# Provincial Prevalence Rates 2009

(15-49) years

| | |
|---|---|
| KwaZulu-Natal | 25.0 % |
| Mpumalanga | 21.8% |
| Free State | 19.5% |
| North West | 19.2% |
| Eastern Cape | 18.5% |
| Gauteng | 16.6% |
| Limpopo | 13.8% |
| Northern Cape | 9.3% |
| Western Cape | 6.2% |

17.8% National

# Provincial Prevalence Rates 2010

(15-49) years

| | |
|---|---|
| KwaZulu-Natal | 24.9 % |
| Mpumalanga | 21.7% |
| Free State | 19.7% |
| North West | 19.1% |
| Eastern Cape | 18.5% |
| Gauteng | 16.9% |
| Limpopo | 14% |
| Northern Cape | 8.9% |
| Western Cape | 6.2% |

17.9% National

# Provincial Prevalence Rates 2009 &2010

(15-49) years

| | 2009 | 2010 |
|---|---|---|
| KwaZulu-Natal | 25.0 % | 24.9 % - |
| Mpumalanga | 21.8% | 21.7% - |
| Free State | 19.5% | 19.7% + |
| North West | 19.2% | 19.1% - |
| Eastern Cape | 18.5%<br>17.8% National | 18.5%<br>17.9% National + |
| Gauteng | 16.6% | 16.9% + |
| Limpopo | 13.8% | 14% + |
| Northern Cape | 9.3% | 8.9% - |
| Western Cape | 6.2% | 6.2% |

# Cervical Cancer Prevention

**Cops and Rubbers**
**Bangkok, Thailand**

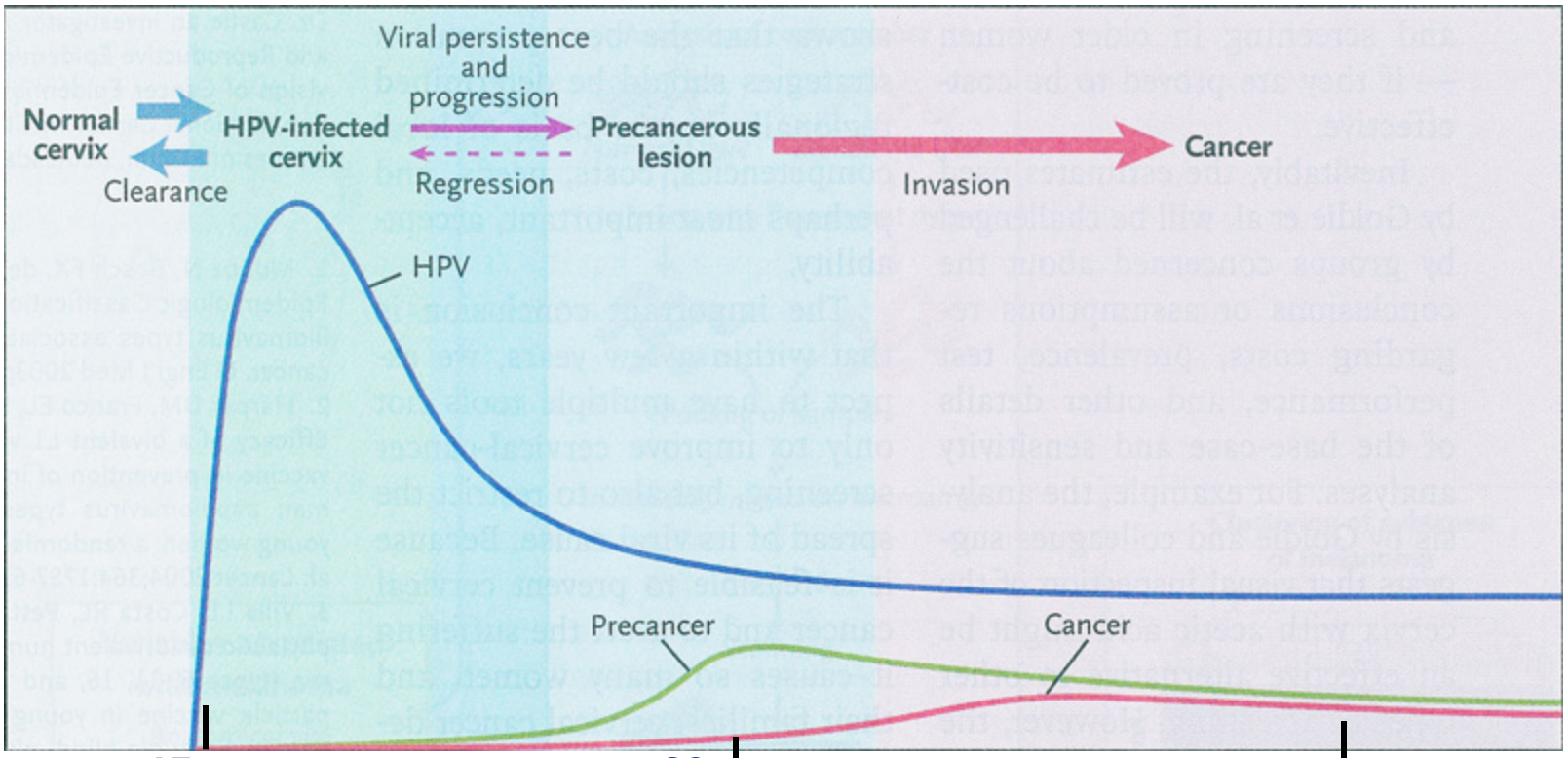
**Primary prevention**

- **Vaccines**
- ***(****Education to reduce high-risk sexual behavior)*
- *(Promotion of condoms)*

**Secondary prevention**

- Identify and treat precancerous lesions before they progress to cervical cancer
- Identify and treat early cancer while the chance of cure is still good (prevents cervical cancer death)

# Continuum of Care for Cervical Cancer Control




**Vaccination**

**Screening and treatment**

**Cancer treatment**

**Source: WHO 2006**

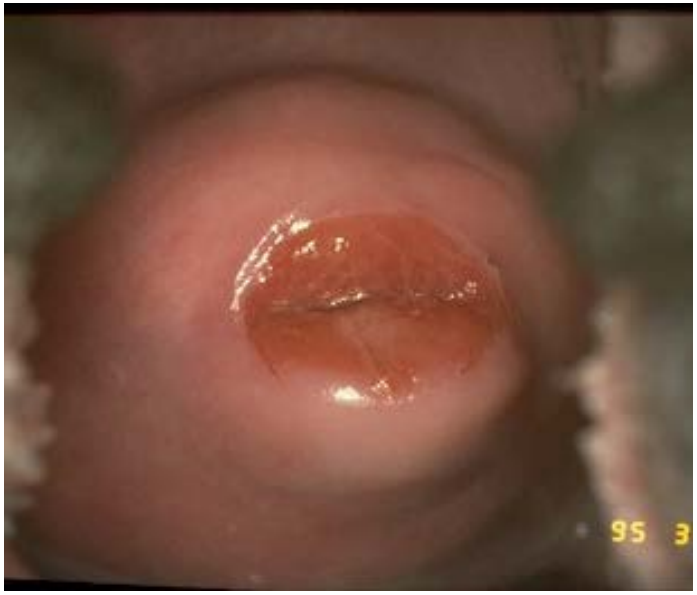
# Detecting Precancer Lesions

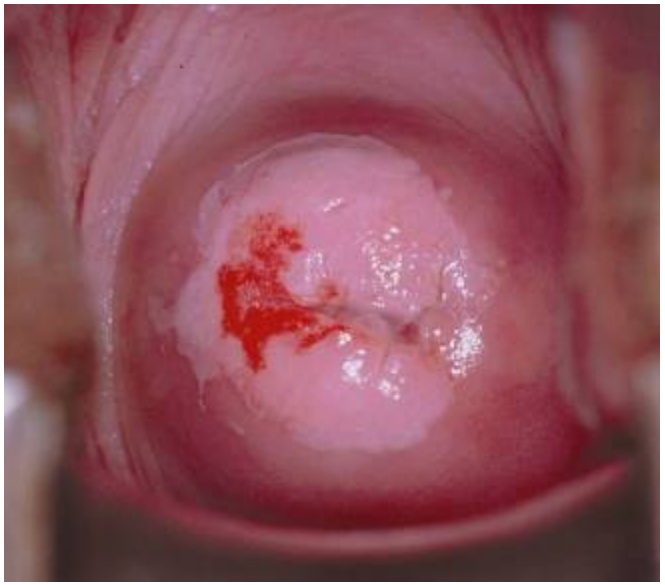
| Characteristics | Conventional cytology | HPV DNA tests | Visual inspection tests | |
|---|---|---|---|---|
| | | | VIA | VILI |
| Sensitivity | 47-62% | 66-100% | 67-79% | 78-98% |
| Specificity for high-grade lesions and invasive cancer | 60-95% | 62-96% | 49-86% | 73-91% |
| Comments | Assessed over the last 50 years in a wide range of settings in developed and developing countries | Assessed over the last decade in many settings in developed and relatively few in developing countries | Assessed over the last decade in many settings in developing countries | Assessed by IARC over the last four years in India and 3 countries in Africa. Need further evaluation for reproducibility |
| Number of visits required for screening and treatment | 2 or more visits | 2 or more visits | Can be used in single-visit or 'see and treat' approach where outpatient treatment is available | |

Source: Sankaranarayan et al. Int J Obstet Gynaecol, 2005.

# What is VIA?

Naked eye inspection of cervix to detect white lesions after applying dilute (3-5%) acetic acid.





# Cervical Cancer Prevention Programs

- THAILAND
- PHILIPPINES
- INDONESIA

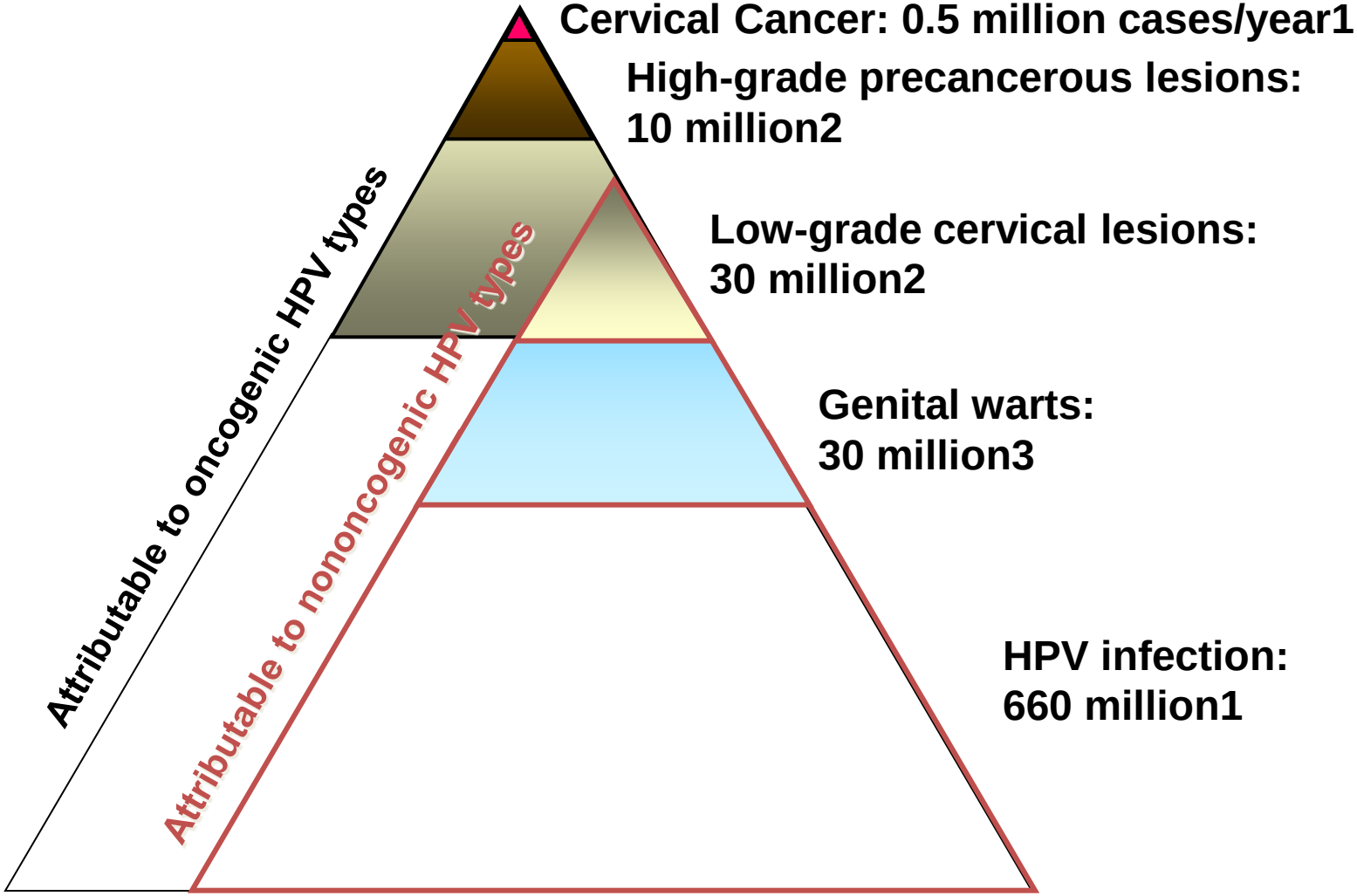
- GHANA
- MALAWI
- NORTHWEST PROVINCE/SOUTH AFRICA

# Potential Integration Models

- VIA and Cryotherapy
- FP services
- Antenatal Care Clinic
- Postpartum/Well Baby Clinic
- Health Center Screening Services
  - Referral from VCT
- **HAART Service**
  - **On site**
  - **Referral**

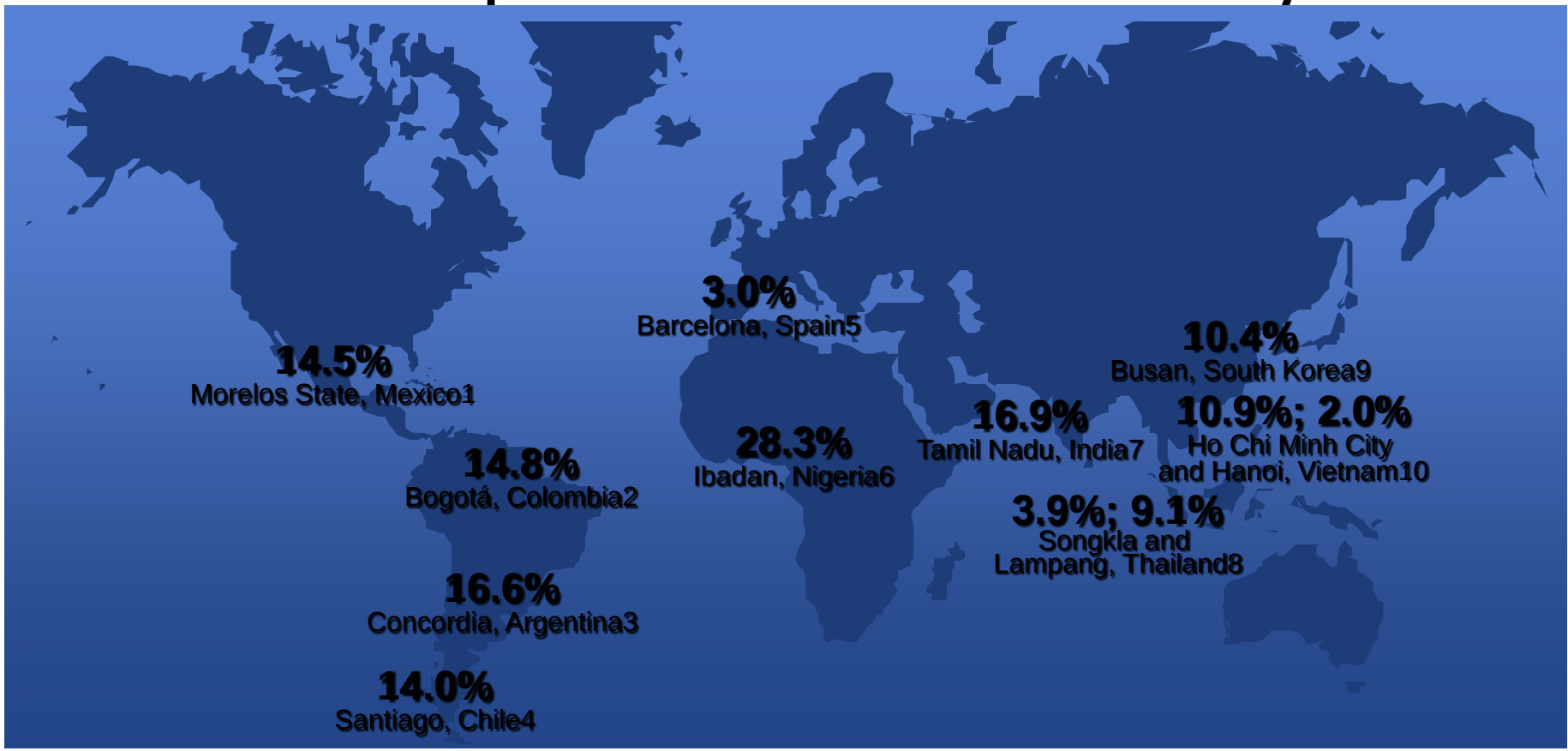

**VCT and VIA Clinics, Chilomoni HC Malawi**

# Estimated World Burden of HPV-Related Diagnoses Focus on Cervical Disease and Genital Warts

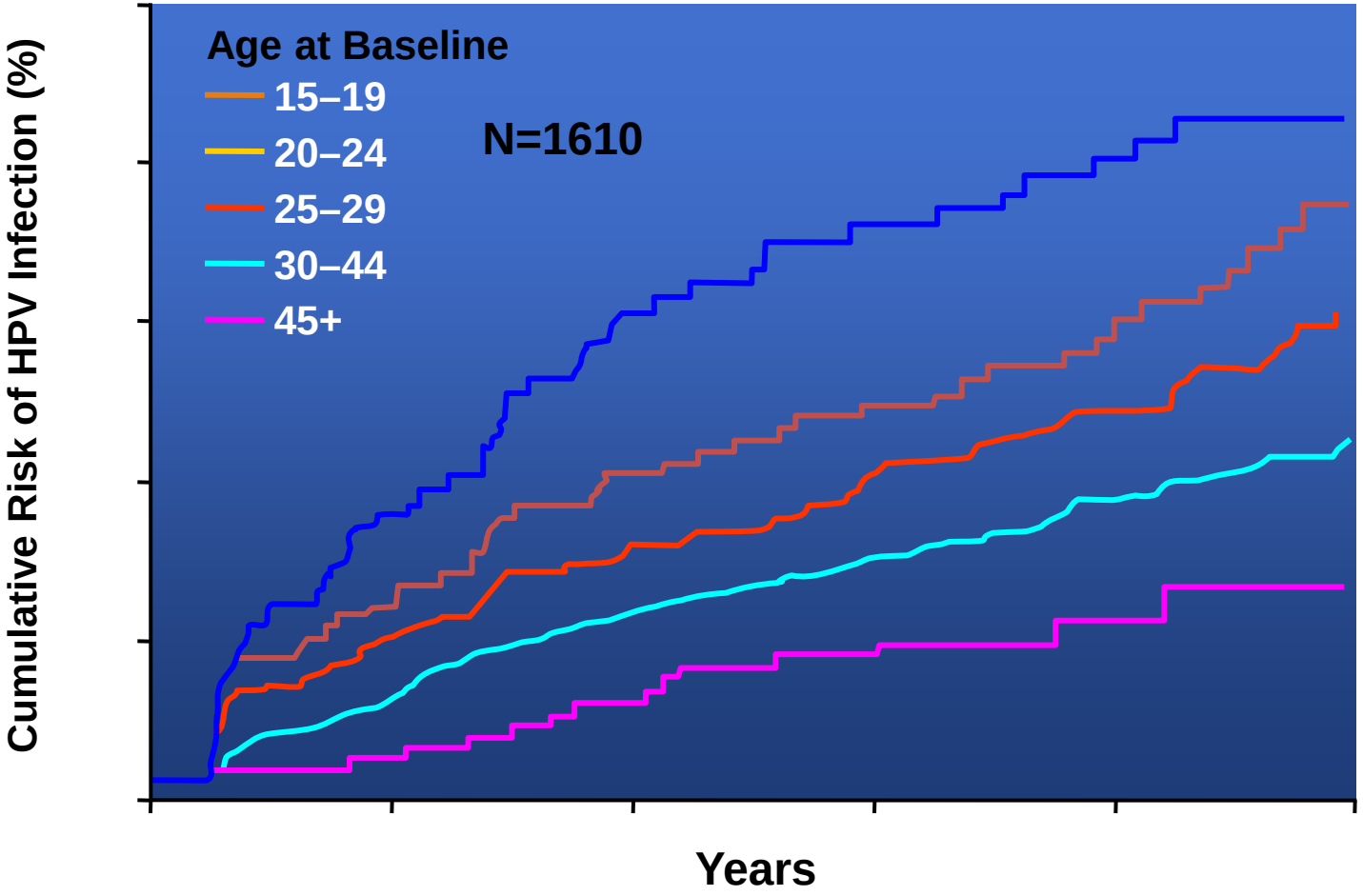



1. World Health Organization, Geneva, Switzerland: World Health Organization; 2005:1–38. 2. World Health Organization. Geneva, Switzerland: World Health Organization; 1999:1–22. 3. World Health Organization. WHO Office of Information. *WHO Features*. 1990;152:1–6.

# Global HPV Prevalence in Females: IARC* Population-Based Surveys



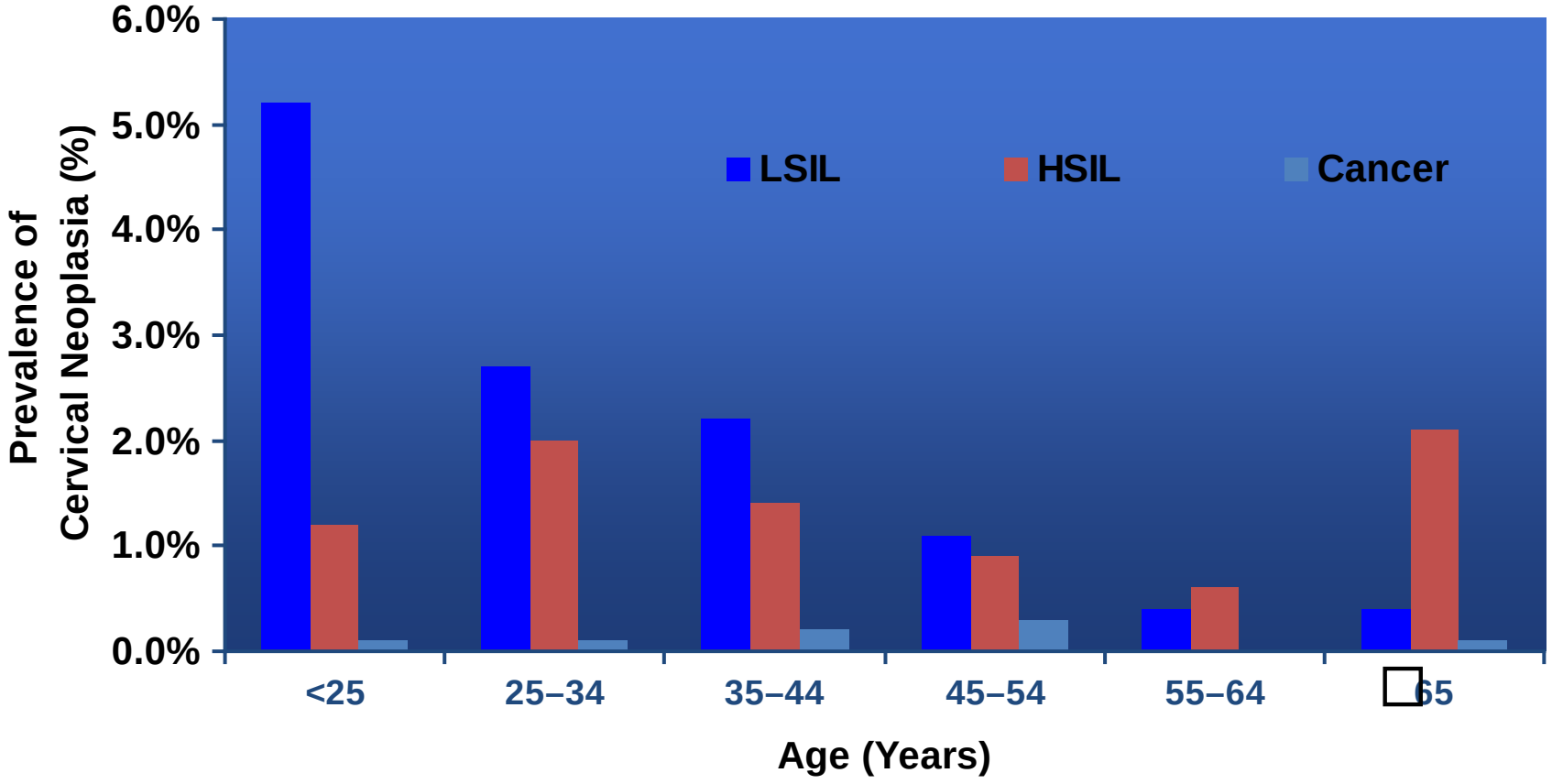
# Cumulative Risk of Any HPV Infection by Age in Women*,[1]




*In a cohort of Colombian women

1. Adapted from Muñoz N, Méndez F, Posso H, et al. *J Infect Dis*. 2004;190:2077–2087. Reprinted with permission from The University of Chicago Press. Copyright © 2004 by the Infectious Diseases Society of America. All rights reserved.

# Prevalence of Cervical SIL and Cancer by Age*,[1]

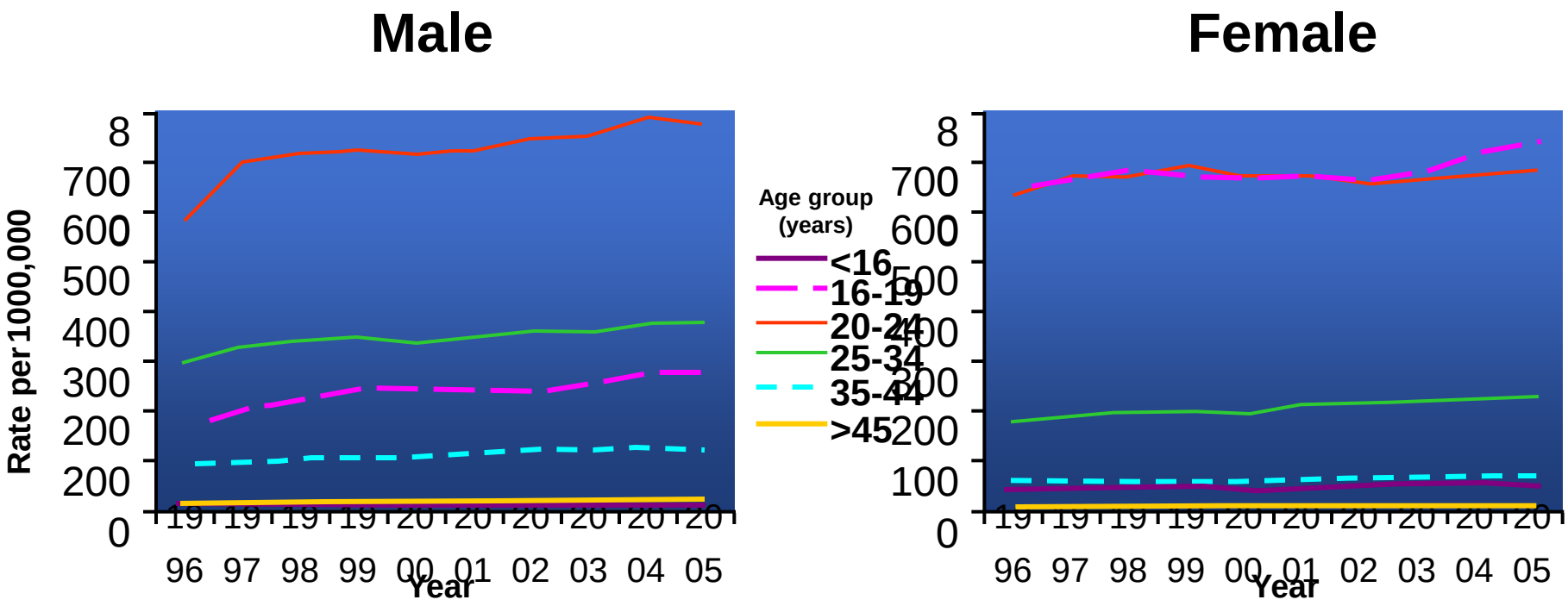



*Study conducted in rural Costa Rica (N=9175)

1. Herrero R, Hildesheim A, Bratti C, et al. Population-based study of human papillomavirus infection and cervical neoplasia in rural Costa Rica. *J Natl Cancer Inst*. 2000;92:464–474.

Adapted with permission from Oxford University Press.

# Genital Warts: A Disease of Young People[1]




*Diagnoses made in GUM clinics.

1. Adapted from *CDR Weekly Online.* 2006;16(48):1–4. Available at http://www.hpa.org.uk/cdr/archives/2006/cdr4806.pdf. Accessed March 29, 2007.

# Prevalence of HPV Infection in Young Men

| Study Author, Year | N | Age Range (Years) | HPV Prevalence (%) |
|---|---|---|---|
| **Kjaer, 2005[1]** | **374 (new military conscripts)** | **18–29** | **34** |
| Baldwin, 2004[2] | 393*,** (STD clinic) | 18–24 | 34 |
| Weaver, 2004[3] | 317 (students) | 18–25 | 33 |
| Svare, 2002**,[4] | 44 (STD clinic) | 18–24 | 48 |
| Kataoka, 1991[5] | 108 (army) | 18–23 | 29 |
| Shin, 2004[6] | 381 (students) | Median = 22 | 9 |

*Number includes all patients included in the study (18–70 years of age).
**Conducted at a sexually transmitted disease clinic

1. Kjaer SK, Munk C, Winther JF, Jorgensen HO, Meijer CJ, van den Brule AJ. *Cancer Epidemiol Biomarkers Prev.* 2005;14:1528–1533. 2. Baldwin SB, Wallace DR, Papenfuss MR, Abrahamsen M, Vaught LC, Giuliano AR. *Sex Transm Dis*. 2004;31:601–607. 3. Weaver BA, Feng Q, Holmes KK, et al. *J Infect Dis.* 2004;189:677–685. 4. Svare EI, Kjaer SK, Worm AM, Østerlind A, Meijer CJ, van den Brule AJ. *Sex Transm Infect.* 2002;78:215–218. 5. Kataoka A, Claesson U, Hansson BG, Eriksson M, Lindh E. *J Med Virol.* 1991;33:159–164. 6. Shin HR, Franceschi S, Vaccarella S, et al. *J Infect Dis.* 2004;190:468–476.

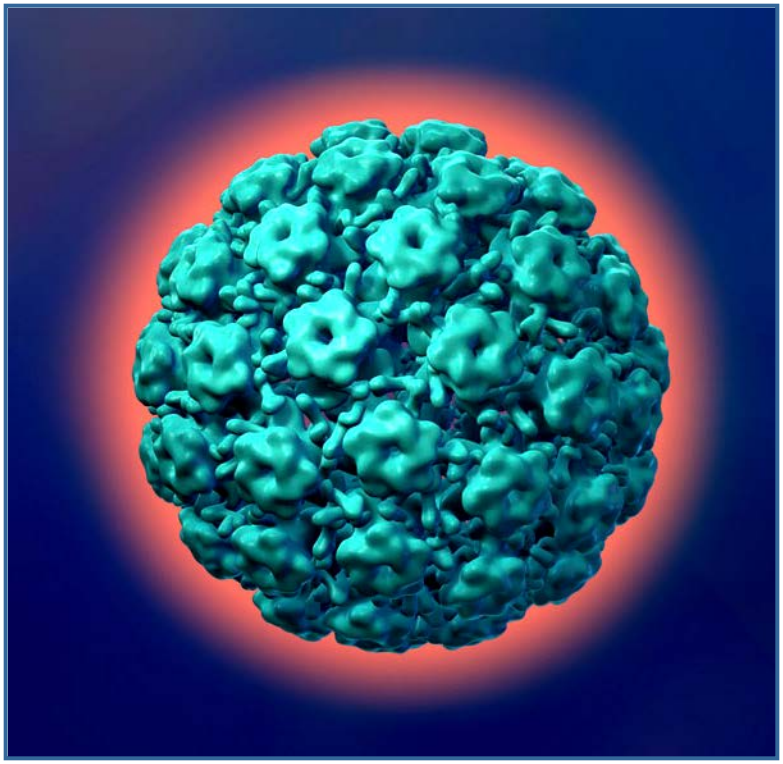
# US HPV Statistics

- Lifetime risk for sexually active men and women is at least 50%.[1]
  - By 50 years of age, at least 80% of women will have acquired genital HPV infection.[1]
- Estimated incidence: 6.2 million per year[1]
- Estimated prevalence: 20 million[1]
- In sexually active individuals 15–24 years of age, ~9.2 million are currently infected.[2]
  - An estimated 74% of new HPV infections occur in this age group.[2]
  - In studies of women <25 years of age, prevalence rates ranged from 28% to 46%.[3,4]

1. Centers for Disease Control and Prevention. Rockville, Md: CDC National Prevention Information Network; 2004. 2. Weinstock H, Berman S, Cates W Jr. *Perspect Sex Reprod Health*. 2004;36:6–10. 3. Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689. 4. Bauer HM, Ting Y, Greer CE, et al. *JAMA*. 1991;265:472–477.

# HPV

Nonenveloped double-stranded DNA virus[1]



- >100 types identified[2]
- ~30–40 anogenital[2,3]
  - ~15–20 oncogenic*,[2,3]
    - HPV 16 and HPV 18 types account for the majority of worldwide cervical cancers.[4]
  - Nononcogenic** types
    - HPV 6 and 11 are most often associated with external anogenital warts.[3]
    - These 2 types are responsible for >90% of genital warts.[5]

1. Howley PM, Lowy DR. In: Knipe DM, Howley PM, eds. Philadelphia, Pa: Lippincott-Raven; 2001:2197–2229.
2. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934. 3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis*. 2002;35(suppl 2):S210–S224. 4. Muñoz N, Bosch FX, Castellsagué X, et al. *Int J Cancer*. 2004;111:278–285.
5. Jansen KU, Shaw AR. *Annu Rev Med*. 2004;55:319–331.

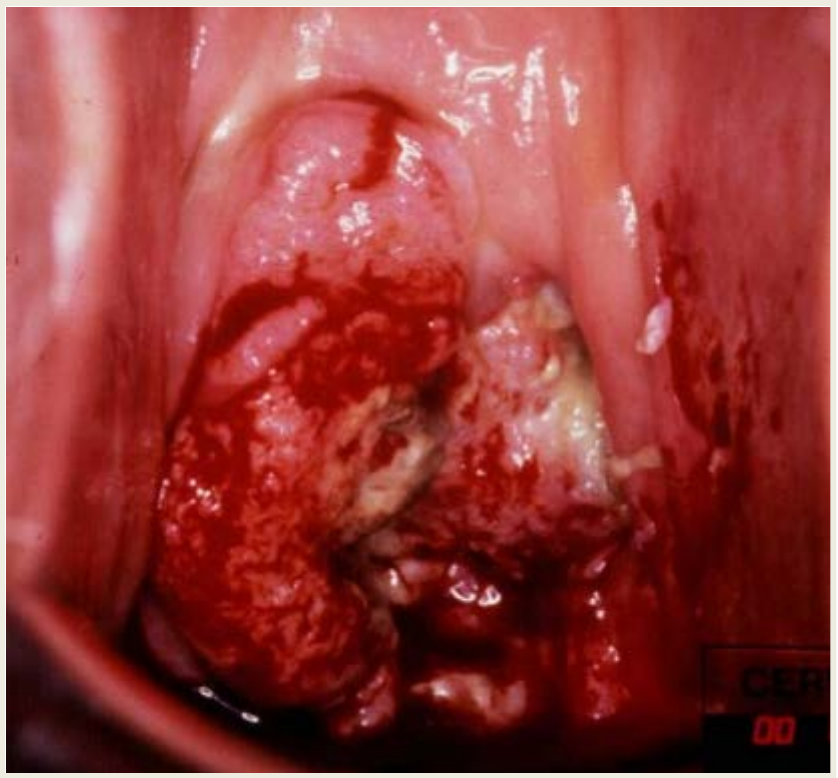
# Major Clinical Associations of HPV Infections[1,2]

| Disease | HPV Type | Transmission |
|---|---|---|
| Cervical cancer | HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 59, and 66 | Sexual |
| Cancer of vulva, vagina, anal canal, penis | HPV 16 and others | Sexual |
| Anogenital warts | HPV 6, 11 | Sexual |
| Juvenile-onset RRP | HPV 6, 11 | Mother-child, at birth |
| Adult-onset RRP | HPV 6, 11 | Unclear |

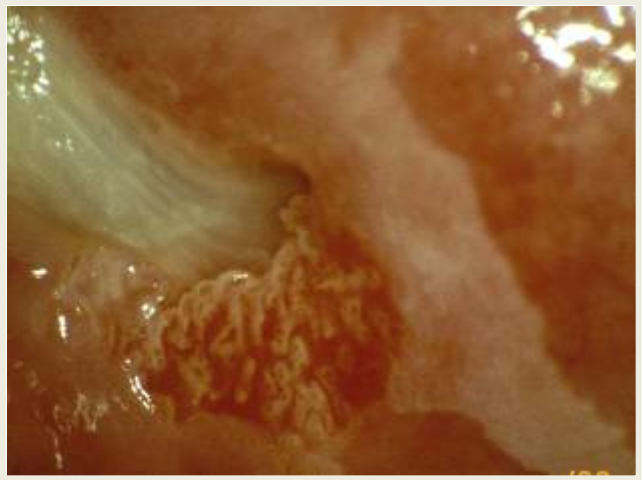
GARDASIL™ is not indicated for RRP.
RRP = Recurrent respiratory papilloma

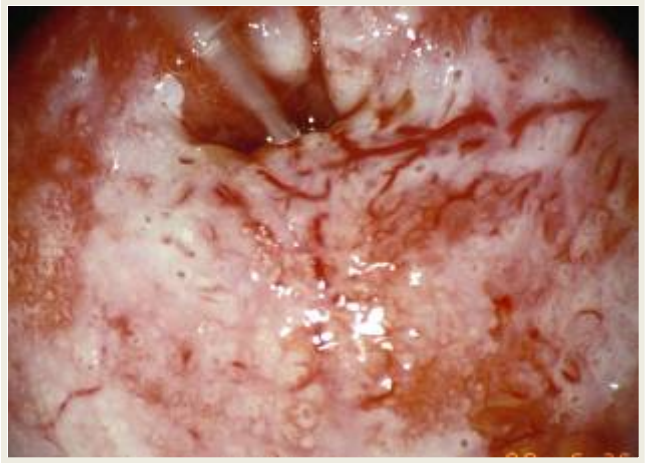
1. Adapted from *Infectious Diseases*, D.Armstrong, J.Cohen, Mosby; 1999; 8:6.3. 2. International Agency for Research on Cancer. 2006. Available at: http://monographs.iarc.fr/ENG/Meetings/90-hpv.pdf. Accessed April 9, 2007.

# Colposcopy: Invasive Cervical Carcinoma



From IARC, 2003.[1]

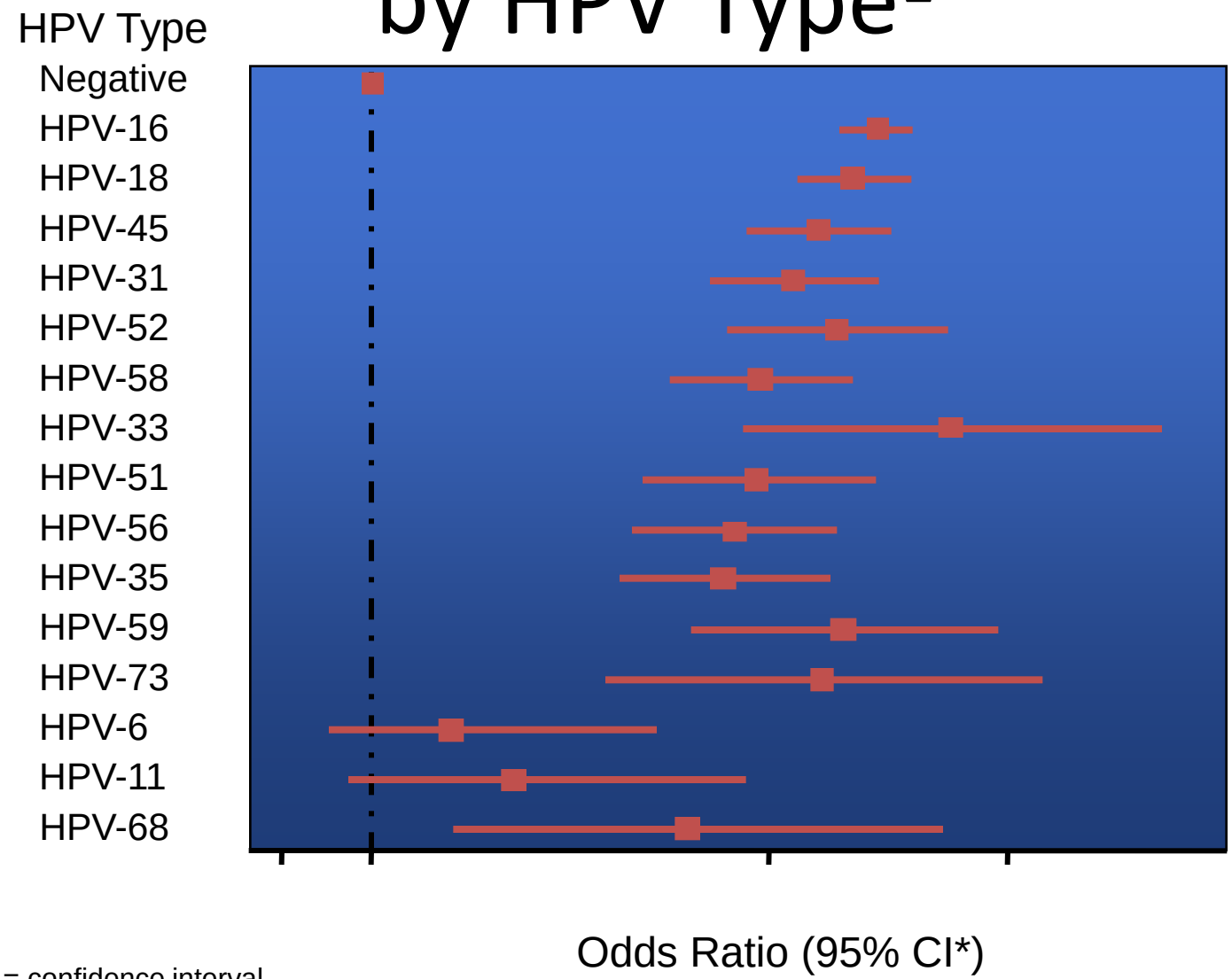




Photos courtesy of Dr. J. Monsonego

1. Reprinted with permission from Sellors JW, Sankaranarayanan R, eds. Colposcopy and Treatment of Cervical Intraepithelial Neoplasia. A Beginner's Manual. Lyon, France: International Agency for Research on Cancer; 2003.

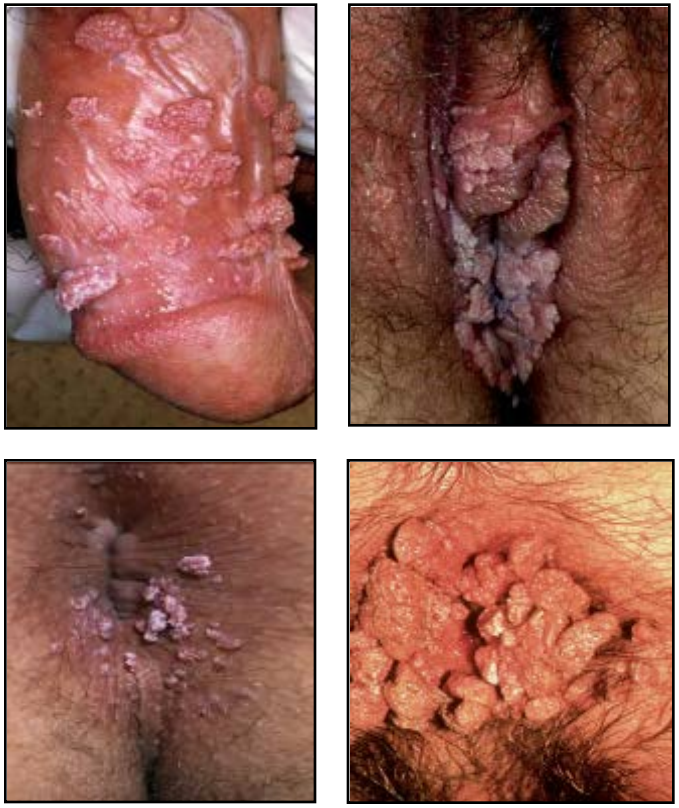
# Risk of Invasive Cervical Cancer by HPV Type[1]




*CI = confidence interval

1. Muñoz N, Castellsagué X, de González AB, Gissmann L. *Vaccine*. 2006;24S3:S3/1–S3/10.

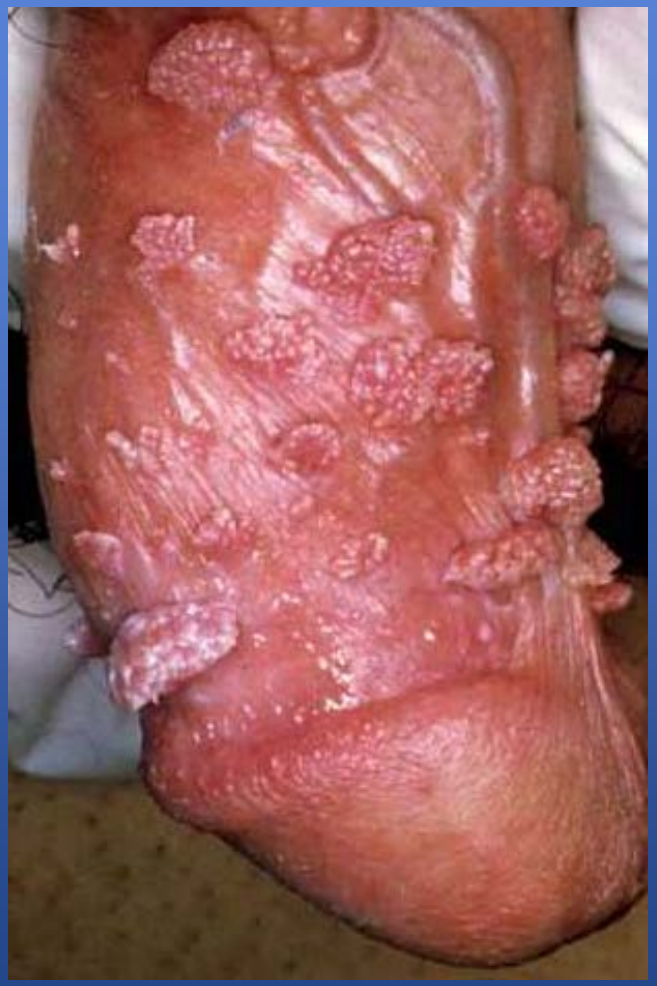
# HPV and Anogenital Warts

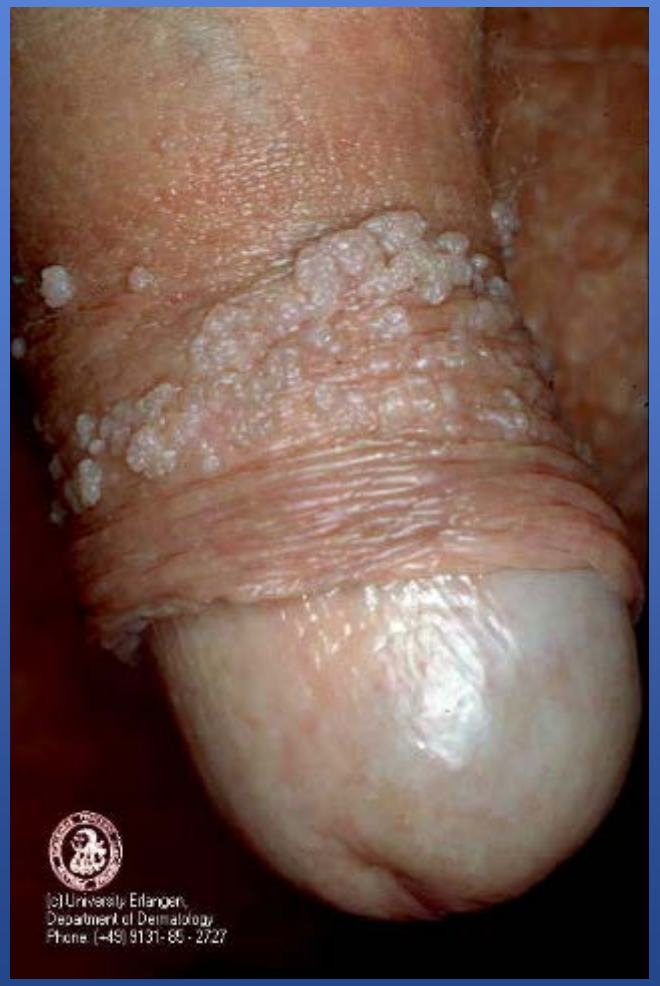


- HPV Types 6 and 11 responsible for >90% of anogenital warts[1]
- Estimated lifetime risk of developing genital warts ~10%[2,3]
- External genital warts are very contagious.[4]
  - Infectivity >75%

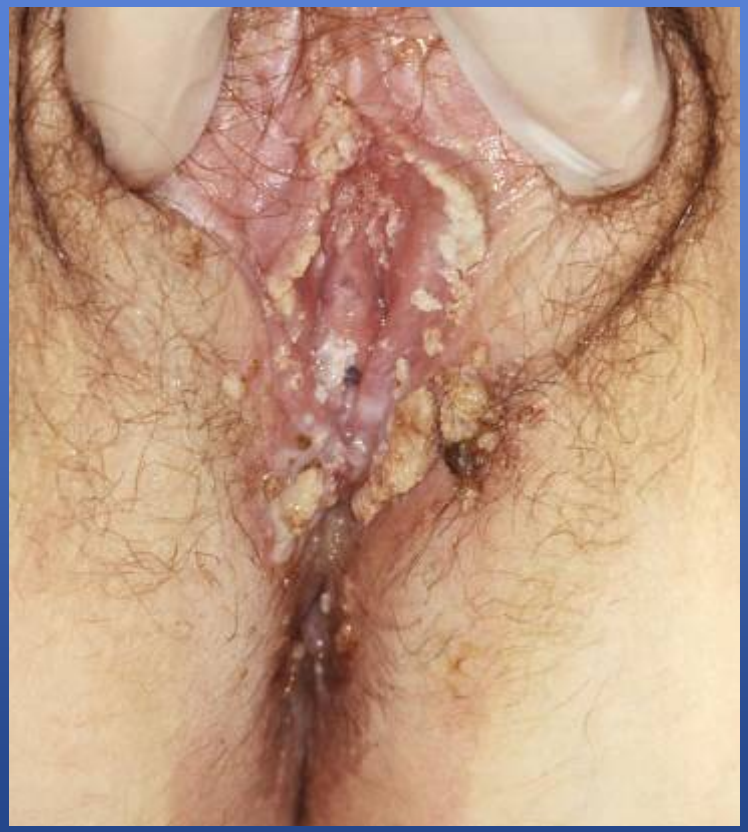
1. Jansen KU, Shaw AR. *Annu Rev Med*. 2004;55:319–331. 2. Franco EL, Villa LL, Richardson H, et al. In: Franco EL, Monsonego J, eds. Oxford, UK: Blackwell Science; 1997:14–22. 3. Tortolero-Luna G. *Hematol Oncol Clin North Am*. 1999;13:245–257, x. 4. Soper DE. In: Berek JS, ed. *Novak's* Gynecology. 13th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2002:453–470.

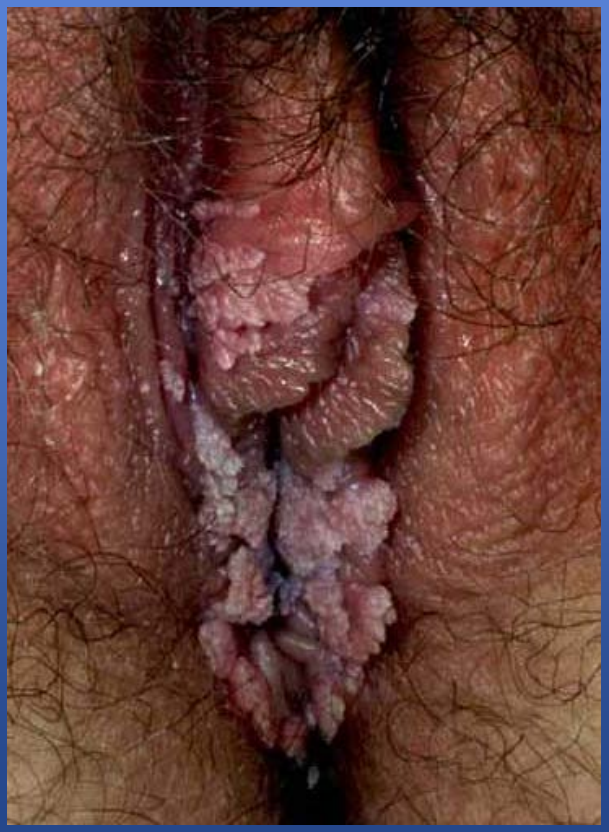
# Presentation of Genital Warts: Penile





# Presentation of Genital Warts: Vulvar





Reprinted with permission from NZ DermNet (www.dermnetnz.org)

# Vulvar Intraepithelial Neoplasia (VIN)

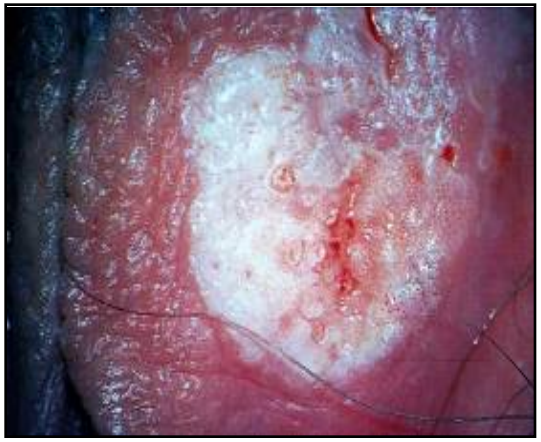
Incidence of VIN is increasing in the United States and worldwide.[1]

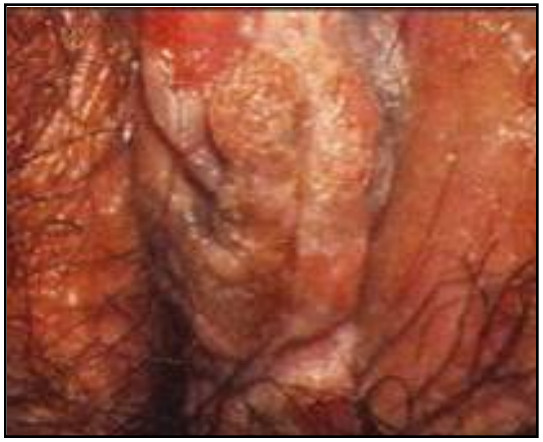
Mean age of women with VIN is decreasing.[2]

Symptoms occur and may be present for a long time prior to diagnosis (median of 1 year).[3]

HPV 16 appears to be the dominant HPV type associated with high-grade VIN.[4]

- Majority of VIN 1 cases are associated with HPV types 6 and 11.[5]
- HPV 6, 11, 16, or 18 can be found in VIN 2 or 3.[6]





Photos courtesy of Dr. E.J. Mayeaux

1. Joura EA. *Curr Opin Obstet Gynecol.* 2002;14:39–43. 2. Jones RW, Rowan DM, Stewart AW. *Obstet Gynecol.* 2005;106:1319–1326. 3. Herod JJ, Shafi MI, Rollason TP, et al. *Br J Obstet Gynaecol.* May 1996;103:446–452. 4. Hampl M, Sarajuuri H, Wentzensen N, et al. *Obstet Gynecol*. 2006;108:1361–1368. 5. Koutsky L. *Am J Med.* 1997;102:3–8. 6. Liaw KL, Kurman RJ, Ronnett B, et al. EUROGIN, April 2006. Paris, France.

# Vaginal Intraepithelial Neoplasia (VaIN)

- Main predisposing factor for VaIN is exposure to HPV.[1]
  - VaIN is often found in conjunction with CIN or VIN.[1,2]
- In recent decades, younger women have been diagnosed with VaIN.[2,3]
- True incidence unknown, but lower than for CIN[1]
  - Incidence expected to rise due to wider use of cytological screening and colposcopy, as well as increased awareness of disease[2]
- VaIN is often asymptomatic and difficult to diagnose.[2]

VaIN 3 and Vulvar Carcinoma Arising in VIN 3

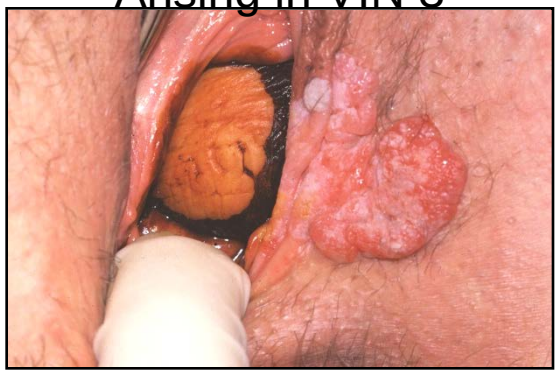


Photo courtesy of Dr. R.W. Jones

VaIN 3

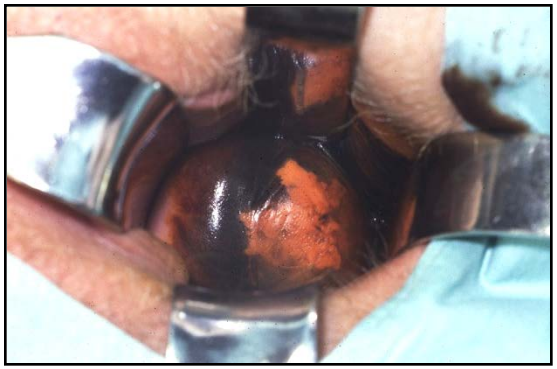


Photo courtesy of Dr. R.W. Jones

# Colposcopy: Cervical Adenocarcinoma

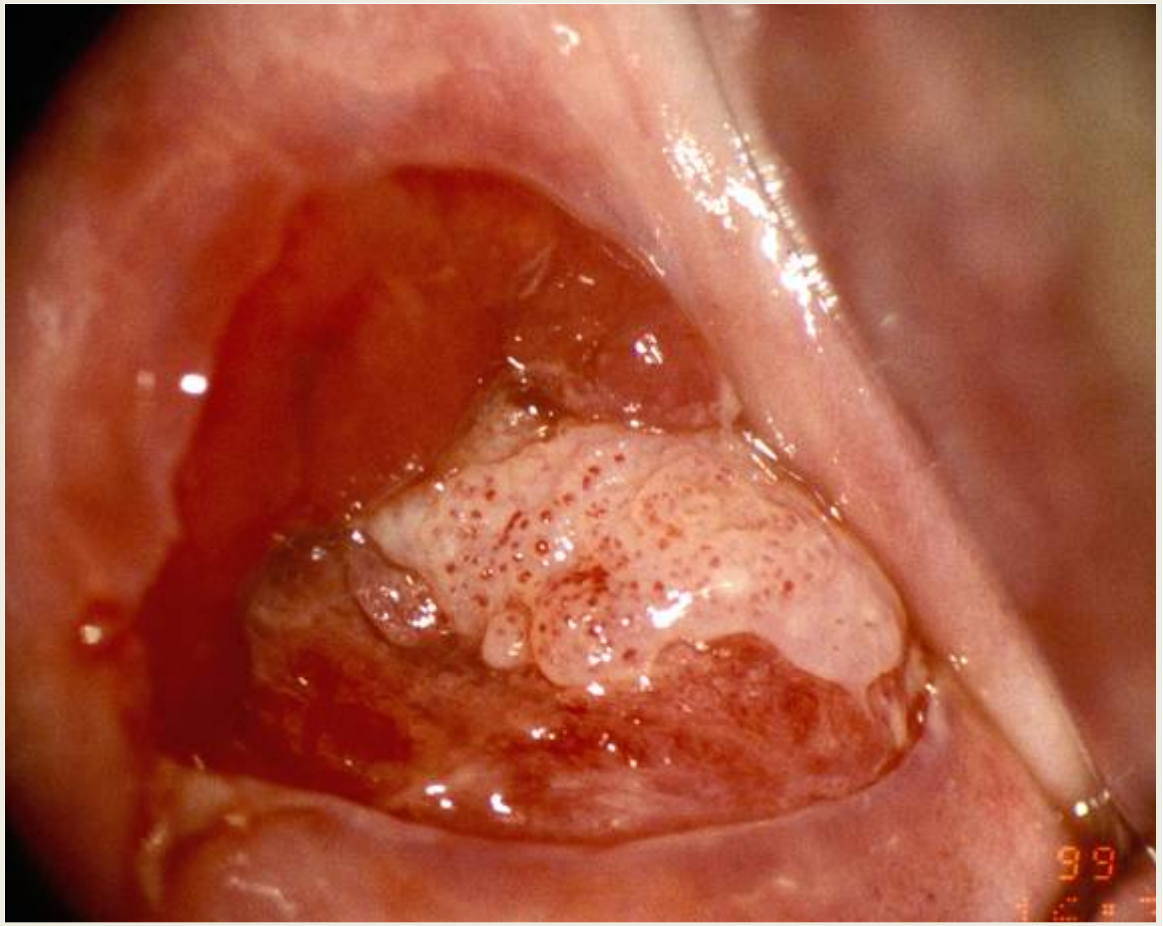


Photo courtesy of Dr. J. Monsonego

# Clinical Spectrum of HPV Infections and HPV-Related Disease in Men as Evidenced Today

- Latent HPV infection (no clinically visible lesions)[1]
- Genital warts
- Penile and anal intraepithelial neoplasia (PIN, AIN)
- Anal cancer
- Penile cancer
- Cancers of the head/neck
- Recurrent respiratory papillomatosis (RRP)

# RRP

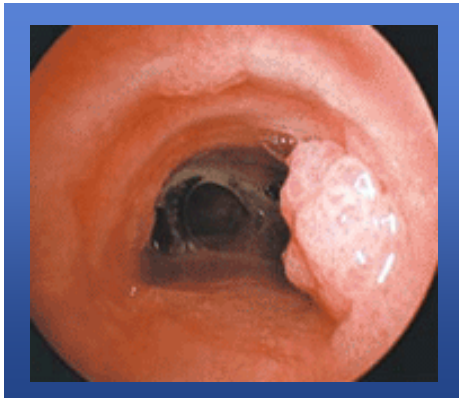


Image reprinted with permission from Glikman D., et al. N Engl J Med 2005; 352:e22. Copyright © 2005 Massachusetts Medical Society. All rights reserved.

Age distribution is bimodal with peaks at[1]:

- 2 to 4 years of age (childhood-onset)
- 20 to 40 years of age (adult-onset)

HPV Types 6 and 11 cause ~100% of both juvenile- and adult-onset RRP.[2]

Papillomas are stratified squamous epithelial masses that can obstruct the airway if not removed.[3]

Although histologically benign, RRP causes significant morbidity and mortality due to recurrent nature.[3]

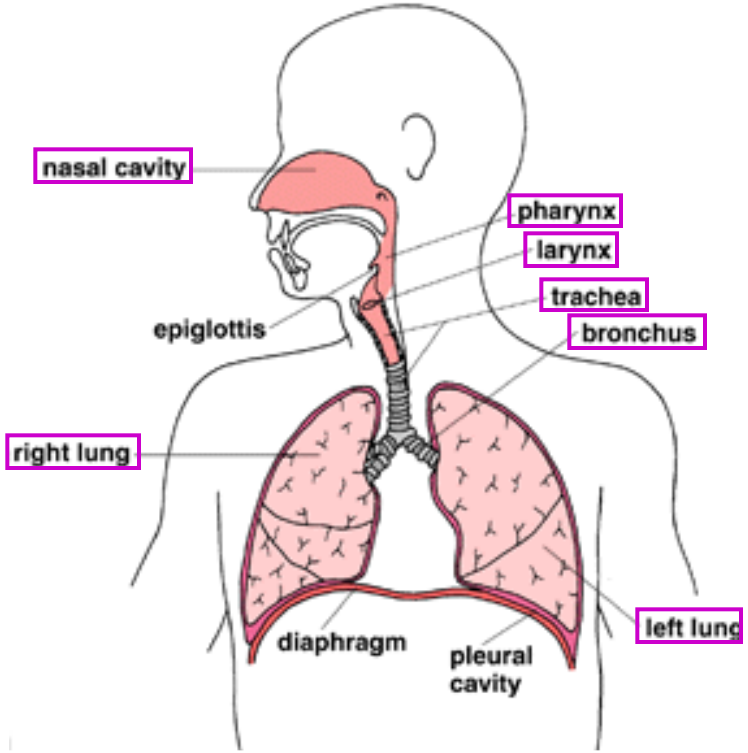
- Could require surgery under general anesthesia as frequently as every few weeks

Possible causative role of RRP in head and neck cancers[3-5]

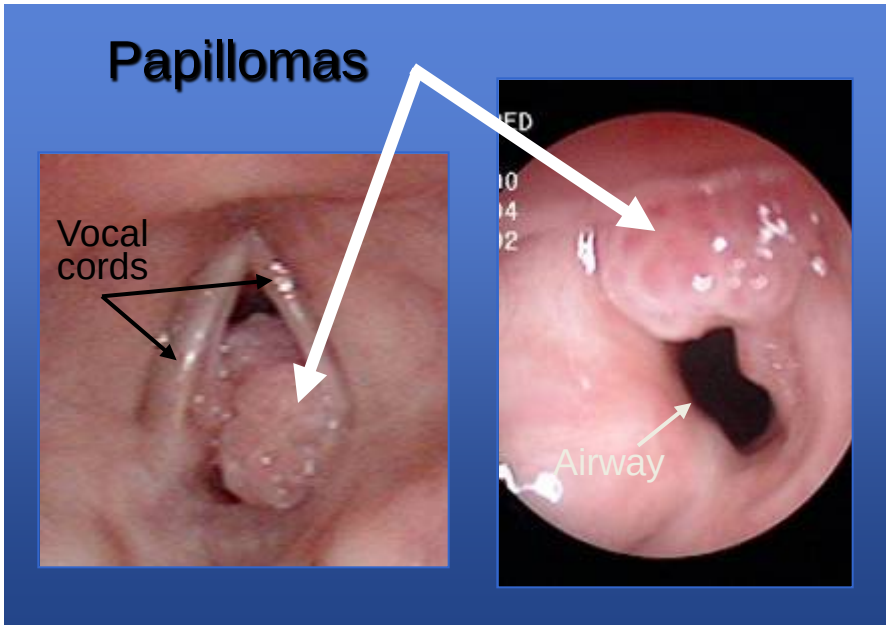
**RRP is rare.[6]**

# Locations of Papillomas in RRP

Normal Anatomy

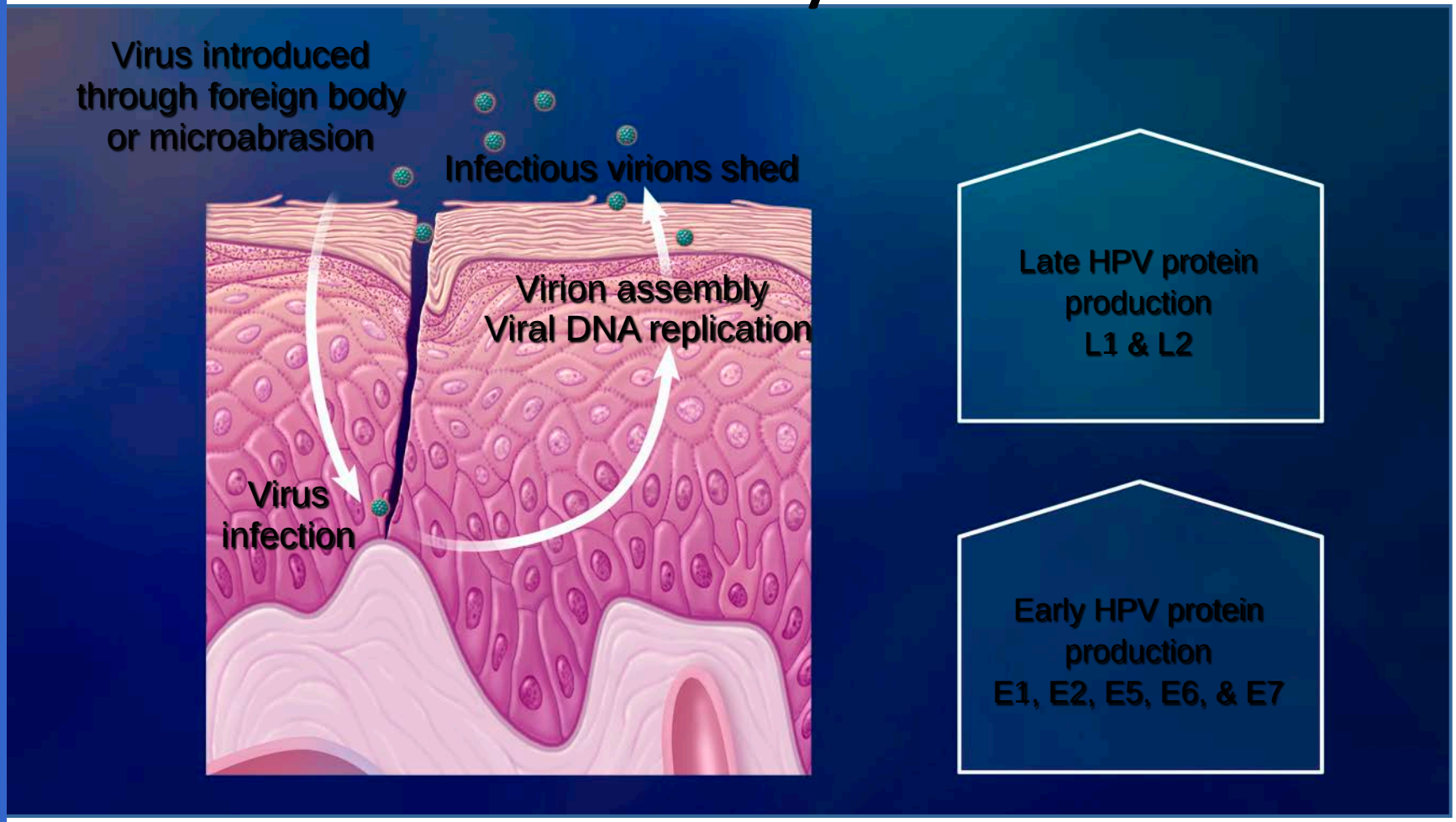



Reprinted with permission of the University of Maryland Medical Center (www.umm.edu)[1]



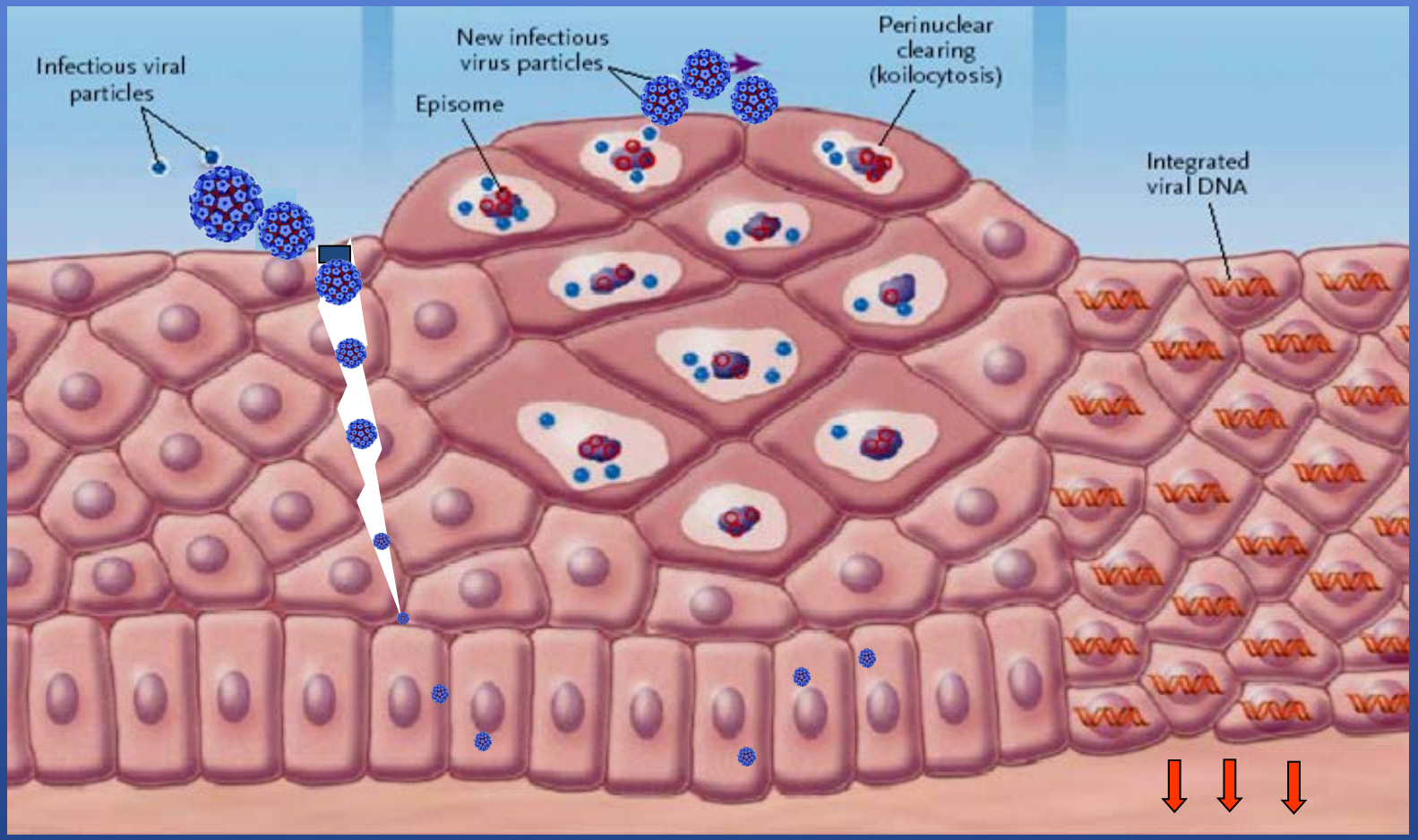

Photos courtesy of Craig S. Derkay, MD
Eastern Virginia Medical School

# HPV Infection and Productive Life Cycle




Adapted from Doorbar J. *J Clin Virol*. 2005;32S:S7–S15.

# Spectrum of Changes in Cervical Squamous Epithelium Caused by HPV Infection




*CIN = cervical intraepithelial neoplasia

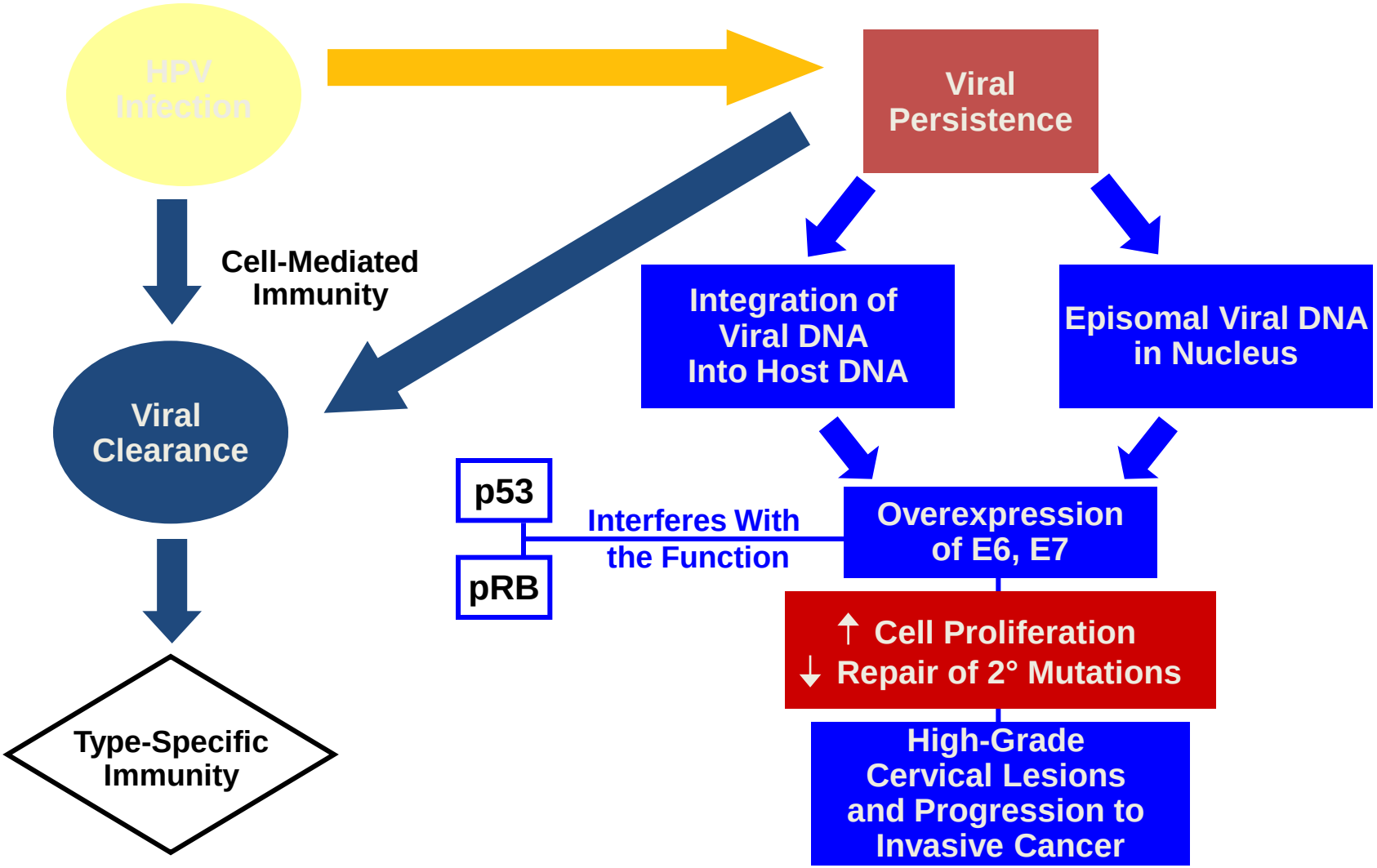
Adapted from Goodman A, Wilbur DC. *N Engl J Med*. 2003;349:1555–1564. Copyright © 2003 Massachusetts Medical Society. All rights reserved. Adapted with permission.

# Cervical Cancer Is Essentially Caused by Oncogenic HPV

- Infection with oncogenic HPV types is the most significant risk factor in cervical cancer etiology.[1]
  - HPV is a main cause of cervical cancer.[2]
- Analysis of 932 specimens from women in 22 countries indicated prevalence of HPV DNA in cervical cancers worldwide = 99.7%.[2]
  - Tissue samples were analyzed for HPV DNA by three different polymerase chain reaction (PCR)–based assays, and the presence of malignant cells was confirmed in adjacent tissue sections.[2]

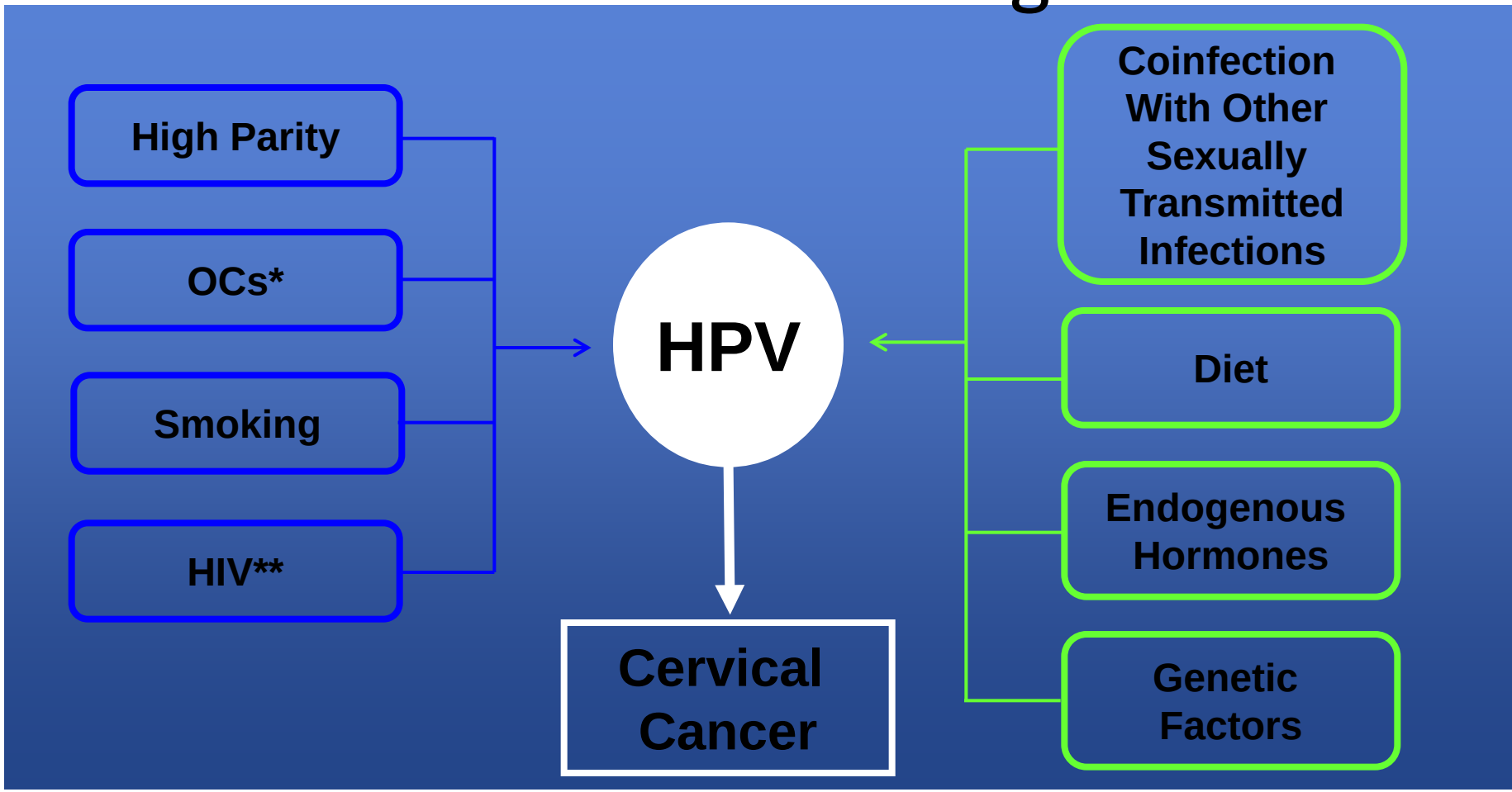
1. Muñoz N, Bosch FX, de Sanjosé, et al. *N Engl J Med*. 2003;348:518–527. 2. Walboomers JM, Jacobs MV, Manos MM, et al. *J Pathol*. 1999;189:12–19.

# Mechanisms of HPV Carcinogenesis[1–5]




1. Castle PE. *Low Genital Tract Dis.*2004;8:224–230. 2. Frazer IH. *Nature Rev Immunol*. 2004;4:46–54. 3. Doorbar J. *J Clin Virol*. 2005;32(suppl):S7–S15. 4. Münger K, Basile JR, Duensing S, et al. *Oncogene*. 2001;20:7888–7898. 5. Furumoto H, Irahara M. *J Med Invest*. 2002;49:124–133.

# Established and Potential Cofactors Involved in HPV Carcinogenesis




*OCs = oral contraceptives
**HIV = human immunodeficiency virus

Castellsagué X, Muñoz N. *J Natl Cancer Inst Monogr*. 2003;31:20–28.

# Mechanisms of HPV Transmission and Acquisition

- Sexual contact
  - Through sexual intercourse[1]
  - Genital–genital, manual–genital, oral–genital[2–4]
  - Genital HPV infection in virgins is rare, but may result from nonpenetrative sexual contact.[2]
  - Proper condom use may help reduce the risk, but is not fully protective against infection.[5]
- Nonsexual routes
  - Mother to newborn (vertical transmission)[6]
  - Fomites (eg, undergarments, surgical gloves, biopsy forceps)[7,8]
    - Hypothesized but not well documented; would be rare
- Most infected individuals are unaware that they are infected and may unknowingly spread the virus.[9]

1. Kjaer SK, Chackerian B, van den Brule AJ, et al. *Cancer Epidemiol Biomarkers Prev*. 2001;10:101–106. 2. Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol*. 2003;157:218–226. 3. Fairley CK, Gay NJ, Forbes A, Abramson M, Garland SM. *Epidemiol Infect*. 1995;115:169–176. 4. Herrero R, Castellsagué X, Pawlita M, et al. *J Natl Cancer Inst*. 2003;95:1772–1783. 5. Manhart LE, Koutsky LA. *Sex Transm Dis*. 2002;29:725–735. 6. Smith EM, Ritchie JM, Yankowitz J, et al. *Sex Transm Dis.* 2004;31:57–62. 7. Ferenczy A, Bergeron C, Richart RM. *Obstet Gynecol.* 1989;74:950–954. 8. Roden RBS, Lowy DR, Schiller JT. *J Infect Dis*. 1997;176:1076–1079. 9.

# Determinants of HPV Infection

## Women

- Young age (peak age group 20–24 years of age)[1]
- Lifetime number of sex partners[2]
- Early age of first sexual intercourse*,[3]
- Male partner sexual behavior[3]
- Smoking*,[4]
- Oral contraceptive use*,[4]
- Uncircumcised male partners[5,6]

## Men

- Young age (peak age group 25–29 years of age)[1]
- Lifetime number of sex partners[7]
- Being uncircumcised[6,7]
- Sexual partner with CIN[8]

*Findings not consistent across studies

1. Insinga RP, Dasbach EF, Myers ER. *Clin Infect Dis.* 2003;36:1397–1403. 2. Burk RD, Ho GY, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689. 3. Murthy NS, Mathew A. *Eur J Cancer Prev*. 2000;9:5–14. 4. Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol*. 2003;157:218–226. 5. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934. 6. Castellsagué X, Bosch FX, Muñoz N, et al. *N Engl J Med*. 2002;346:1105–1112. 7. Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJ, van den Brule AJ. *Sex Transm Infect*. 2002;78:215–218. 8. Bleeker MC, Hogewoning CJ, Voorhorst FJ, et al. *Int J Cancer*. 2005;113:36–41.

# Role of Men in HPV Transmission

- Men acquire and transmit HPV.[1]
- Risk factors for HPV acquisition and/or transmission by men include:
  - Young age (peak age group 25–29 years of age)[2,3]
  - Recent multiple sexual partners[2,4]
  - Sexual partner with CIN[5]
  - Lack of circumcision[2,6]

1. Castellsagué X, Bosch FX, Muñoz N. *Salud Publica Mex.* 2003;45(suppl 3):S345–353. 2. Svare EI, Kjaer SK, Worm AM, Østerlind A, Meijer CJLM, van den Brule AJC. *Sex Transm Infect.* 2002;78:215–218. 3. Insinga RP, Dasbach EF, Myers ER. *Clin Infect Dis.* 2003;36:1397–1403. 4. Chin-Hong PV, Vittinghoff E, Cranston RD, et al. *J Infect Dis.* 2004;190:2070–2076. 5. Bleeker MC, Hogewoning CJ, Voorhorst FJ, et al. *Int J Cancer.* 2005;113:36–41. 6. Castellsagué X, Bosch FX, Muñoz N, et al. *N Engl J Med*. 2002;346:1105–1112.

# Several Factors May Minimize/Prevent HPV Exposure to the Immune System

- No blood-borne phase of infection[1]
  - No viremia
- Limited and delayed expression of late viral capsid proteins[1,2]
- HPV does not kill or lyse keratinocytes.[1]
  - No release of pro-inflammatory cytokines[1]
  - Little tissue destruction associated with HPV[3]
- E6 and E7
  - Interfere with the activation of the innate immune response[4]
  - Suppress interferon signaling necessary for cell-mediated immune response[1]
  - Down-regulate antiviral cytokines[4]
- No activation of antigen-presenting cells (APCs)[1]

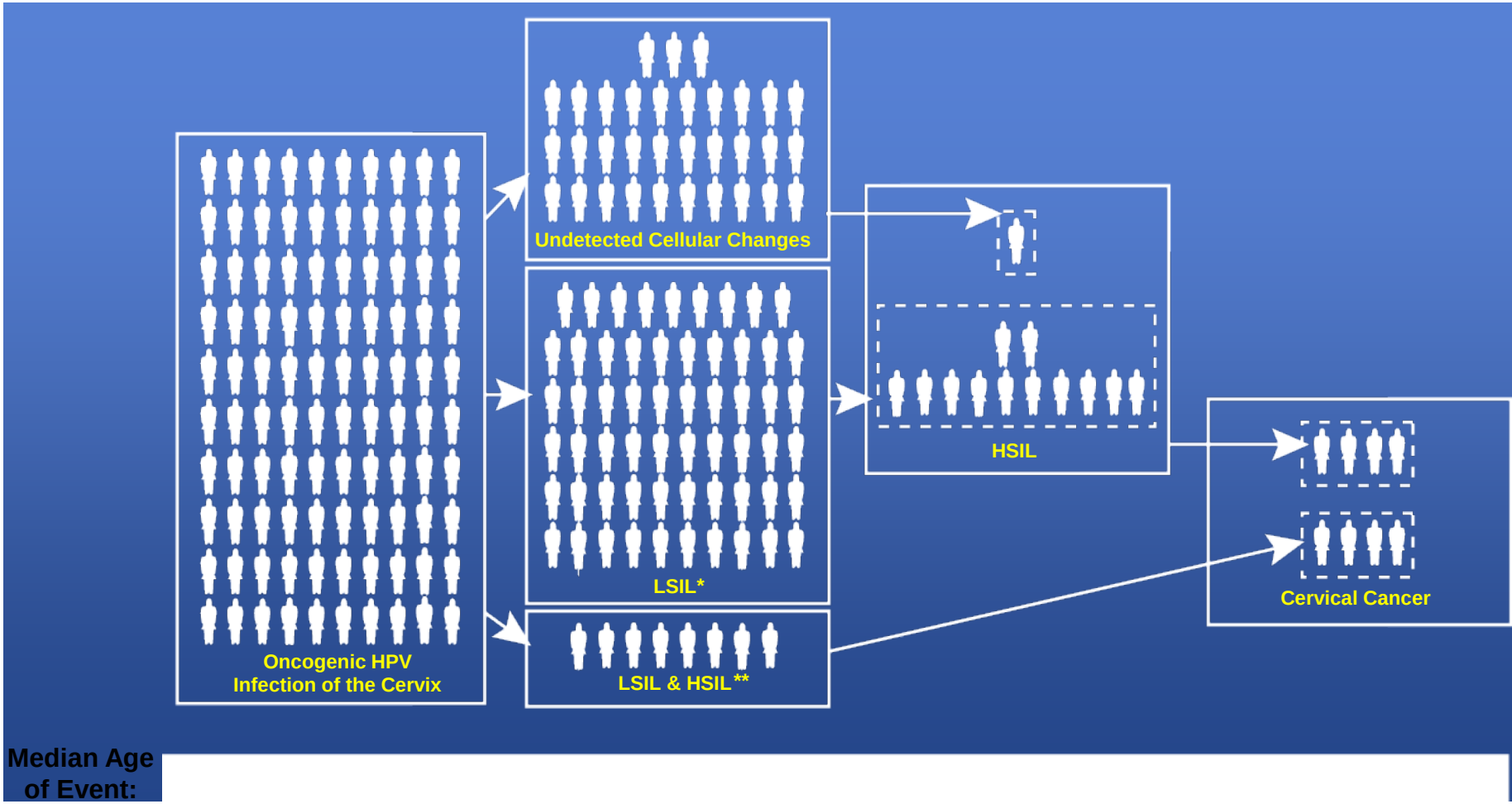
1. Tindle RW. *Nat Rev Cancer*. 2002;2:1–7. 2. Scott M, Nakagawa M, Moscicki A-B. *Clin Diagn Lab Immunol*. 2001;8:209–220. 3. Frazer IH. *Nature Rev Immunol*. 2004;4:46–54. 4. Hasan UZ, Bates E, Takeshita F, et al. *J Immunol*. 2007;178:3186–3197.

# Cell-Mediated Immune Response Against HPV Infection

- Required for eliminating established HPV infections[1]
- Early proteins are expressed throughout much of the life cycle of HPV.[2]
- E2, E6, and E7 appear to be targets for cell-mediated immune responses.[3–5]
  - Capsid proteins are expressed only in terminally differentiated cells in the upper strata of the epithelium, not in infected basal cells.[1]
- T-cell responses to HPV proteins have been shown to be type-specific.[5]

1. Roden R, Wu T-C. *Expert Rev Vaccines*. 2003;2:495–516. 2. Doorbar J. *Clin Sci*. 2006;110:525–541. 3. Stanley M, Lowy DR, Frazer I. *Vaccine*. 2006;24(suppl 1):S16–S22. 4. Nakagawa M, Viscidi R, Deshmukh I, et al. *Clin Diagn Lab Immunol*. 2002;9(4):877–892. 5. Welters MJP, de Jong A, van den Eeden SJF, et al. *Cancer Res*. 2003;63:636–641.

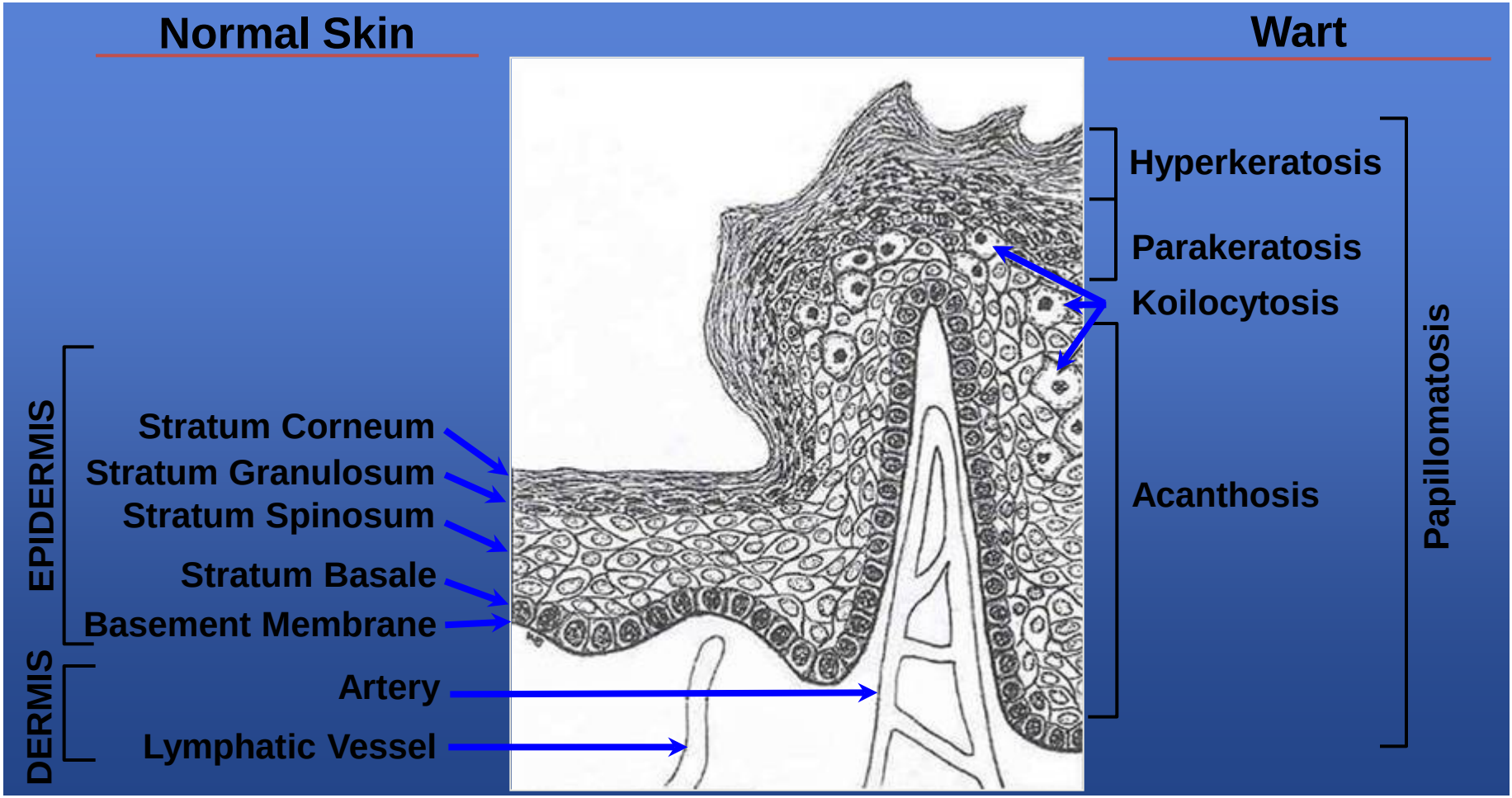
# Natural History from HPV Infection to Cervical Cancer




*LSIL = low-grade squamous intraepithelial lesion
**HSIL = high-grade squamous intraepithelial lesion

Adapted from Baseman JG, Koutsky LA. *J Clin Virol.* 2005;32S:S16–S24, with permission from Elsevier.

# Histologic Features of Normal Skin and of a Wart




Adapted with permission from

# Cervical Cancer Occurs Despite Established Screening Programs Example of Europe

| Country | Recommendation | | % Regularly Screened | Cervical Cancer Mortality/100,000[3] | Cervical Cancer Incidene/100,000[3] |
|---|---|---|---|---|---|
| | Age Range (Years) | Interval (Years) | | | |
| Finland[1] | 30–60 | 5 | 93 | 3.0 | 6.2 |
| England[1] | 25–64 | 3–5 | 83 | 5.1 | 10.5 |
| Sweden[1] | 23–60 | 3 | 83 | 5.6 | 10.9 |
| Belgium[2] | 25–64 | 3 | 78 | 6.2 | 12.8 |
| The Netherlands[1] | 30–60 | 5 | 77 | 3.8 | 9.4 |
| Denmark[1] | 23–59 | 3 | 75 | 8.6 | 16.3 |
| France[1] | 25–65 | 3 | 69 | 5.4 | 13.6 |
| Italy[1] | 25–64 | 3 | 53–74 | 4.0 | 11.6 |
| Germany[1] | 20–85 | 1 | 50 | 7.1 | 14.7 |
| Spain[2] | 25–65 | 3 | 27 | 3.6 | 10.3 |

1. Anttila A, Ronco G, Clifford G, et al. *Br J Cancer.* 2004;91:935–941. 2. van Ballegooijen M, van den Akker-van Marle E, Patnick J, et al. *Eur J Cancer.* 2000;36:2177–2188. 3. Ferlay J, Bray F, Pisani P, Parkin DM. Lyon, France: IARC Press; 2004.

# Targeting High Disease Burden

| Type | Women | Men |
|---|---|---|
| 6/11 | >90% of genital warts[2]<br>~10% of low-grade cervical lesions[3]<br>Recurrent respiratory papillomatosis (RRP)*,[4]<br>Transmission to men[5] | >90% of genital warts[2]<br>Transmission to women[9]<br>RRP*,[4] |
| 16/18 | ~70% of cervical cancer[3]<br>~50% of high-grade cervical lesions[6]<br>~25% of low-grade cervical lesions[3]<br>~70% of high-grade vulvar/vaginal lesions[7]<br>Oropharyngeal cancer†,[8]<br>Other cancers†,[8]<br>Transmission to men[5] | ~60% of anal cancer[10]<br>Penile cancer†,[8]<br>Oropharyngeal cancer†,[8]<br>Other cancers†,[8]<br>Transmission to women[9] |

1. Villa LL, Costa RLR, Petta CA, et al. *Lancet Oncol*. 2005;6:271–278. 2. Gissmann L, Wolnik L, Ikenberg H, et al. *Proc Natl Acad Sci USA*. 1983;80:560–563. 3. Clifford GM, Rana RK, Franceschi S, Smith JS, Gough G, Pimenta JM. *Cancer Epidemiol Biomarkers Prev*. 2005;14:1157–1164. 4. Kashima HK, Mounts P, Shah K. *Obstet Gynecol Clin North Am*. 1996;23:699–706. 5. Dunne EF, Nielson CM, Stone KM, et al. *J Infect Dis*. 2006;194:1044–1057. 6. Clifford GM, Smith JS, Aguado T, Franceschi S. *Br J Cancer*. 2003;89:101–105. 7. GARDASIL Worldwide Product Circular. Merck & Co., Inc., Whitehouse Station, NJ, USA. 8. Parkin DM. *Int J Cancer*. 2006;118:3030–3044. 9. Castellsagué X, Bosch FX, Muñoz N. *Salud Publica Mex.* 2003;45(suppl 3):S345–353. 10. Frisch M, Glimelius B, van den Brule AJC, et al. *N Engl J Med*. 1997;337:1350–1358.

# What does it mean for us?

Screening - Only find what you look for.

Education and Awareness

Risk identified already – HIV - pregnant

Aggressive CA

HIV treatment to start at right time

# Update

NSP: our new **Bible**

Resistance Guidelines in review

Adult Guidelines – early 2012