cervical cancer range >99% to 18% depending on stage and extent

J Clin Invest. 2006 May;116(5):1167-73.  
Vaccine. 2006 May 15

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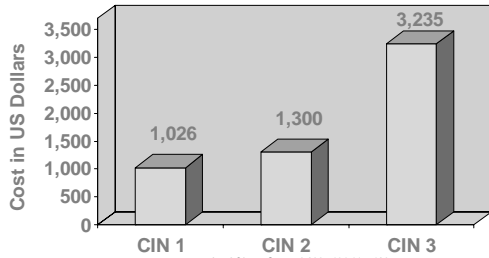
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## Burden of HPV

Cost per episode in 2002



CIN = cervical intraepithelial neoplasia *Am J Obstet Gynecol.* 2004;191:114-120

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## Patient Scenario 1

- Mrs. Stevens comes into your pharmacy to pick up a prescription. While there she see's your "Ask Me About HPV" badge.
- Mrs. Stevens has a daughter and states "I've heard a lot of conflicting information recently, and I'm more confused than ever! What are your thoughts about the new HPV vaccine?"

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## Patient scenario cont.

- To help answer Mrs. Stevens question what additional information would you like to ask Mrs. Stevens?
  - How old is her daughter?
  - What is her daughter's vaccination history?
  - Is her daughter sexually active?
    - If so, has her daughter been tested for STDs?
  - Is there a family history of cervical cancer?

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Patient scenario cont.

- Mrs. Stevens informs you that her daughter:
  - Is 15 years old
  - Received all of her childhood vaccinations
  - Has a boyfriend, but she hopes and prays she isn't sexually active
  - No one in her or her husbands family has been diagnosed with cancer that she can remember

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Patient scenario cont.

- With this information, what recommendation(s) could you make to Mrs. Stevens?
  - Re-enforce abstinence
  - If sexually active, re-enforce condom use
  - Regular gynecologic visits and Pap smears
  - HPV vaccination
  - Symptomatic treatment should she develop HPV related genital warts in the future

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Vaccination options for prevention

- Gardasil®
  - FDA approved in the U.S
  - Quadrivalent vaccination
    - Types 6, 11, 16 and 18
  - Females ages 9 to 26
- Ceravix®
  - Non-FDA approved at this time
  - Bivalent vaccination
    - Types 16 and 18
  - Females ≥10 years old

Gardasil® [package insert], Whitehouse Station, NJ: Merck & CO, Inc; December 2007.  
Ceravix [package insert], Research Triangle Park, NC: GlaxoSmithKline, Inc; September 2007.

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## Indications for Vaccination

- Prevention of:
  - Human Papillomavirus
  - Genital Warts
  - Precancerous or dysplastic lesions
  - Cervical Cancer
- Cannot be used to treat patients with active HPV infection or cervical dysplasia and/or cancer

Gardasil [package insert], Whitehouse Station, NJ: Merck & CO, Inc; December 2007.  
Cervix [package insert], Research Triangle Park, NC: GlaxoSmithKline, Inc; September 2007.

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## Bivalent vs. Quadrivalent

- Bivalent vaccination:
  - Vaccinates against types 16 and 18
- Quadrivalent vaccination:
  - Vaccinates against types 6, 11, 16 and 18

What impact does this difference have clinically?

Gardasil [package insert], Whitehouse Station, NJ: Merck & CO, Inc; December 2007.  
Cervix [package insert], Research Triangle Park, NC: GlaxoSmithKline, Inc; September 2007.

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## Vaccinations cont.

- Both vaccines provide coverage against:
  - Types 16 and 18:
    - Associated with 70% of all cervical cancers
- The quadrivalent vaccine provides additional coverage against:
  - Types 6 and 11:
    - Associated with 90% of all genital warts

Gardasil [package insert], Whitehouse Station, NJ: Merck & CO, Inc; December 2007.  
Cervix [package insert], Research Triangle Park, NC: GlaxoSmithKline, Inc; September 2007.

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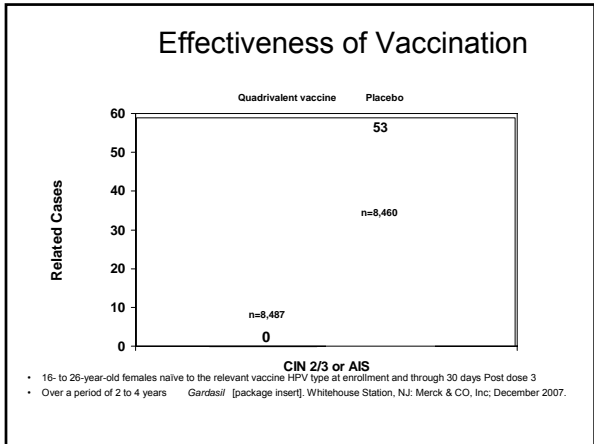
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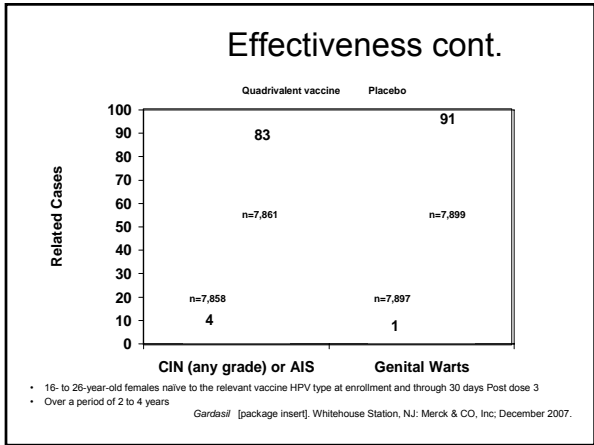
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### Patient Scenario revisited

- Recall Mrs. Stevens, you provided her information about the HPV vaccine, its efficacy and who is appropriate to receive it, but she wants to know more about its safety and use.

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### Return to Patient Scenario.

- What information would help you in answering this question?
  - What adverse reactions have been reported with the use of the vaccination?
  - What contraindications to use exist?
  - How is this vaccine administered?
  - Can this vaccine be co-administered with other vaccines or medications?
  - Any other considerations?

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### Reported adverse events

- Quadrivalent vaccination compared to placebo:
  - Injection site:
    - Pain: 83.9% vs. 75.4%
    - Swelling: 25.4% vs. 15.8%
    - Erythema: 24.6 vs. 18.4%
    - Pruritis: 3.1% vs. 2.8%
  - Systemic:
    - Fever: 10.3% vs. 8.6%
    - Nausea: 4.2% vs. 4.1%
    - Dizziness: 2.8% vs. 2.6%

Gardasil [package insert], Whitehouse Station, NJ: Merck & CO, Inc; December 2007.

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### Contraindications and Precautions

- Contraindications:
  - Hypersensitivity to vaccine or its excipients
- Precautions:
  - Pregnancy Category B
    - Not recommended, administer only if necessary
  - Breastfeeding safety not established

Gardasil [package insert], Whitehouse Station, NJ: Merck & CO, Inc; December 2007.

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## Vaccination Schedule

- Vaccination should be administered intramuscularly:
  - Three separate doses according to the following schedule:
    - First dose: at elected date
    - Second dose: 2 months after the first dose
    - Third dose: 6 months after the first dose
- Syncope (fainting) may occur after vaccination:
  - Observe patients for 15 minutes after administration

Gardasil [package insert]. Whitehouse Station, NJ: Merck & CO, Inc; December 2007.

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Oops!  
I forgot to come back for my next dose

- Variation of dosing regimen from clinical studies:

	Minimum	Maximum
Interval between first and second dose	36 days (~5 weeks)	84 days (~3 months)
Interval between second and third dose	80 days (~3 months)	160 days (~5 months)

- Ongoing studies evaluating various dosing schedules:
  - 0, 3, 9 months; 0, 6, 12 months; or 0, 12, 24 months

Gardasil [package insert]. Whitehouse Station, NJ: Merck & CO, Inc; December 2007.

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## Co-Administration

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| <ul style="list-style-type: none"> <li>• Other vaccines:                     <ul style="list-style-type: none"> <li>– May be administered concomitantly with hepatitis B vaccine</li> <li>– No data for other vaccinations at this time</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>• Other medications:                     <ul style="list-style-type: none"> <li>– Hormonal contraception                             <ul style="list-style-type: none"> <li>• Use did not alter efficacy</li> </ul> </li> <li>– Immunosuppressants                             <ul style="list-style-type: none"> <li>• May reduce immune response to all vaccines</li> </ul> </li> </ul> </li> </ul> |
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Gardasil [package insert]. Whitehouse Station, NJ: Merck & CO, Inc; December 2007.

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**Additional Vaccination Considerations**

- Role of a booster vaccine
  - No booster vaccination recommended at this time
  - Current studies have only evaluated women up to 5 years post-vaccination, but length of immunity is unknown
- Role of vaccinating males
  - Men can be asymptomatic carriers and transmitters of HPV
  - No approved indication for vaccination at this time, but trials are ongoing to evaluate effectiveness

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**Additional Considerations Cont.**

- Role of vaccination outside of genital warts and cervical cancer:
  - Recently published case control studies suggest that HPV is a risk factor for oral and oropharyngeal carcinomas
- Role of vaccinating women outside approved age ranges:
  - Studies ongoing evaluating the use of HPV vaccinations in females ages up to 45 years

NEJM 2007;356:1993-1995  
NEJM 2007;356:1944-56

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**Patient Scenario 2**

- A provider in your ambulatory care clinic calls you to inquire about treatment options for a patient of theirs found to have genital warts

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### Treatment of Genital Warts

Which one of the following agents may be used as treatment of genital warts?

- A. Acyclovir
- B. Famciclovir
- C. Imiquimod (correct answer)
- D. Valganciclovir

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### Patient Scenario 2 cont.

- What options are available for this patient?
  - Podofilox (Condylox) 0.5% topical external solution or gel
    - Applied twice daily x 3 days, then rest for 4 days
      - May repeat up to 4 cycles
  - Imiquimod (Aldara) 5% topical external cream
    - Applied three times weekly for up to 16 weeks

CDC, MMWR 2006  
Am Fam Phys. 2004;70:12:2335

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### Comparison of available Agents

- |                                   |                                      |
|-----------------------------------|--------------------------------------|
| • Podofilox 0.5%:                 | • Imiquimod 5%:                      |
| – Clear rates: 45 to 80%          | – Clear rates: 30 to 50%             |
| – Risk of recurrence: 5 to 30%    | – Risk of recurrence: 15%            |
| – Avg. cost per episode: \$200.00 | – Avg. cost of per episode: \$500.00 |
| – Generic available               | – Brand only                         |

Am Fam Phys. 2004;70:12:2335  
2006 Drug Topics Red Book. Montvale, N.J.: Thompson Medical Economics; 2007.

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### Additional Considerations

- Adverse effects:
  - Erythema: 95-100%
  - Epithelial erosion, depigmentation and scarring: 9 to 54%
- Pregnancy category C:
  - Infant risk cannot be ruled out

Am Fam Phys. 2004;70:12:2335

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### Putting it together cont.

Please review the following case:

- MR is a 19 yo woman
  - All vaccinations up to date
  - Sexually active, monogamous relationship
    - Both tested and negative for STDs/HIV
  - Last pap smear revealed abnormal cervical cells
  - Brings in a new prescription to your pharmacy for the HPV vaccination

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### Putting it all together

- MR says “I’ve heard a lot about this vaccine, but I’m not sure if I need it. My boyfriend and I don’t have HPV, but my doctor recommended anyways. Do you have any additional information?”

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Putting it together cont.

Please think of at least two different responses to help answer MR's question

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MR cont.

- After your discussion MR thanks you for your advise and states that she will fill the prescription.
- Once you fill the medication, you tell MR that you wanted to make her aware of a few things about the use and potential adverse reactions with this particular vaccination

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MR cont.

Please come up with at least two different counseling points for MR related to this vaccination

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### MR Returns

- It's six month later and MR returns to your pharmacy. You find out that subsequent to your last conversation MR ended up not receiving the vaccination and shortly after that MR contracted genital warts from her boyfriend.

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### MR cont.

- MR still has two refills on her vaccine prescription and wants to fill it ASAP and go to her doctor's office before they close.
- Please formulate an appropriate response to MR's request

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### HPV vaccination in review

Which one of the following choices is correct regarding the quadrivalent HPV vaccine?

- A. It is approved for use in women ages <9 and >26 years of age
- B. It is approved for use to prevent both genital warts and cervical cancer (correct answer)
- C. It is approved for use to treat both genital warts and cervical cancer
- D. It is approved for use in men and women

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### In Review

- What options are currently available in the U.S. to prevent HPV strains?
- Who is eligible for this vaccination?
- What is the dosing schedule?
- What counseling points should you offer patients regarding the HPV vaccine?

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### Review cont.

- What suppressive therapy options exist for those with genital warts?
- What is the dosing schedule for each?
- What counseling points should you offer your patients regarding suppressive therapy?

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THANK YOU FOR YOUR  
PARTICIPATION AND TIME

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