HSV and HPV

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I have no disclosures

Many thanks to Drs. Khalil Ghanem and Jean Anderson for slides and expertise!

Objectives

- By the end of the presentation, participants should be able to:
  - Describe the epidemiology, common clinical manifestations, and management of Herpes Simplex Virus and Human Papilloma Virus

Part I

HERPES SIMPLEX VIRUSES (HSV)

What is the Epidemiology of HSV-1 & 2?

- Both HSV-1 and HSV-2 cause genital herpes
- HSV-2 mainly causes genital herpes
- HSV-1 also causes herpetic stomatitis (fever blisters) and can be transmitted in childhood via oral secretions
- NHANES Study of Adult U.S. Population:
  - Seroprevalence of HSV-1: 68%
  - Seroprevalence of HSV-2: 17%
- NHANES Study of U.S. Children:
  - Seroprevalence of HSV-1: 36%
- When an adult acquires HSV-1, it is 3X more likely that it was acquired sexually

Schillinger et al. *Sex Transm Dis*. 2004;31:753-60

MMWR. 2010;59(15):456-9

Xu, F, et al. *J Pediatr.* 2007;151(4):374-7

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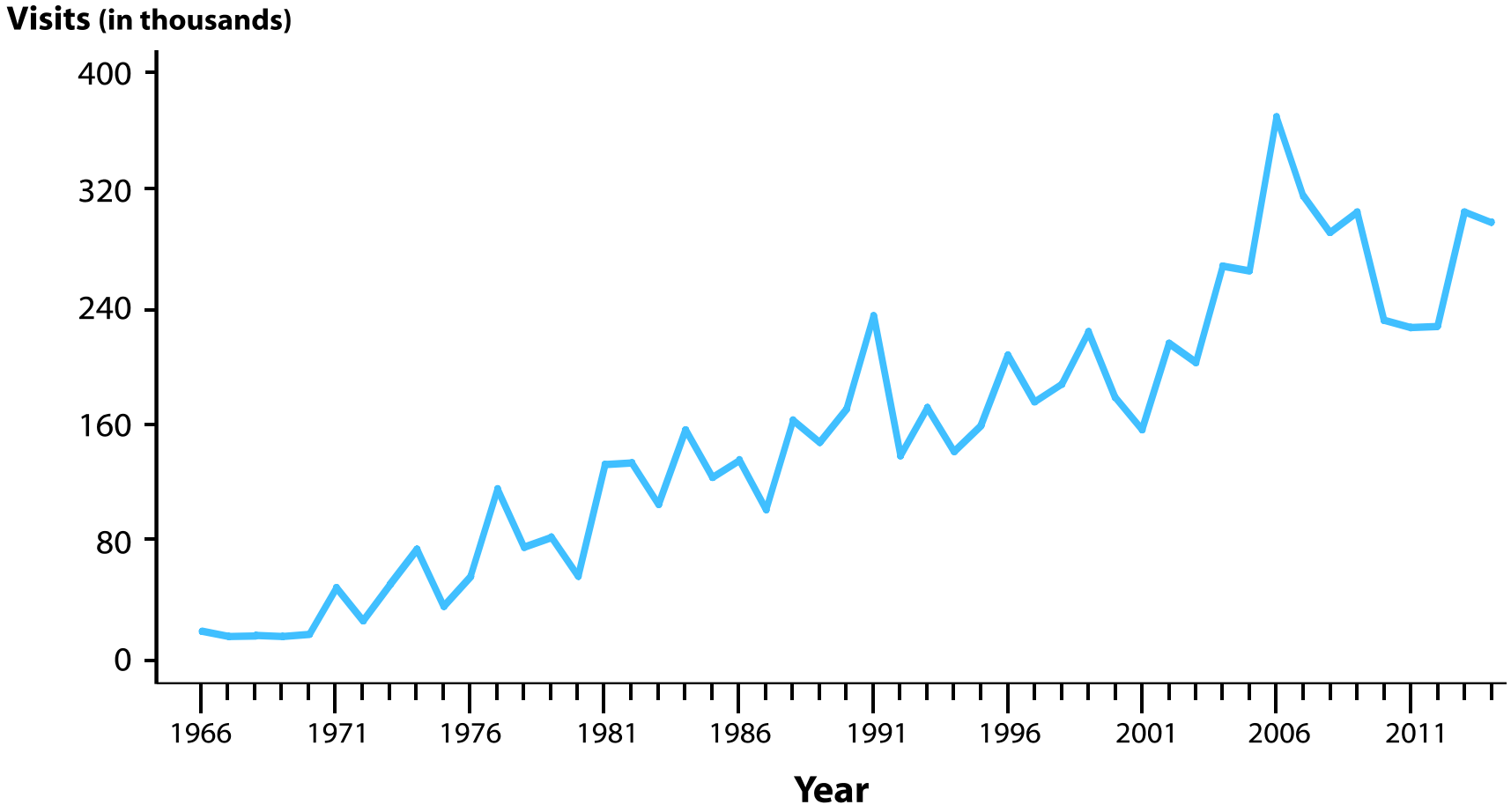
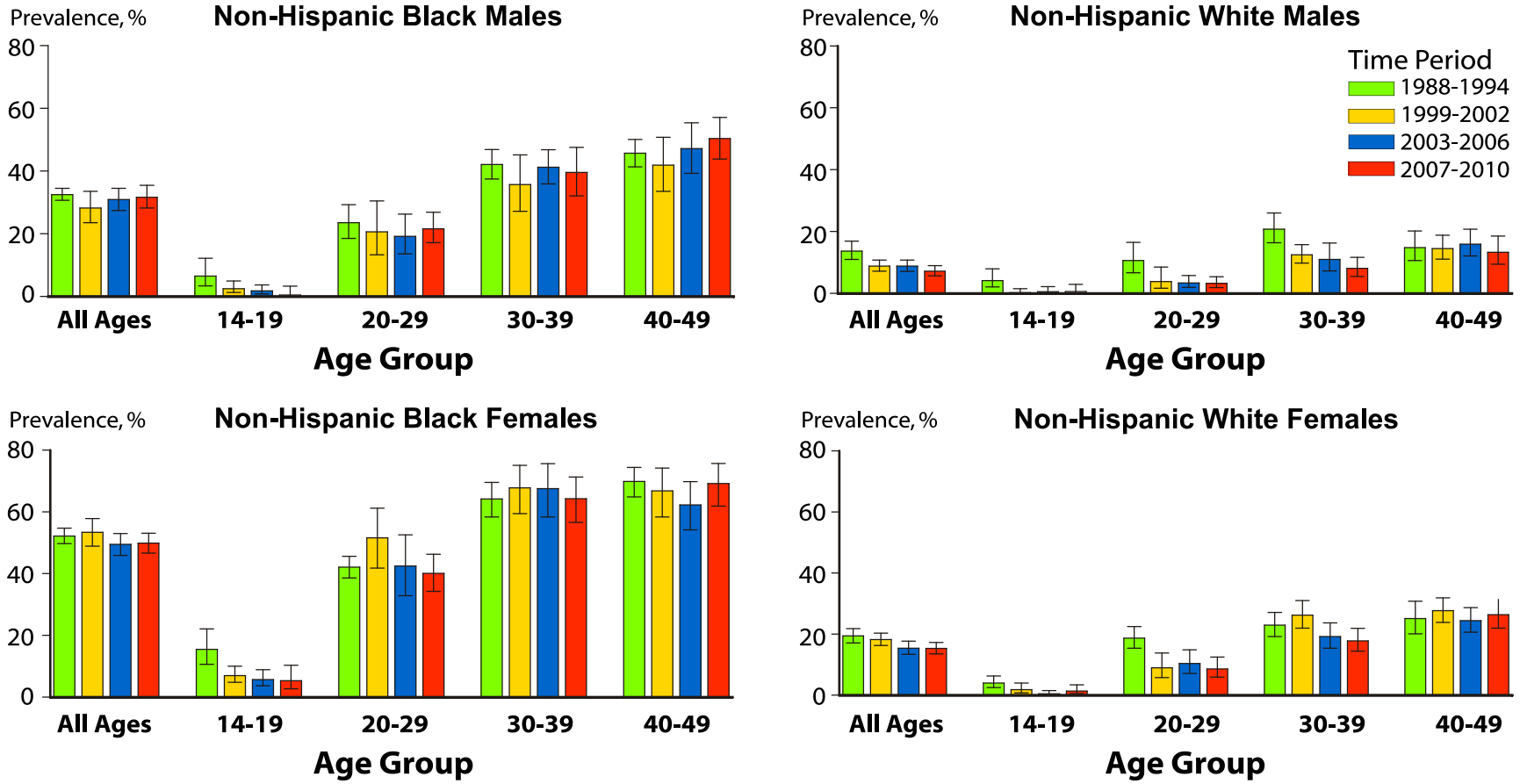
Genital Herpes Simplex Virus (HSV) Infections — Initial Visits to Physicians' Offices, United States, 1966–2014



NOTE: The relative standard errors for genital HSV infection estimates of more than 100,000 range from 18% to 23%.

SOURCE: National Disease and Therapeutic Index, IMS Health, Integrated Promotional Services™. IMS Health Report, 1966–2014. The 2015 data were not obtained in time to include them in this report.

Herpes Simplex Virus (HSV) Type 2 — Seroprevalence Among Non-Hispanic Whites and Non-Hispanic Blacks by Sex and Age Group, National Health and Nutrition Examination Survey, 1988–1994, 1999–2002, 2003–2006, and 2007–2010



NOTE: Error bars indicate 95% confidence interval.

SOURCE: Fanfair RN, Zaidi A, Taylor LD, Xu F, Gottlieb S, Markowitz L. Trends in seroprevalence of herpes simplex virus type 2 among non-Hispanic blacks and non-Hispanic whites aged 14 to 49 years — United States, 1988 to 2010. Sex Transm Dis. 2013;40(11):860–4.

If Infected with One Virus can you Become Infected with the Other?

- Previous HSV-1 infection did not reduce the rate of HSV-2 infection, but it did increase the likelihood of asymptomatic seroconversion 2.6 fold as compared with symptomatic seroconversion
- Acquisition of HSV-1 infections in persons with prior HSV-2 infections is rare

Langenberg AG, et al. *NEJM* 1999:341:1432-8

- Prior orolabial HSV-1 infection appears to protect against HSV-1 genital infection

Corey L, et al. *Ann Int Med* 1983:98:958-72

Reeves W, et al. *NEJM* 1981:305:315

What are the symptoms of primary HSV infection?

- 74% of HSV-1 and 63% of HSV-2 infections did not produce **participant-recognized** symptoms
- No differences in clinical presentation of primary infection between HSV-1 and 2

Diagnostic Rule	Sensitivity	Specificity	PPV	NPV	Accuracy
Ulcers	0.63	0.89	0.69	0.86	0.82
Ulcers or vesicles	0.76	0.81	0.60	0.90	0.79
Ulcers or vesicles or pain	0.87	0.68	0.51	0.93	0.73
Ulcers or vesicles or painful urination or pain	0.98	0.26	0.34	0.97	0.46
Rule based on No. of the following signs/symptoms: ulcers, vesicles, painful urination, or pain					
At least 1 of 4	0.98	0.26	0.34	0.97	0.46
At least 2 of 4	0.85	0.73	0.55	0.93	0.76
At least 3 of 4	0.59	0.95	0.82	0.86	0.85
All 4	0.39	1.00	1.00	0.81	0.83

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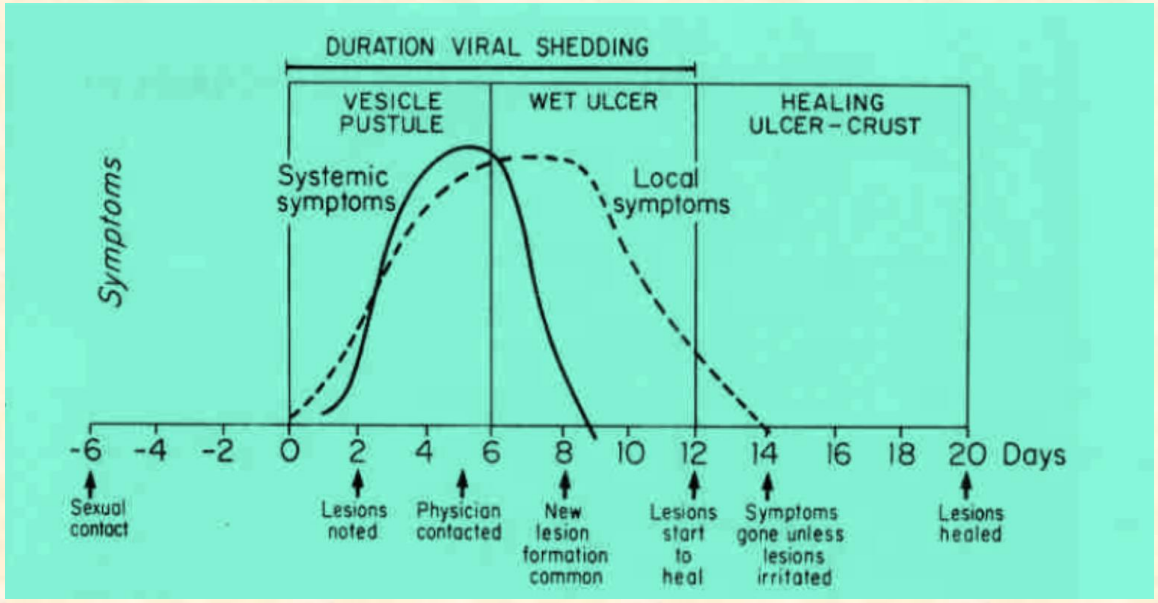
Bernstein DI, et al. *Clin Infect Dis*. 2013;56(3):344-51

What are the symptoms of primary HSV infection?

Symptom	Men	Women
Meningitis sx	11%	36%
Local pain	95%	99%
Dysuria	44%	83%
Urethral/vaginal discharge	27%	85%

*HSV causes 23% of cases of non-gonococcal proctitis



- Systemic symptoms (fever, headache, malaise, and myalgias occur early in the course of infection and peak 3-4 days after onset of lesions
- Severity of symptoms, duration of lesions, and viral shedding are similar in **primary** HSV1 and HSV-2 infections
- Symptoms of primary HSV infection tend to be more severe in **women** than in men

Corey L, et al. *Ann Int Med* 1983:98:958-72

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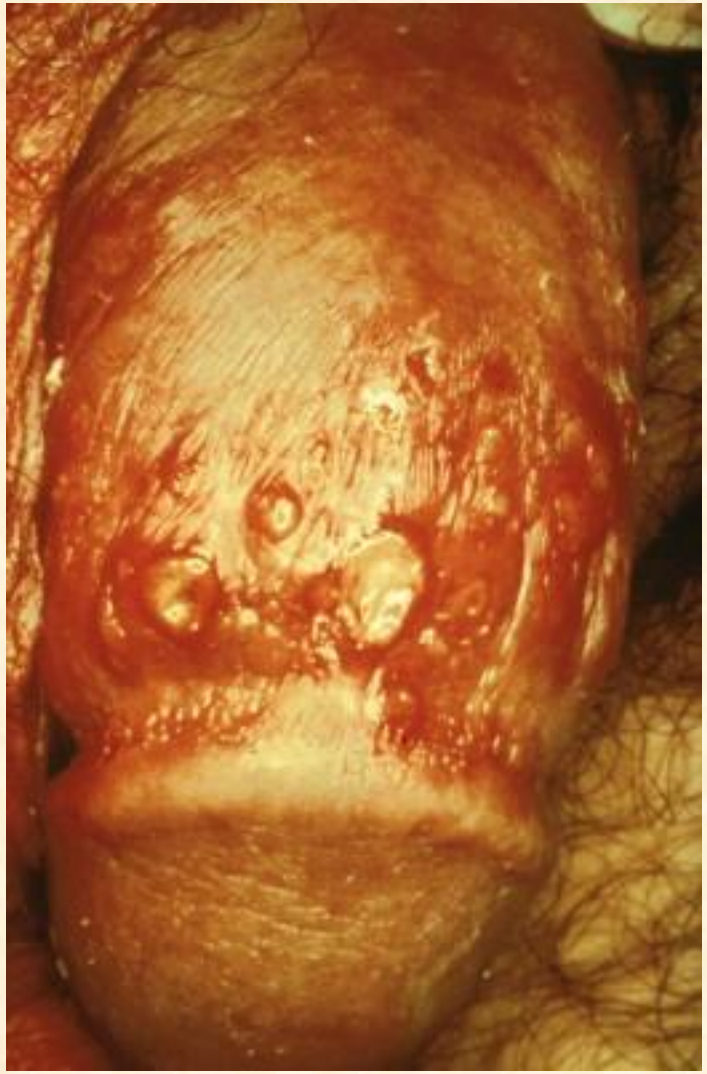
Primary herpes, male



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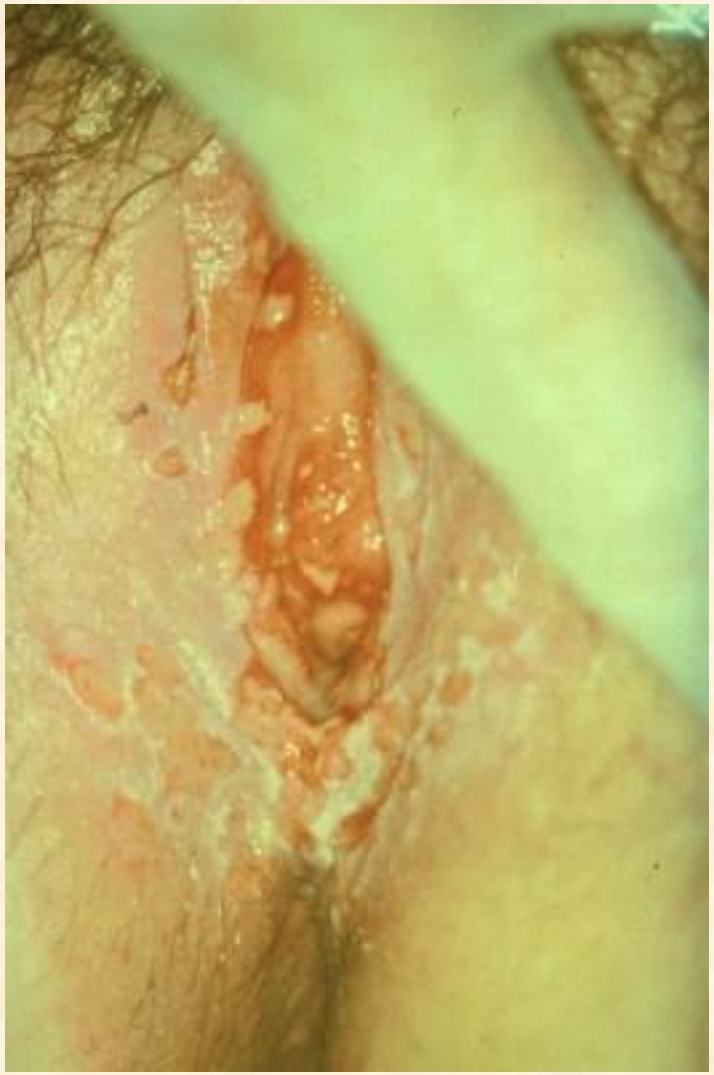
Primary herpes, female



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How well do clinicians perform when attempting to diagnose HSV infections clinically?

- The performance of clinical diagnosis is good when a patient presents with classic signs and symptoms
- Overall, the sensitivity of clinical diagnosis is 39% and PPV is 81% (because most patients do not present with classic manifestations)
- 20% of those given a clinical diagnosis did not have herpes

- Note: 25% of **clinically** discordant couples are **serologically** concordant

Langenberg AG, et al. *NEJM* 1999:341:1432-8
Corey L and Wald A. *Sexually Transmitted Diseases* 4th edition, Chapter 24

What about Recurrences of HSV-1 & 2?

- Recurrences are less severe than primary infection and of shorter duration
- Recurrences of HSV-2 tend to be more frequent and more severe than recurrences of HSV-1
  - 90% of symptomatic persons with primary **HSV-2** had a recurrence in subsequent 12 months; 38% had at least 6 recurrences; a longer duration of primary infection increases risk of recurrences
  - 57%of symptomatic persons with primary **HSV-1** had a recurrence in subsequent 12 months and <4% will have 4 or more recurrences

Benedetti JK, et al. *Ann Int Med* 1994;121:847-54
Engleberg R, et al. Sex Transm Dis 2003;30:174-7

How Frequently does Viral Shedding Occur?

- Shedding occurs even in the absence of symptoms
- The number of viral copies in subclinical shedding is similar to the number of viral copies with recurrent lesions
- Shedding tends to precede symptoms
- Shedding occurs on 30% of days during the first year following primary infection

Corey L and Wald A. *Sexually Transmitted Diseases* 4th edition, Chapter 24

How Well do Condoms Work to Prevent Transmission of HSV?

- **Per coital act**:
  - 3.6% increased odds of acquisition without condoms vs. 0.8% odds of acquisition with 100% condom use (i.e. 78% reduction in odds of acquisition per coital act when condoms are used)
    - Limited data on MSM
    - Small sample size

Stanaway JD, et al. *Sex Transm Dis*. 2012;39:388-393

- **Over time**:
  - Consistent condom users (used 100% of the time) had a 30% lower risk of HSV-2 acquisition compared with those who never used condoms

Martin ET, et al. *Arch Intern Med*. 2009;169(13):1233-40

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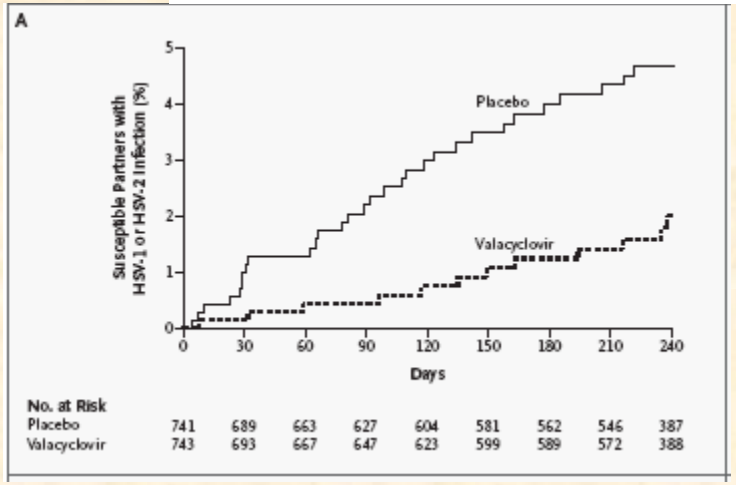
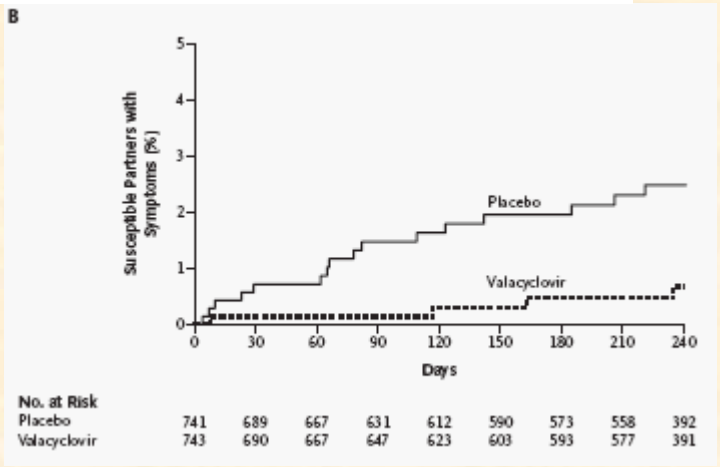
How well does the combination of antiviral suppression and condoms work for preventing transmission?

Table 2. Acquisition of HSV Infection among the Susceptible Partners, According to the Source Partner's Treatment Assignment.*

Variable	Valacyclovir (N=743)	Placebo (N=741)	Total No.	Hazard Ratio (95% CI)	P Value
	no. (%)				
Acquisition of symptomatic HSV-2 infection	4 (0.5)	16 (2.2)	20	0.25 (0.08–0.75)	0.008
Overall acquisition of HSV-2 infection	14 (1.9)	27 (3.6)	41	0.52 (0.27–0.99)	0.04
Acquisition of HSV-1 or HSV-2 infection	14 (1.9)	31 (4.2)	45	0.45 (0.24–0.84)	0.01





Consistent condom use and viral suppressive therapy decreased the risk of HSV acquisition by about 55%

Corey L et al. *NEJM* 2004;350(1):11-20

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How do we Diagnose HSV?

- **Symptomatic Patient**
  - Tzanck smear (only 40% sensitive)
  - Culture (sensitivity 30-70%)
  - Antigen detection (~70% sensitive)
  - PCR (FDA cleared, >90% sensitive)

REMEMBER:

- Antibodies may be negative in early primary infection
- The specificity of these tests is high but not perfect. As such, if the pre-test probability of having herpes is low, a positive test result has a high likelihood of being a false positive

- **Asymptomatic Patient**

  - Use Glycoprotein G-based type-specific assays (gG1 & gG2)

  - If gG2 is positive, pt has genital herpes

  - If gG1 is positive, patient either has oral herpes or genital herpes

  - Do **NOT** use crude antigen-based serological assays

  - **NEVER order or try to interpret IgM serologies**

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Who Should Have Serological Testing for HSV?

- Type-specific HSV serologic assays may be performed in the following patients:
  - Patients with recurrent genital symptoms, or atypical symptoms in whom HSV cultures have been negative
  - Patients who have been given a clinical diagnosis of genital herpes without laboratory confirmation
  - Patients who have a partner with genital herpes
  - Consider in persons presenting for an STD evaluation, persons HIV+, and MSM

MMWR Recomm Rep. 2010;59(RR-12):1-110

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What is the treatment for primary HSV infections?

- Acyclovir/ Valcyclovir / Famciclovir
  - All have ~the same efficacy; differences in price and convenience in dosing
  - Treat for 10-14 days
  - Extend course by 7 days if lesions not healed
  - Reduce duration of symptoms, viral shedding , and enhance lesion healing
  - Treatment does not impact probability of future recurrences

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MMWR Recomm Rep. 2010;59(RR-12):1-

HSV Treatment: First Clinical Episode

- All patients with first episodes of genital herpes should receive antiviral therapy

Recommended Regimens*
Acyclovir 400 mg orally three times a day for 7–10 days OR **Acyclovir** 200 mg orally five times a day for 7–10 days OR **Valacyclovir** 1 g orally twice a day for 7–10 days OR **Famciclovir** 250 mg orally three times a day for 7–10 days

*Treatment can be extended if healing is incomplete after 10 days of therapy.

What is the treatment for recurrent HSV infections?

- Acyclovir/ Valcyclovir/ Famciclovir
  - Suppressive therapy vs. episodic therapy (2-5 days)
    - Depends on the number of recurrences and patient preferences
  - In immunocompetent persons, no difference in emergence of drug resistance between suppressive therapy and episodic therapy
  - In immunocompromised persons, suppressive therapy may decrease the probability of emergence of resistance

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MMWR Recomm Rep. 2010;59(RR-12):1-

HSV Treatment: Suppressive Therapy

- Suppressive therapy reduces the frequency of recurrences by 70%–80%

Recommended Regimens
Acyclovir 400 mg orally twice a day OR **Valacyclovir** 500 mg orally once a day* OR **Valacyclovir** 1 g orally once a day OR **Famiciclovir** 250 mg orally twice a day
*Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).

Recommended Regimens for Daily Suppressive Therapy in Persons with HIV
Acyclovir 400–800 mg orally twice to three times a day OR **Valacyclovir** 500 mg orally twice a day OR **Famciclovir** 500 mg orally twice a day

HSV Therapy: Episodic Therapy

- Effective episodic treatment requires initiation of therapy within 1 day of lesion onset or during the prodrome

Recommended Regimens
Acyclovir 400 mg orally three times a day for 5 days
OR
Acyclovir 800 mg orally twice a day for 5 days
OR
Acyclovir 800 mg orally three times a day for 2 days
OR
Valacyclovir 500 mg orally twice a day for 3 days
OR
Valacyclovir 1 g orally once a day for 5 days
OR
Famciclovir 125 mg orally twice daily for 5 days
OR
Famciclovir 1 gram orally twice daily for 1 day
OR
Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days

Recommended Regimens for Episodic Infection in Persons with HIV
Acyclovir 400 mg orally three times a day for 5–10 days
OR
Valacyclovir 1 g orally twice a day for 5–10 days
OR
Famciclovir 500 mg orally twice a day for 5–10 days

Who is likely to develop acyclovir resistance?

- **Immunocompetent persons**: exceedingly rare instances of acyclovir-resistance with treatment failures
- **Immunocompromised persons**: 5% prevalence of resistance particularly in those who received multiple courses of acyclovir therapy
  - HIV risk factors for acyclovir resistance include low CD4 count and topical antiviral use

Corey L and Wald A. *Sexually Transmitted Diseases* 4th edition, Chapter 24

What are some options for treating acyclovir-resistant herpes?

- Famciclovir (oral)
  - If resistant HSV result from altered viral TK
  - Only 10% of resistant strains will respond
- Cidofovir (topical, IM, or IV)
  - Activated by cellular kinases not viral TK
  - Long half-life; IM or IV; associated with renal insufficiency
  - Topical formulation can be compounded but can still case renal insufficiency
- Foscarnet (IV)
  - Does not require activation by viral TK
  - Must be given IV; associated with renal insufficiency
- ****Imiquimod (Not FDA Cleared)** (topical)
  - Immune modulating effect (⇧IL-12; ⬇IL4/5)

Gilbert et al. *Arch Dermatology* 2001;137:1013
Perkins et al. *Sex Transm Infect* 2011;87:292

What about HSV in pregnancy?

- Risk of vertical transmission if mom acquires FIRST episode of herpes at time of delivery= 30-50%
- Risk of vertical transmission if mom has RECURRENT episode of herpes at time of delivery=1%
- A woman with a history of HSV-2 who does NOT have ACTIVE lesions at time of delivery can deliver vaginally. C-sections are recommended ONLY IF ACTIVE LESION PRESENT AT DELIVERY
- Risk of transmission of HSV1 to neonate > risk of transmission of HSV-2
- Limited data on safety of acyclovir in pregnancy but it is being used, especially in 3rd trimester. HOWEVER, routine use of acyclovir reduces probability of c-section but HAS NOT BEEN SHOWN TO REDUCE RISK OF NEONATAL HERPES

Gardella C et al. *Am J Obstet Gynecol* 2005;193:1891-99
Corey L, et al. *NEJM* 2009; 361:1376-85
Sheffield JS, et al. Obstet Gynecol 2003; 102:1396-1403

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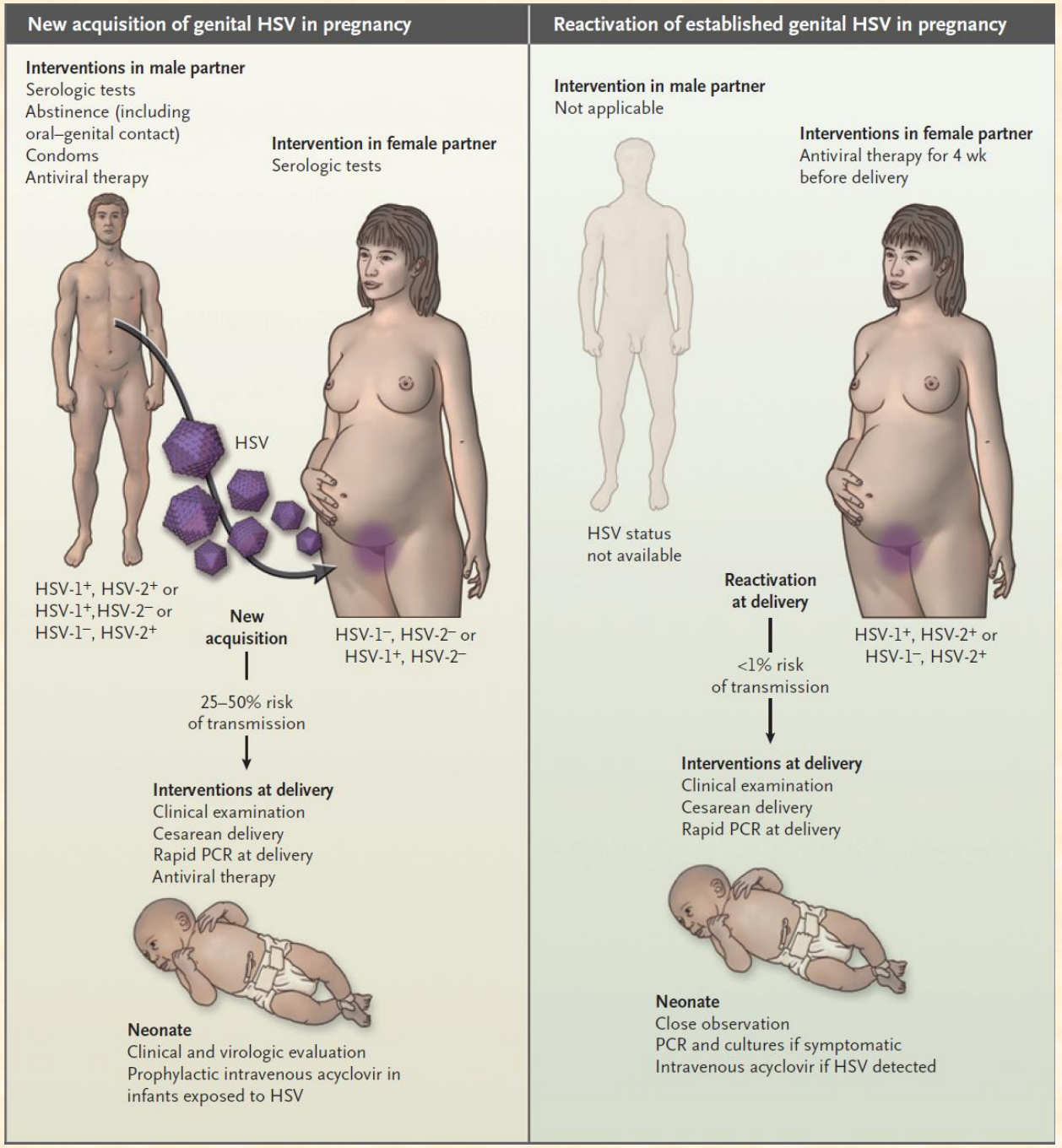

Corey L, et al. *NEJM* 2009; 361:1376-85

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Part II

HUMAN PAPILLOMA VIRUS (HPV)

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Human Papilloma Virus (HPV)

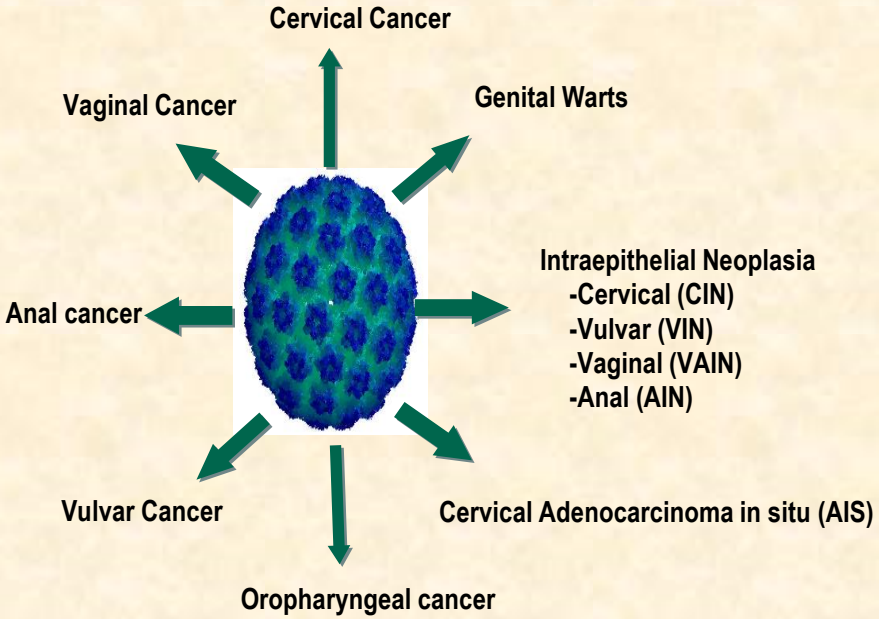
- Over 150 types identified: 40 infect the genital area
  - 15 oncogenic types
    - ❖ 99.7% of all cervical cancer cases
      - » 16 & 18 → 70% of cases
    - ❖ 70% of vaginal and vulvar cancers

Carcinogenic Risk	***Genotype***	***Pathology***
Low Risk	**6, 11**, 40, 42, 43, 44,54,61,70,72,81	Genital warts, low-grade cervical dysplasia
Intermediate Risk	26,53,*66*	
High Risk	***16, 18, 31, 33***, *35*, *39*, ***45***, *51*, ***52***, *56*, ***58***, *59*, *68*, 73, 82, 83	Low- and high-grade cervical dysplasia, squamous cell carcinoma, adenocarcinoma

Genotypes: found in vaccines; *genotypes*: detected with commercial tests

Division of Cancer Prevention and Control, National Center for Chronic Disease Prevention and Health Promotion. CDC.HPV Vaccination. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR vol 63 (5); August 29, 2014; Walboomers JM. J Pathol (1999);189(1):12

HPV Transmission and Diseases



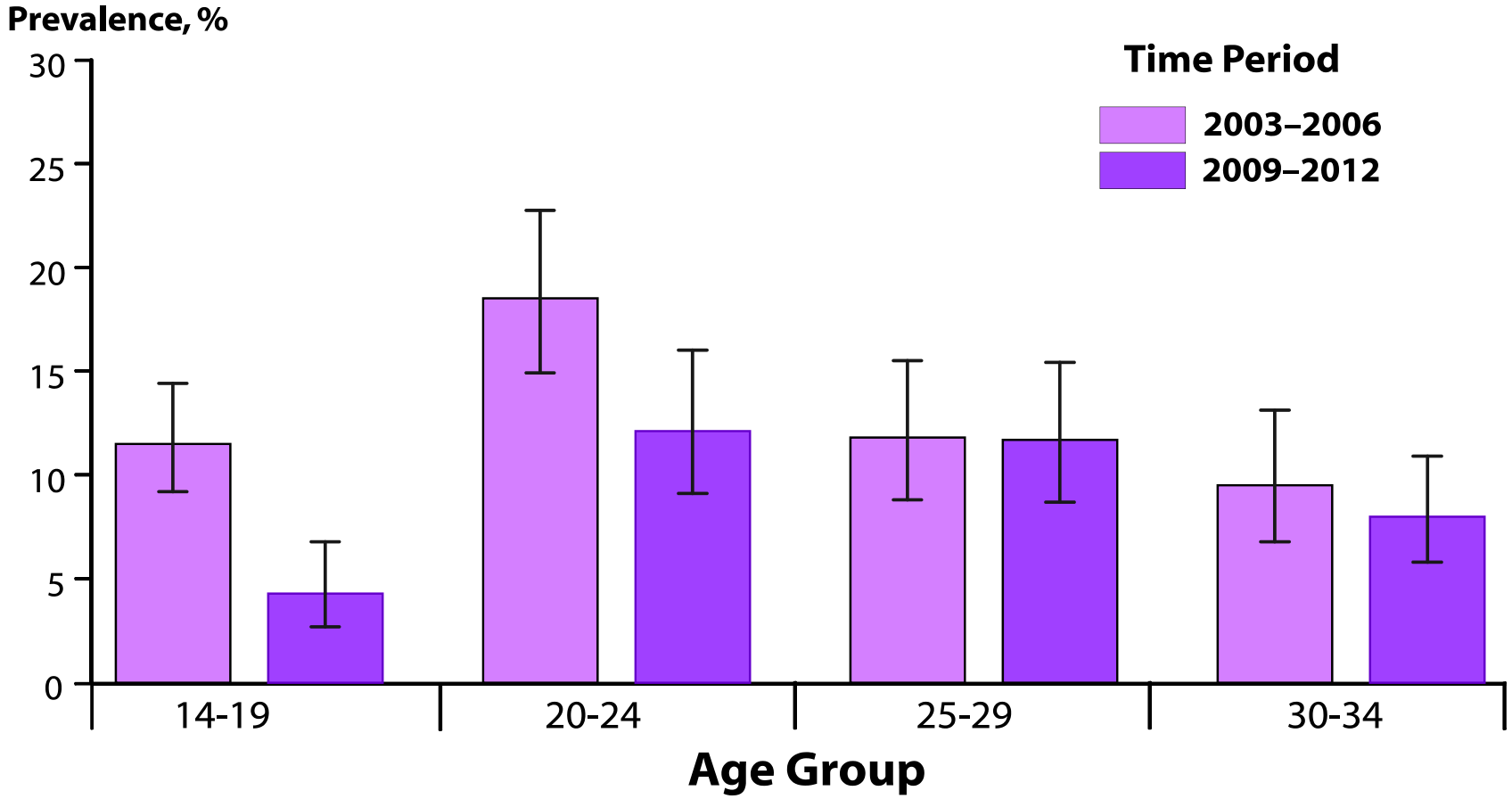
- Most common STI in the U.S.
  - 79 million prevalent cases
  - 14 million incident cases/year among 15 - 59 yr olds
  - Genital warts: incid up to 100/100,000; 1.4 mil affected at any one time
- Sexually transmitted
  - Condom use reduces the risk, but it is not fully protective

Most HPV infections are transient and asymptomatic

- 70% will clear in 1yr, 90% in 2yrs
- Risk of persistence varies by HPV type and host factors

CDC. HPV Vaccination. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR vol 63 (5); August 29, 2014

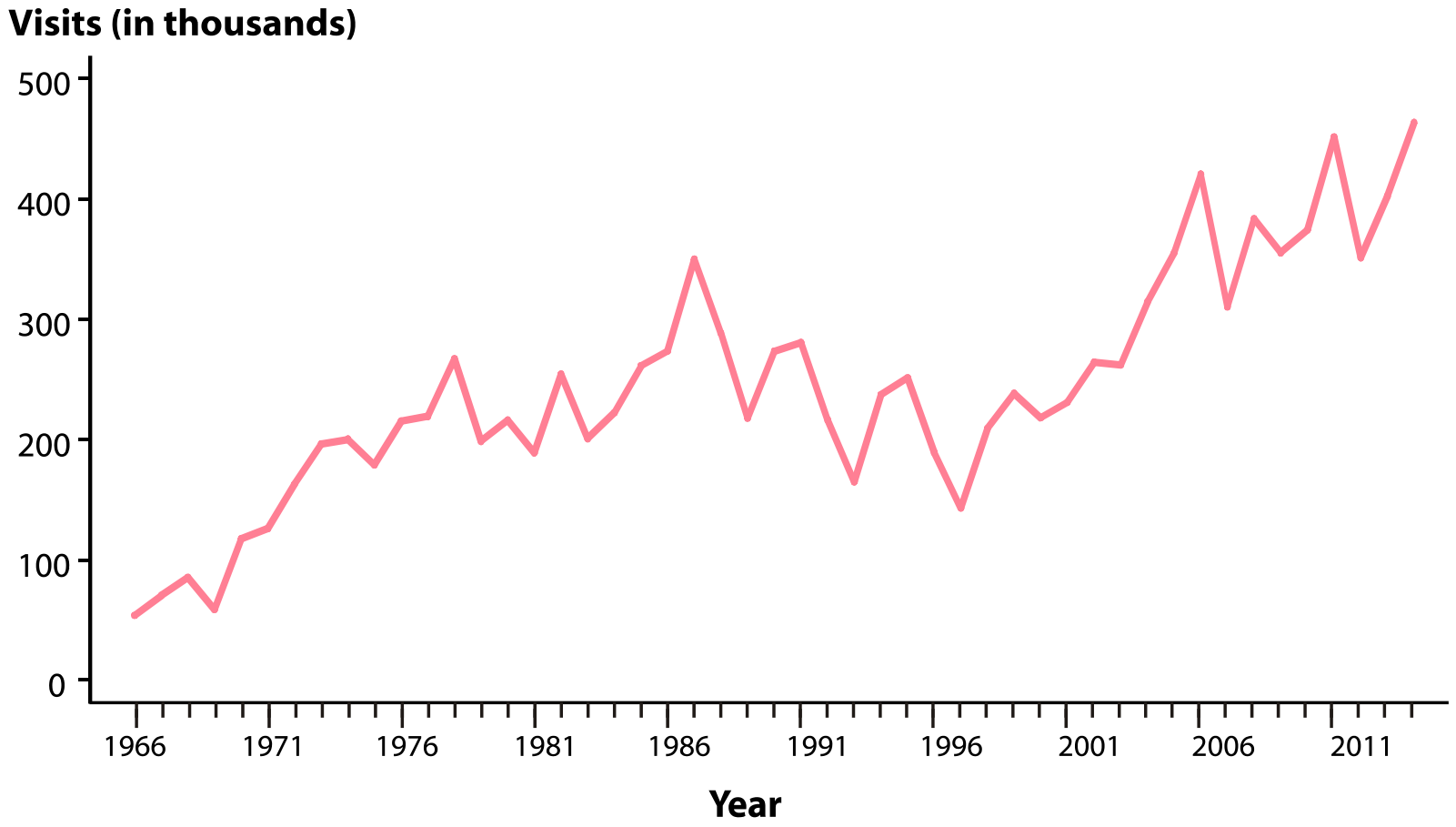
Human Papillomavirus — Cervicovaginal Prevalence of Types 6, 11, 16 and 18 Among Women Aged 14–34 Years by Age Group and Time Period, National Health and Nutrition Examination Survey, 2003–2006 and 2009–2012



NOTE: Error bars indicate 95% confidence interval.

SOURCE: Markowitz LE, Liu G, Hariri S, et al. Prevalence of HPV after introduction of the vaccination program in the United States. Pediatrics 2016;137(3):e20151968.

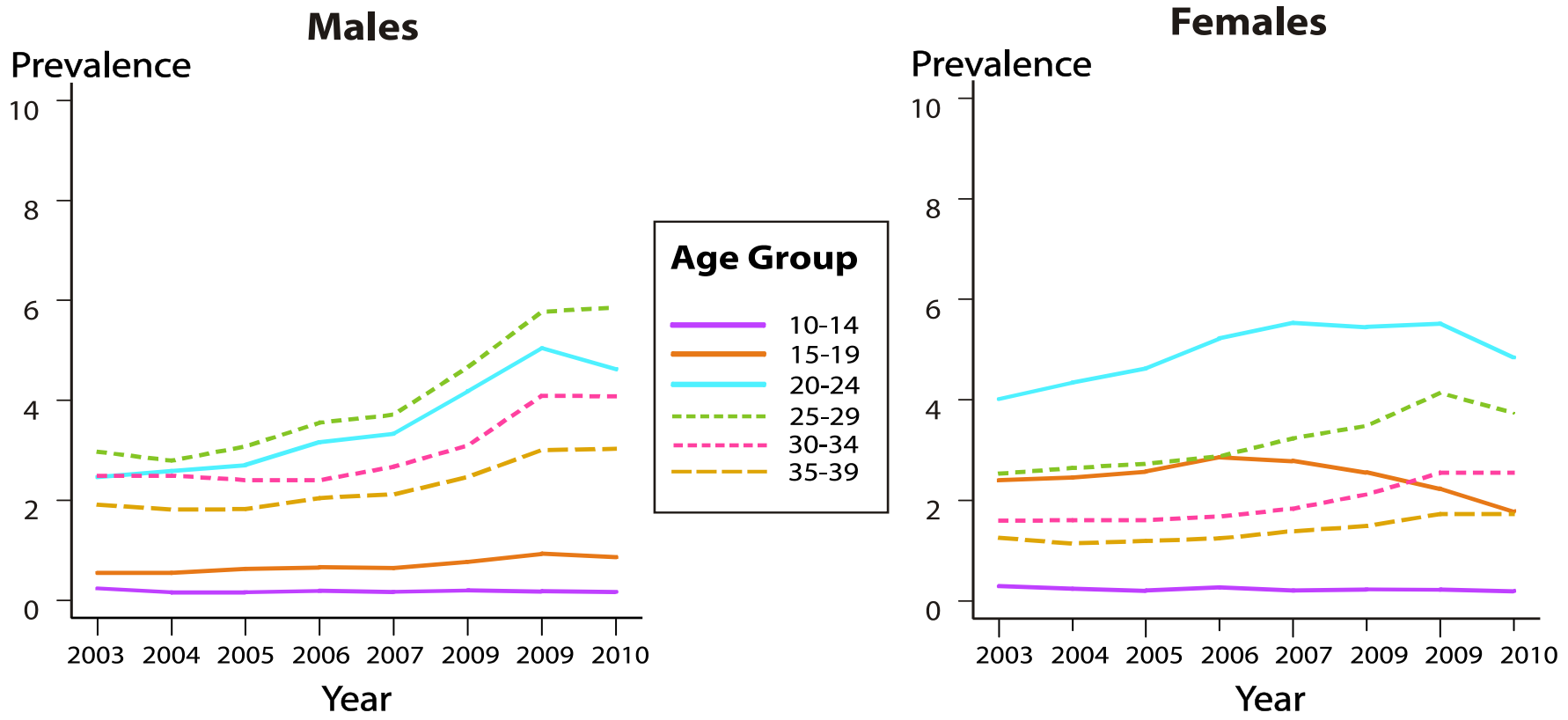
Genital Warts — Initial Visits to Physicians' Offices, United States, 1966–2014



NOTE: The relative standard errors for genital warts estimates of more than 100,000 range from 18% to 23%.

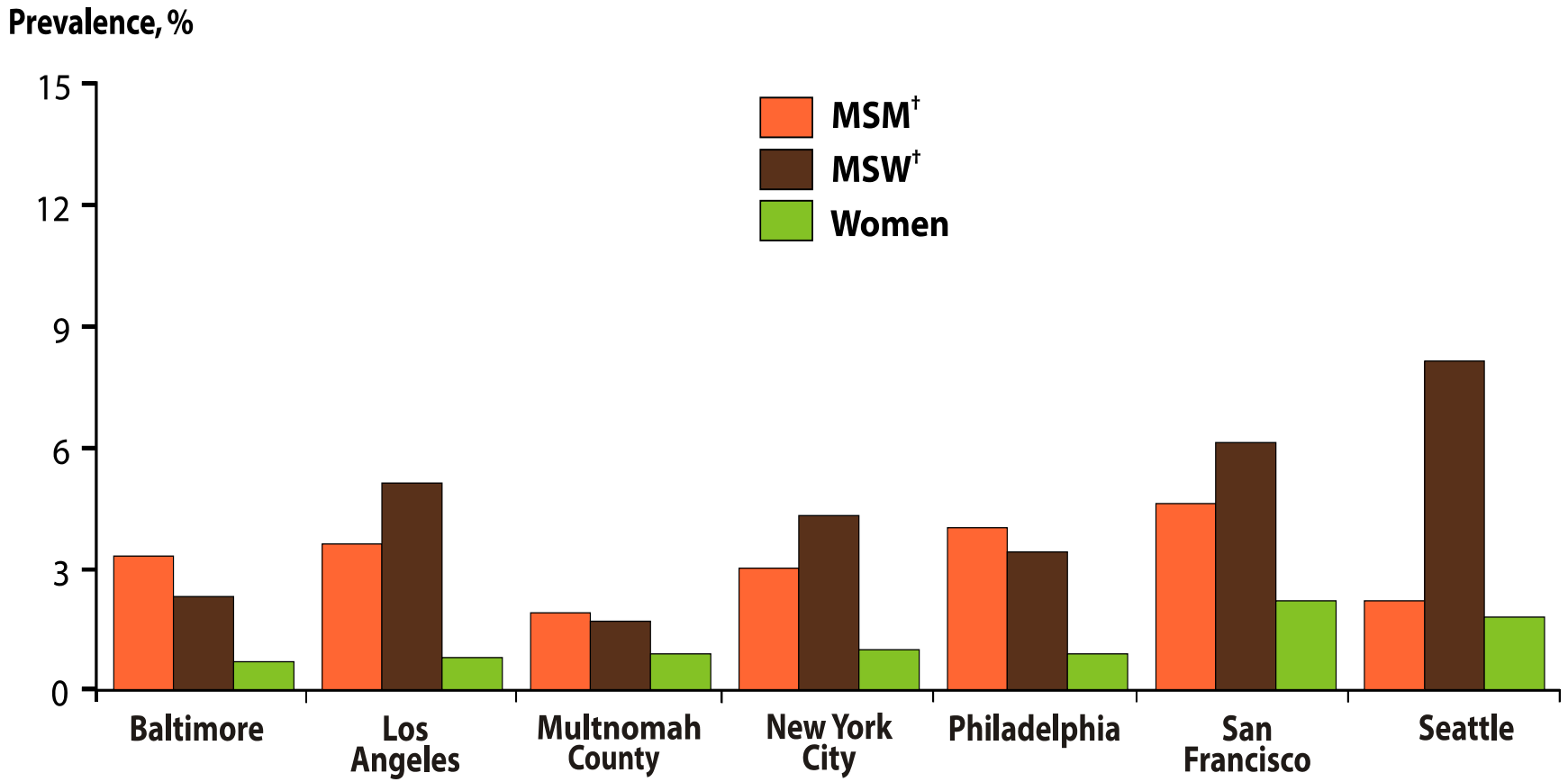
SOURCE: National Disease and Therapeutic Index, IMS Health, Integrated Promotional Services™. IMS Health Report, 1966–2014. The 2015 data were not obtained in time to include them in this report.

Genital Warts — Prevalence per 1000 Person-Years Among Participants in Private Health Plans Aged 10–39 Years by Sex, Age Group, and Year, 2003–2010



SOURCE: Flagg EW, Schwartz R, Weinstock H. Prevalence of anogenital warts among participants in private health plans in the United States, 2003–2010: potential impact of human papillomavirus vaccination. Am J Public Health 2013;103(8):1428–35.

Genital Warts — Prevalence Among STD Clinic Patients by Sex, Sex of Partners, and Jurisdiction*, STD Surveillance Network (SSuN), 2015



* Includes SSuN jurisdictions that contributed data for all of 2015.

† MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.

HPV-associated cancers United States, 2004-2008

Anatomic Area	Average annual number of cases*	Estimated+ HPV attributable	Estimated+ HPV 16/18 attributable
Cervix	11,967	11,500	9,100
Vagina	729	500	400
Vulva	3,136	1,600	1,400
Anus (F)	3,089	2,900	2,700
Oropharynx (F)	2,370	1,500	1,400
Total (Females)	**21,291**	**18,000**	**15,000**
Penis	1,046	400	300
Anus (M)	1,678	1,600	1,500
Oropharynx (M)	9,356	5,900	5,600
Total (Males)	**12,080**	**7,900**	**7,400**

* Defined by histology and anatomic site; Watson M et al. Cancer 2008. Data source: National Program of Cancer Registries and SEER, covering 100% coverage of US population. + Gillison ML, et al. Cancer 2008 . Ref: Human Papillomavirus-Associated Cancers MMWR 2012;61(15):258-261.

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Genital Warts-Appearance

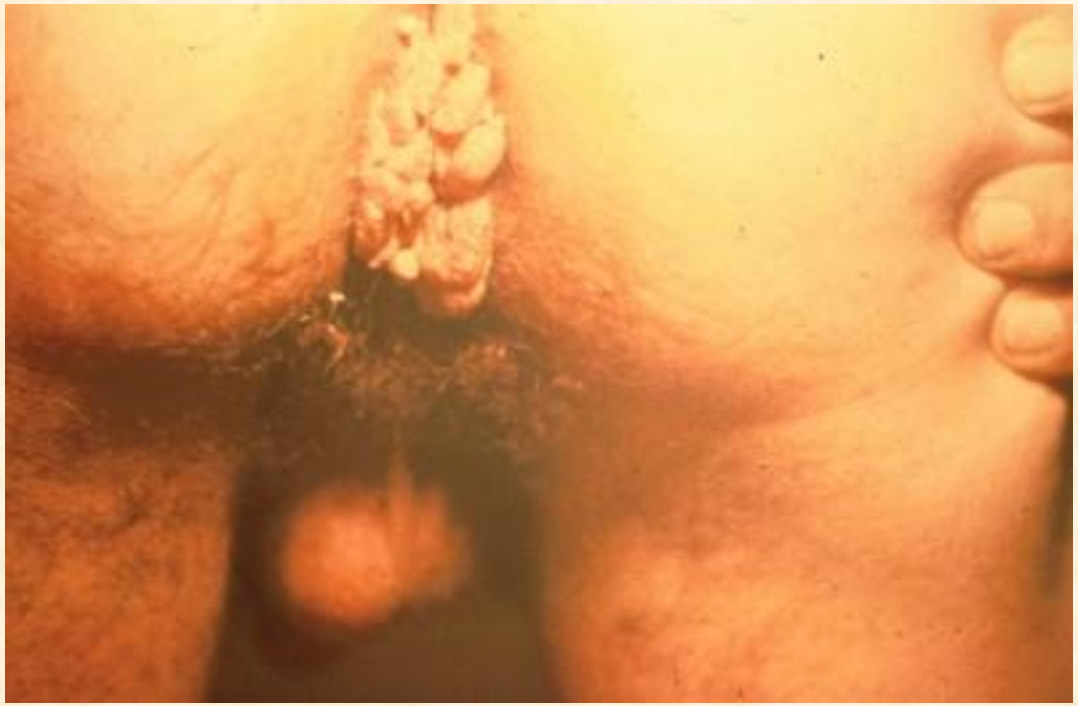
- Condylomata acuminata
  - Cauliflower-like appearance
  - Skin-colored, pink, or hyperpigmented
  - May be keratotic on skin; generally nonkeratinized on mucosal surfaces
- Smooth papules
  - Usually dome-shaped and skin-colored
- Flat papules
  - Macular to slightly raised
  - Flesh-colored, with smooth surface
  - More commonly found on internal structures (i.e., cervix), but also occur on external genitalia
- Keratotic warts
  - Thick horny layer that can resemble common warts or seborrheic keratosis

Genital Warts-Location

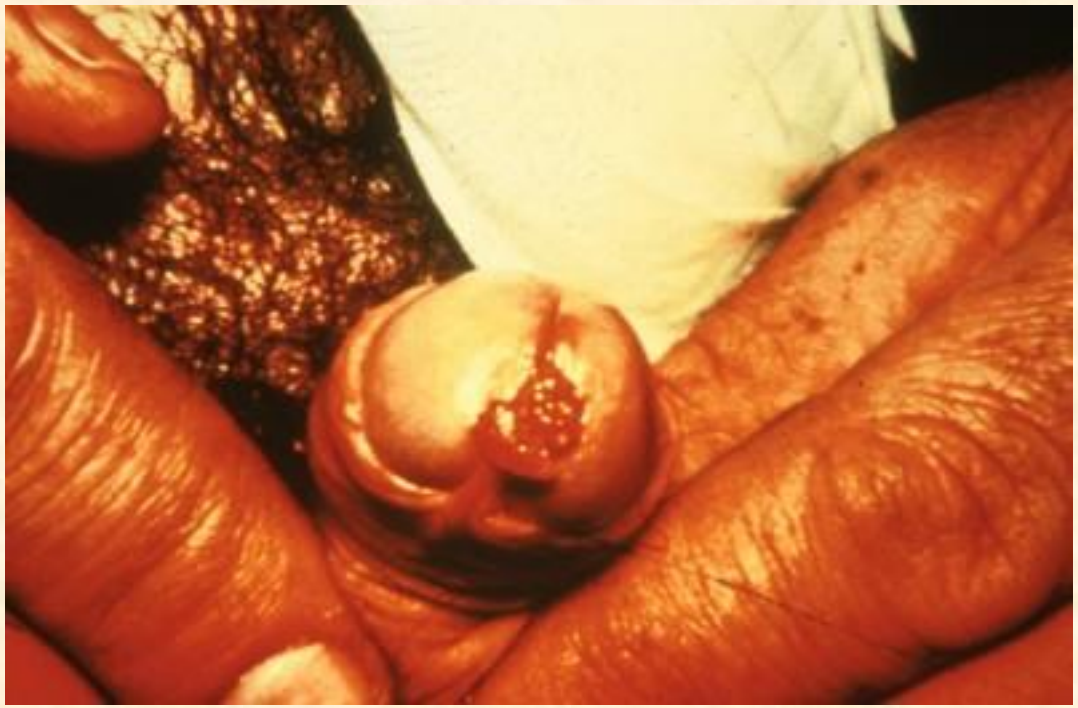
- Most commonly occur in areas of coital friction
- Perianal warts do not necessarily imply anal intercourse.
  - May be secondary to autoinoculation, sexual activity other than intercourse, or spread from nearby genital wart site
- Intra-anal warts are seen predominantly in patients who have had receptive anal intercourse.
- HPV types causing genital warts can occasionally cause lesions on oral, upper respiratory, upper GI, and ocular locations.
- Patients with visible warts are frequently simultaneously infected with multiple HPV types.

Condyloma acuminata, penile

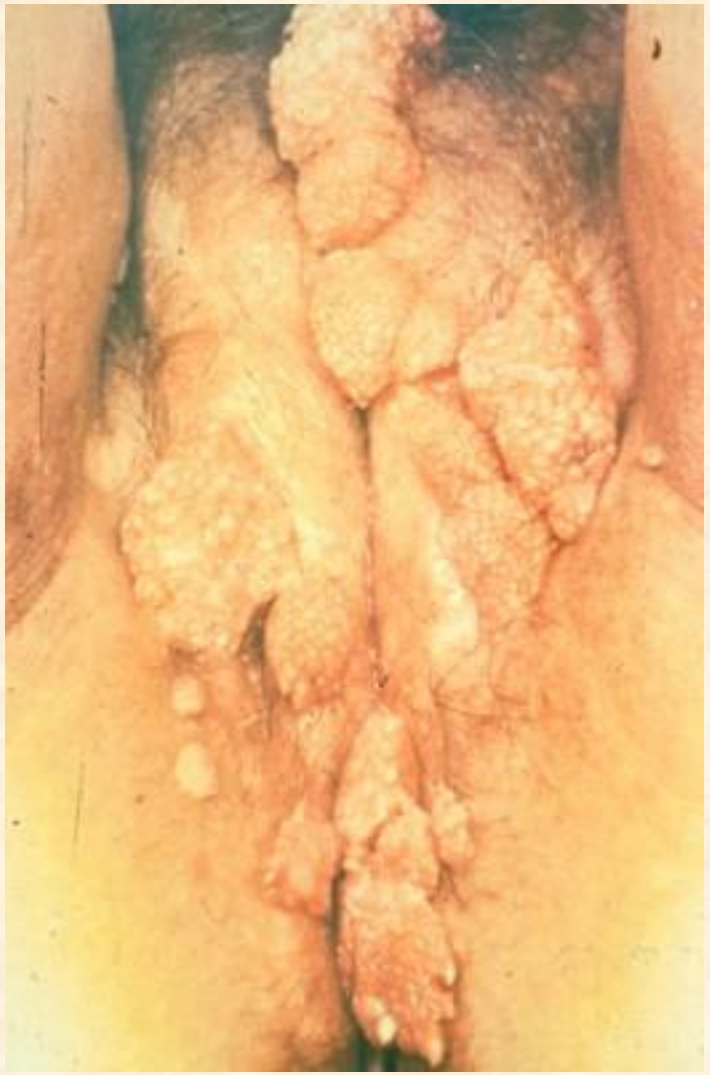
Condyloma acuminata, anal



Condyloma acuminata, meatal



Condyloma acuminata, vulva



Genital Warts-Symptoms

- Genital warts usually cause no symptoms. Symptoms that can occur include:
  - Vulvar warts-dyspareunia, pruritis, burning discomfort;
  - Penile warts-occasional itching;
  - Urethral meatal warts-hematuria or impairment of urinary stream;
  - Vaginal warts-discharge/bleeding, obstruction of birth canal (secondary to increased wart growth during pregnancy); and
  - Perianal and intra-anal warts-pain, bleeding on defecation, itching

- Most patients have fewer than ten genital warts, with total wart area of 0.5–1.0 cm^2.

Genital Warts-Duration and Transmission

- May regress spontaneously, or persist with or without proliferation.
  - Frequency of spontaneous regression is unclear, but estimated at 10–30% within three months.
  - Persistence of infection occurs, but frequency and duration are unknown.
  - Recurrences after treatment are common.

Diagnosis of Genital Warts

- Diagnosis is usually made by visual inspection with bright light.
- Consider biopsy when
  - Diagnosis is uncertain;
  - Patient is immunocompromised;
  - Warts are pigmented, indurated, or fixed;
  - Lesions do not respond or worsen with standard treatment; or
  - There is persistent ulceration or bleeding.

Differential Diagnosis of Genital Warts

- Other infections
  - Condylomata lata
    - Tend to be smoother, moist, more rounded, and darkfield-positive for *Treponema pallidum*
  - Molluscum contagiosum
    - Papules with central dimple, caused by a pox virus; rarely involves mucosal surfaces
- Acquired dermatologic conditions
  - Seborrheic keratosis
  - Lichen planus
  - Fibroepithelial polyp, adenoma
  - Melanocytic nevus
  - Neoplastic lesions

Differential Diagnosis of Genital Warts- continued

- Normal anatomic variants
  - "Pink pearly penile papules"
  - Vestibular papillae (micropapillomatosis labialis)
  - Skin tags (acrochordons)

- External genital squamous intraepithelial lesions (SIL)
  - Squamous cell carcinoma *in situ*
  - Bowenoid papulosis
  - Erythroplasia of Queyrat
  - Bowen's disease of the genitalia

Treatment Regimens

- Factors influencing treatment selection include
  - Wart size,
  - Number of warts,
  - Anatomic site of wart,
  - Wart morphology,
  - Patient preference,
  - Cost of treatment,
  - Convenience, and
  - Adverse effects.

Treatment Response

- Affected by
  - Number, size, duration, and location of warts, and immune status
  - In general, warts located on moist surfaces and in intertriginous areas respond better to topical treatment than do warts on drier surfaces.
- Many patients require a course of therapy over several weeks or months rather than a single treatment.
  - Evaluate the risk-benefit ratio of treatment throughout the course of therapy to avoid over-treatment.
- There is no evidence that any specific treatment is superior to any of the others.
  - The use of locally developed and monitored treatment algorithms has been associated with improved clinical outcomes

CDC-Recommended Regimens For External Genital Warts (Patient-Applied)

- Podofilox 0.5% solution or gel*
  - Apply solution with cotton swab or gel with a finger to visible warts twice a day for 3 days, followed by 4 days of no therapy.
  - Cycle may be repeated as needed up to 4 cycles

or

- Imiquimod 3.75% or 5% cream*
  - Apply cream once daily at bedtime, 3 times a week for up to 16 weeks.
  - Treatment area should be washed with soap and water 6–10 hours after application

or

- Sinecatechins 15% ointment*,**
  - Apply ointment 3 times daily for up to 16 weeks.
  - ***Do not wash off*** post-application

**Safety not established in pregnancy*

***Safety not established in HIV- or HSV-co-infected individuals*

CDC-Recommended Regimens For External Genital Warts (Provider-Administered)

- Cryotherapy with liquid nitrogen or cryoprobe
  - Repeat applications every 1–2 weeks, or
- Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90%
  - Apply small amount only to warts and allow to dry
  - Treatment may be repeated weekly if needed, or
- Surgical removal - tangential scissor excision, tangential shave excision, curettage, or electrosurgery

**Safety not established in pregnancy*

Recurrence After Treatment

- As many as two-thirds of patients will experience recurrences of warts within 6–12 weeks of therapy; after 6 months most patients have clearance.
  - If persistent after 3 months, or if there is poor response to treatment, consider biopsy to exclude a premalignant or neoplastic condition, especially in an immunocompromised person.
- Treatment modality should be changed if patient has not improved substantially after 3 provider-administered treatments or if warts do not completely clear after 6 treatments

Genital Warts in HIV-Infected Patients

- No data that treatment should be different
- Larger, more numerous warts
- Might not respond as well to therapy
- More frequent recurrence of lesions after treatment
- Squamous cell carcinomas arising in or resembling genital warts might occur more frequently among immunosuppressed persons, therefore, requiring biopsy for confirmation of diagnosis for suspicious cases, and referral to a specialist.

Transmission Issues

- Usually sexually transmitted
- Infection is often shared between partners
- Determining source of infection is usually difficult (incubation period variable)
- Recurrences usually are not reinfection
- Transmission risk to current and future partners after treatment is unclear.
- Likelihood of transmission and duration of infectivity with or without treatment are unknown.
- Value of disclosing a past diagnosis of genital HPV infection to future partners is unclear, although candid discussions about past STD should be encouraged.

HPV DNA Testing

- HPV DNA tests
  - FDA-approved:
    - To triage women with ASC-US Pap test results, and
    - As an adjunct to Pap test screening for cervical cancer in women 30 years or older.
    - Use of type-specific HPV DNA tests for routine diagnosis and management of genital warts is not recommended

- HPV DNA tests should not be used
  - In men,
  - In adolescents <21 years,
  - To screen partners of women with Pap test abnormalities,
  - To determine who will receive HPV vaccine, or
  - STD screening for HPV.

Pap and HPV Testing Guidelines, 2015

	HIV (-)	HIV (+)
Age at initiation	21yrs	Within 1 year of coitarche or at time of HIV diagnosis if ≥21yrs
Frequency Age 21-29 Age ≥ 30	 Every 3yrs Every 3yrs OR every 5yrs if Pap & hrHPV(-)	 Every yr; 3 consecutive nl Pap→ 3yrs Every 3yrs if cytology & hrHPV(-)
hrHPV	Primary hrHPV screening (≥ 26yrs) Co-testing w/ pap (≥ 30yrs) Triage ASCUS result	No primary hrHPV screening Co-testing w/ Pap (≥ 30yrs) Triage ASCUS result
Age at discontinuation	65yrs	No age cut-off
Prior hysterectomy	No screening, unless prior dysplasia ≥ CIN 2 or cancer w/i past 20 yrs	No screening, unless prior dysplasia ≥ CIN 2 or cancer
Prior HPV vaccination	Same as unvaccinated women	

https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/343/hpv

Table 1. Use and Efficacy of the Bivalent, Quadrivalent, and 9-valent Human Papillomavirus Vaccines

Vaccine	HPV Types	Disease Reduction	Efficacy*
Bivalent	16 and 18	HPV genotypes 16- and 18-related cervical cancer, CIN 1, CIN 2/3, and adenocarcinoma in situ	HPV disease related to genotypes 16 and 18; 98.1%[†,‡]
Quadrivalent	6, 11, 16, and 18	HPV genotypes 6, 11, 16, and 18-related cervical, vulvar, and vaginal cancer; CIN 1; CIN 2/3; adenocarcinoma in situ; VIN 2/3; and vaginal intraepithelial neoplasia 2/3 in females Penile intraepithelial neoplasia 1/2/3 and penile cancer in males Warts, anal intraepithelial neoplasia, and anal cancer in males and females	HPV disease related to genotypes 6, 11, 16, and 18; up to 100%[§,‖] External genital disease in men; 90.4%[‖]
9-valent	6, 11, 16, 18, 31, 33, 45, 52, and 58	HPV genotypes 6, 11, 16, 18, 31, 33, 45, 52, and 58-related cervical, vulvar, and vaginal cancer; CIN 2/3; adenocarcinoma in situ; VIN 2/3; and vaginal intraepithelial neoplasia 2/3 in females Penile intraepithelial neoplasia 1/2/3 and penile cancer in males[¶] Warts, anal intraepithelial neoplasia, and anal cancer in males and females	HPV disease related to genotypes 6, 11, 16, 18; greater than 99% HPV related to genotypes 31, 33, 45, 52, and 58; 96.7%[¶]

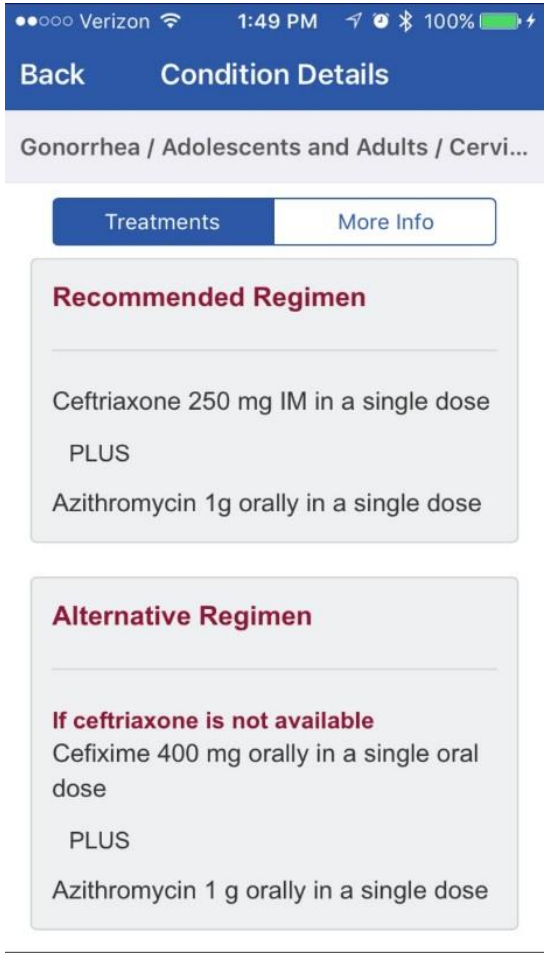
HPV Vaccine Indications

- Indicated for the prevention of cervical, vaginal, and vulvar cancers; precancerous or dysplastic lesions; and genital warts (Gardasil)
- Vaccinate all women and men age 9-26 regardless of sexual activity, history of cervical dysplasia, or genital warts
  - Rationale: some cross-reactivity or patient might not have been exposed to vaccine types
- U.S. ACIP guidelines: 3 doses (0, 2, 6 months)
  - If 1st dose <15 yr, only 2 doses need (0,6-12 mo)
- Immunocompromised persons
  - Vaccines are well tolerated and immunogenic in HIV(+) women
  - Unclear if there are vaccine differences in effectiveness
  - Vaccination is recommended
- Testing for HPV DNA is not recommended before vaccination. Vaccination is recommended even if the patient is tested for HPV DNA and the results are positive.
- Women who have received HPV vaccine should continue routine cervical cancer screening

Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR vol 63 (5); August 29, 2014

STD Treatment Guidelines Apps

STD Tx Guidelines



Available on iTunes & Google Play

STD Clinical Toolbox

Available on iTunes

STD Treatment Guidelines wall charts, pocket guides, and the full MMWR article at:

www.cdc.gov/std/tg2015

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