



Complete Summary

GUIDELINE TITLE

Human papillomavirus infection. Sexually transmitted diseases treatment guidelines 2002.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention. Human papillomavirus infection. Sexually transmitted diseases treatment guidelines. MMWR Recomm Rep 2002 May 10; 51(RR-6):53-7.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Human papillomavirus (HPV) infection, including genital warts and subclinical genital HPV infection (without exophytic warts)

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Internal Medicine
Obstetrics and Gynecology
Preventive Medicine
Urology

INTENDED USERS

Health Care Providers
Managed Care Organizations
Physicians

GUIDELINE OBJECTIVE(S)

- To update the 1998 Guidelines for Treatment of Sexually Transmitted Diseases (MMWR 1998; 47[No. RR-1])
- To assist physicians and other health-care providers in preventing and treating sexually transmitted diseases (STDs)
- To present updated recommendations for the treatment of genital warts caused by human papillomavirus (HPV) infection and subclinical genital HPV infection

TARGET POPULATION

Patients with human papillomavirus (HPV) infection

INTERVENTIONS AND PRACTICES CONSIDERED

Note from the National Guideline Clearinghouse and the Centers for Disease Control and Prevention: These guidelines focus on the treatment and counseling of individual patients and do not address other community services and interventions that are important in sexually transmitted disease/human immunodeficiency virus (STD/HIV) prevention.

Treatment

External genital warts

Patient-applied

1. Podofilox 0.5% solution or gel
2. Imiquimod 5% cream

Provider-administered

1. Cryotherapy with liquid nitrogen or cryoprobe
2. Podophyllin resin 10%-25% in a compound tincture of benzoin
3. Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%
4. Surgical removal by tangential scissor excision, tangential shave excision, curettage or electrosurgery
5. Intralesional interferon
6. Laser surgery

Cervical warts

1. Exclude diagnosis of high-grade squamous intraepithelial lesions (SIL)
2. Consultation with specialist

Vaginal warts

1. Cryotherapy with liquid nitrogen
2. Trichloroacetic acid or bichloroacetic acid 80%-90%

Urethral meatus warts

1. Cryotherapy with liquid nitrogen
2. Podophyllin 10%-25% in compound tincture or benzoin

Anal warts

1. Cryotherapy with liquid nitrogen
2. Trichloroacetic acid or bichloroacetic acid 80%-90%
3. Surgical removal
4. Specialist consultation for warts on rectal mucosa

Oral warts

1. Cryotherapy with liquid nitrogen
2. Surgical removal

Special considerations in pregnancy, in persons who are immunosuppressed, and in patients with squamous cell carcinoma in situ of the genitalia

Subclinical genital HPV infection (without exophytic warts)

[Note: In the absence of coexistent squamous intraepithelial lesions, treatment is not recommended when subclinical genital human papillomavirus infection is diagnosed by colposcopy, biopsy, acetic acid application, or the detection of human papillomavirus by laboratory test.]

Management

1. Education and counseling, using patient education materials, pamphlets, hotlines, and web sites
2. Follow-up evaluation
3. Counseling of sex partners

MAJOR OUTCOMES CONSIDERED

- Microbiologic cure
- Alleviation of signs and symptoms
- Prevention of sequelae
- Prevention of transmission

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Beginning in 2000, Centers for Disease Control and Prevention (CDC) personnel and professionals knowledgeable in the field of sexually transmitted diseases (STDs) systematically reviewed literature (i.e., published abstracts and peer-reviewed journal articles) concerning each of the major STDs, focusing on information that had become available since publication of the 1998 Guidelines for Treatment of Sexually Transmitted Diseases. Background papers were written and tables of evidence constructed summarizing the type of study (e.g., randomized controlled trial or case series), study population and setting, treatments or other interventions, outcome measures assessed, reported findings, and weaknesses and biases in study design and analysis. A draft document was developed on the basis of the reviews.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse and the Centers for Disease Control and Prevention: When more than one therapeutic regimen is recommended, the sequence is alphabetized unless the choices for therapy are prioritized based on efficacy, convenience, or cost. For sexually transmitted diseases (STDs) with more than one recommended regimen, almost all regimens have similar efficacy and similar rates of intolerance or toxicity unless otherwise specified.

Genital Warts

More than 30 types of human papillomavirus (HPV) can infect the genital tract. Most HPV infections are asymptomatic, unrecognized, or subclinical. Visible genital warts usually are caused by HPV types 6 or 11. Other HPV types in the anogenital region (e.g., types 16, 18, 31, 33, and 35) have been strongly associated with cervical neoplasia. Diagnosis of genital warts can be confirmed by biopsy, although biopsy is needed only under certain circumstances (e.g., if the diagnosis is uncertain; the lesions do not respond to standard therapy; the disease worsens during therapy; the patient is immunocompromised; or warts are pigmented, indurated, fixed, and ulcerated). No data support the use of type-specific HPV nucleic acid tests in the routine diagnosis or management of visible genital warts.

In addition to the external genitalia (i.e., the penis, vulva, scrotum, perineum, and perianal skin), genital warts can occur on the uterine cervix and in the vagina, urethra, anus, and mouth; these warts are sometimes symptomatic. Intra-anal warts are seen predominantly in patients who have had receptive anal intercourse; these warts are distinct from perianal warts, which can occur in men and women who do not have a history of anal sex. In addition to the genital area, HPV types 6 and 11 have been associated with conjunctival, nasal, oral, and laryngeal warts. HPV types 6 and 11 rarely are associated with invasive squamous cell carcinoma of the external genitalia. Depending on the size and anatomic location, genital warts can be painful, friable, and pruritic, although they are commonly asymptomatic.

HPV types 16, 18, 31, 33, and 35 are found occasionally in visible genital warts and have been associated with external genital (i.e., vulvar, penile, and anal) squamous intraepithelial neoplasia (i.e., squamous cell carcinoma in situ, bowenoid papulosis, Erythroplasia of Queyrat, or Bowen's disease of the genitalia). These HPV types also have been associated with vaginal, anal, and

cervical intraepithelial dysplasia and squamous cell carcinoma. Patients who have visible genital warts can be infected simultaneously with multiple HPV types.

Treatment

The primary goal of treating visible genital warts is the removal of symptomatic warts. In most patients, treatment can induce wart-free periods. If left untreated, visible genital warts may resolve on their own, remain unchanged, or increase in size or number. Determining whether treatment of genital warts will reduce transmission is difficult, because no laboratory marker of infectivity has been established and because clinical studies evaluating the persistence of HPV deoxyribonucleic acid (DNA) in genital tissue after treatment have shown variable results. Existing data indicate that currently available therapies for genital warts may reduce, but probably do not eradicate, infectivity. Whether the reduction in viral DNA that results from current treatment regimens impacts future transmission remains unclear. No evidence indicates that either the presence of genital warts or their treatment is associated with the development of cervical cancer.

Regimens

Treatment of genital warts should be guided by the preference of the patient, the available resources, and the experience of the health-care provider. No definitive evidence suggests that any of the available treatments is superior to the others, and no single treatment is ideal for all patients or all warts. The use of locally developed and monitored treatment algorithms has been associated with improved clinical outcomes and should be encouraged. Because of uncertainty regarding the effect of treatment on future transmission and the possibility for spontaneous resolution, an acceptable alternative for some patients is to forego treatment and await spontaneous resolution.

Most patients have ≤ 10 genital warts, with a total wart area of 0.5--1.0 cm². These warts respond to most treatment modalities. Factors that may influence selection of treatment include wart size, wart number, anatomic site of wart, wart morphology, patient preference, cost of treatment, convenience, adverse effects, and provider experience. Many patients require a course of therapy rather than a single treatment. In general, warts located on moist surfaces and/or in intertriginous areas respond better to topical treatment than do warts on drier surfaces.

The treatment modality should be changed if a patient has not improved substantially after three provider-administered treatments or if warts have not completely cleared after six treatments. The risk-benefit ratio of treatment should be evaluated throughout the course of therapy to avoid overtreatment. Both patient-applied therapies and provider-administered therapies are available. Providers should be knowledgeable about, and have available to them, at least one patient-applied and one provider-administered treatment.

Complications rarely occur if treatments for warts are employed properly. Patients should be warned that persistent hypopigmentation or hyperpigmentation are common with ablative modalities. Depressed or hypertrophic scars are uncommon but can occur, especially if the patient has had insufficient time to heal between

treatments. Rarely, treatment can result in disabling chronic pain syndromes (e.g., vulvodynia or hyperesthesia of the treatment site).

Recommended Regimens for External Genital Warts

Patient-Applied:

Podofilox 0.5% solution or gel. Patients should apply podofilox solution with a cotton swab, or podofilox gel with a finger, to visible genital warts twice a day for 3 days, followed by 4 days of no therapy. This cycle may be repeated, as necessary, for up to four cycles. The total wart area treated should not exceed 10 cm², and the total volume of podofilox should be limited to 0.5 mL per day. If possible, the health-care provider should apply the initial treatment to demonstrate the proper application technique and identify which warts should be treated. The safety of podofilox during pregnancy has not been established.

OR

Imiquimod 5% cream. Patients should apply imiquimod cream once daily at bedtime, three times a week for up to 16 weeks. The treatment area should be washed with soap and water 6--10 hours after the application. The safety of imiquimod during pregnancy has not been established.

Provider-Administered:

Cryotherapy with liquid nitrogen or cryoprobe. Repeat applications every 1--2 weeks.

OR

Podophyllin resin 10% --25% in a compound tincture of benzoin. A small amount should be applied to each wart and allowed to air dry. The treatment can be repeated weekly, if necessary. To avoid the possibility of complications associated with systemic absorption and toxicity, some specialists recommend that application be limited to ≤ 0.5 mL of podophyllin or an area of < 10 cm² of warts per session. Some specialists suggest that the preparation should be thoroughly washed off 1-4 hours after application to reduce local irritation. The safety of podophyllin during pregnancy has not been established.

OR

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80% -90%. A small amount should be applied only to warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate (i.e., baking soda), or liquid soap

preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

OR

Surgical removal either by tangential scissor excision, tangential shave excision, curettage, or electrosurgery.

Alternative Regimens for External Genital Warts

Intralesional interferon

OR

Laser surgery

For patient-applied treatments, patients must be able to identify and reach warts to be treated. Podofilox 0.5% solution or gel, an antimitotic drug that destroys warts, is relatively inexpensive, easy to use, safe, and self-applied by patients. Most patients experience mild/moderate pain or local irritation after treatment. Imiquimod is a topically active immune enhancer that stimulates production of interferon and other cytokines. Local inflammatory reactions are common with the use of imiquimod; these reactions usually are mild to moderate. Traditionally, follow-up visits are not required for patients using self-administered therapy. However, follow-up may be useful several weeks into therapy to determine appropriateness of medication use and response to treatment.

Cryotherapy destroys warts by thermal-induced cytolysis. Health-care providers must be trained on the proper use of this therapy, because over- and under-treatment may result in poor efficacy or increased likelihood of complications. Pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, is common. Local anesthesia (topical or injected) may facilitate therapy if warts are present in many areas or if the area of warts is large.

Podophyllin resin, which contains several compounds including antimitotic podophyllin lignans, is another treatment option. The resin is most frequently compounded at 10%--25% in a tincture of benzoin. However, podophyllin resin preparations differ in the concentration of active components and contaminants. The shelf life and stability of podophyllin preparations are unknown. A thin layer of podophyllin resin must be applied to the warts and allowed to air dry before the treated area comes into contact with clothing; over-application or failure to air dry can result in local irritation caused by spread of the compound to adjacent areas.

Both TCA and BCA are caustic agents that destroy warts by chemical coagulation of the proteins. Although these preparations are widely used, they have not been investigated thoroughly. TCA solutions have a low viscosity comparable with that of water and can spread rapidly if applied excessively; thus, they can damage adjacent tissues. Both TCA and BCA should be applied sparingly and allowed to dry before the patient sits or stands. If pain is intense, the acid can be neutralized with soap or sodium bicarbonate.

Surgical therapy is a treatment option that has the advantage of usually eliminating warts at a single visit. However, such therapy requires substantial clinical training, additional equipment, and a longer office visit. Once local anesthesia is applied, the visible genital warts can be physically destroyed by electrocautery, in which case no additional hemostasis is required. Care must be taken to control the depth of electrocautery to prevent scarring. Alternatively, the warts can be removed either by tangential excision with a pair of fine scissors or a scalpel or by curettage. Because most warts are exophytic, this can be accomplished with a resulting wound that only extends into the upper dermis. Hemostasis can be achieved with an electrosurgical unit or a chemical styptic (e.g., an aluminum chloride solution). Suturing is neither required nor indicated in most cases when surgical removal is done properly. Surgical therapy is most beneficial for patients who have a large number or area of genital warts. Carbon dioxide laser and surgery may be useful in the management of extensive warts or intraurethral warts, particularly for those patients who have not responded to other treatments.

Interferons, either natural or recombinant, used for the treatment of genital warts have been administered systemically (i.e., subcutaneously at a distant site or intramuscularly [IM]) and intralesionally (i.e., injected into the warts). Systemic interferon is not effective. The efficacy and recurrence rates of intralesional interferon are comparable to other treatment modalities. Interferon is likely effective because of its anti-viral and/or immunostimulating effects. However, interferon therapy is not recommended for routine use because of inconvenient routes of administration, frequent office visits, and the association between its use and a high frequency of systemic adverse effects.

Because of the shortcomings of all available treatments, some clinics employ combination therapy (i.e., the simultaneous use of two or more modalities on the same wart at the same time). However, some specialists believe that combining modalities may increase complications without improving efficacy.

Cervical Warts

For women who have exophytic cervical warts, high-grade squamous intraepithelial lesions (SIL) must be excluded before treatment is initiated. Management of exophytic cervical warts should include consultation with a specialist.

Recommended Regimens for Vaginal Warts

Cryotherapy with liquid nitrogen. The use of a cryoprobe in the vagina is not recommended because of the risk for vaginal perforation and fistula formation.

OR

TCA or BCA 80% --90% applied to warts. A small amount should be applied only to warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate

(i.e., baking soda), or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

Recommended Regimens for Urethral Meatus Warts

Cryotherapy with liquid nitrogen

OR

Podophyllin 10% --25% in compound tincture of benzoin. The treatment area must be dry before contact with normal mucosa. This treatment can be repeated weekly, if necessary. The safety of podophyllin during pregnancy has not been established.

Note: Although data evaluating the use of podofilox and imiquimod for the treatment of distal meatal warts are limited, some specialists recommend their use in certain patients.

Recommended Regimens for Anal Warts

Cryotherapy with liquid nitrogen

OR

TCA or BCA 80% --90% applied to warts. A small amount should be applied only to warts and allowed to dry, at which time a white "frosting" develops. If an excess amount of acid is applied, the treated area should be powdered with talc, sodium bicarbonate (i.e., baking soda), or liquid soap preparations to remove unreacted acid. This treatment can be repeated weekly, if necessary.

OR

Surgical removal

Note: Warts on the rectal mucosa should be managed in consultation with a specialist.

Recommended Regimens for Oral Warts

Cryotherapy with liquid nitrogen

OR

Surgical removal

Education and counseling are important aspects of managing patients with genital warts. Patients can be educated through patient education materials, including pamphlets, hotlines, and web sites (www.ashastd.org). Attempts should be made to cover the following key messages.

- Genital HPV infection is a viral infection that is common among sexually active adults.
- Infection is almost always sexually transmitted, but the incubation period is variable and it is often difficult to determine the source of infection. Within ongoing relationships, sex partners usually are infected by the time of the patient's diagnosis, although they may have no symptoms or signs of infection.
- The natural history of genital warts is generally benign; the types of HPV that usually cause external genital warts are not associated with cancer. Recurrence of genital warts within the first several months after treatment is common and usually indicates recurrence rather than reinfection.
- The likelihood of transmission to future partners and the duration of infectivity after treatment are unknown. The use of latex condoms has been associated with a lower rate of cervical cancer, an HPV-associated disease.
- Because genital HPV is common among persons who have been sexually active and because the duration of infectivity is unknown, the value of disclosing a past diagnosis of genital HPV infection to future partners is unclear. Candid discussions about other STDs should be encouraged and attempted whenever possible.

Follow-Up

After visible genital warts have cleared, a follow-up evaluation is not mandatory but may be helpful. Patients should be cautioned to watch for recurrences, which occur most frequently during the first 3 months. Because the sensitivity and specificity of self-diagnosis of genital warts are unknown, patients concerned about recurrences should be offered a follow-up evaluation 3 months after treatment. Earlier follow-up visits also may be useful for some patients to document the absence of warts, to monitor for or treat complications of therapy, and to provide an additional opportunity for patient education and counseling. Women should be counseled to undergo regular Papanicolaou (Pap) screening as recommended for women without genital warts. The presence of genital warts is not an indication for a change in the frequency of Pap tests or for cervical colposcopy.

Management of Sex Partners

Examination of sex partners is not necessary for the management of genital warts because no data indicate that reinfection plays a role in recurrences. Additionally, providing treatment solely for the purpose of preventing future transmission cannot be recommended because the value of treatment in reducing infectivity is not known. However, because self- or partner-examination has not been evaluated as a diagnostic method for genital warts, sex partners of patients who have genital warts may benefit from examination to assess the presence of genital warts and other STDs. The counseling of sex partners provides an opportunity for these partners to a) learn about implications of having a partner who has genital warts and about their potential for future disease transmission and b) receive STD and Pap screening. Female sex partners of patients who have genital warts should be reminded that cytologic screening for cervical cancer is recommended for all sexually active women.

Special Considerations

Pregnancy

Imiquimod, podophyllin, and podofilox should not be used during pregnancy. Because genital warts can proliferate and become friable during pregnancy, many specialists advocate their removal during pregnancy. HPV types 6 and 11 can cause respiratory papillomatosis in infants and children. The route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood. The preventive value of cesarean section is unknown; thus, cesarean delivery should not be performed solely to prevent transmission of HPV infection to the newborn. Cesarean delivery may be indicated for women with genital warts if the pelvic outlet is obstructed or if vaginal delivery would result in excessive bleeding.

Immunodeficient Patients

Persons who are immunosuppressed because of human immunodeficiency virus (HIV) or other reasons may not respond as well as immunocompetent persons to therapy for genital warts, and they may have more frequent recurrences after treatment. Squamous cell carcinomas arising in or resembling genital warts may occur more frequently among immunosuppressed persons, thus requiring biopsy for confirmation of diagnosis. Because of the increased incidence of anal cancer in HIV-infected homosexual men, screening for anal SIL by cytology in this population is advocated by some specialists. However, until more data about the natural history of anal SIL and treatment efficacy are available, such a screening approach is not recommended.

Squamous Cell Carcinoma in Situ

Patients in whom squamous cell carcinoma in situ of the genitalia is diagnosed should be referred to a specialist for treatment. Ablative modalities usually are effective, but careful follow-up is important. The risk for these lesions leading to invasive squamous cell carcinoma of the external genitalia in immunocompetent patients is unknown but is probably low. Female partners of male patients who have squamous cell carcinoma in situ are at high risk for cervical abnormalities.

Subclinical Genital HPV Infection (Without Exophytic Warts)

Subclinical genital HPV infection is a term often used to refer to manifestations of infection in the absence of genital warts, including situations where infection is detected on the cervix by Pap test, colposcopy, or biopsy; on the penis, vulva, or other genital skin by the appearance of white areas after application of acetic acid; or on any genital skin by a positive test for HPV.

Subclinical genital HPV infection occurs more frequently than visible genital warts among both men and women. Subclinical infection of the cervix is most commonly diagnosed by Pap screening with the detection of squamous intraepithelial lesions. The application of 3%--5% acetic acid usually turns HPV-infected genital mucosal tissue a whitish color. However, acetic acid application is not a specific test for HPV infection, and the specificity and sensitivity of this procedure for screening have not been defined. Thus, the routine use of this procedure for screening to detect subclinical infection is not recommended. However, some experienced clinicians find this test useful for identification of flat genital warts.

A definitive diagnosis of HPV infection is based on detection of viral nucleic acid (DNA or ribonucleic acid [RNA]) or capsid protein. Pap-test diagnosis of HPV does not always correlate with detection of HPV DNA in cervical cells. Cell changes attributed to HPV in the cervix are similar to those of SIL and often regress spontaneously without treatment. Tests that detect several types of HPV DNA in cells scraped from the cervix are available and may be useful in the triage of women with atypical squamous cells of undetermined significance (ASCUS) but not other types of cytologic abnormalities. Screening for subclinical genital HPV infection using DNA or RNA tests is not recommended.

Treatment

In the absence of coexistent SIL, treatment is not recommended for subclinical genital HPV infection diagnosed by colposcopy, biopsy, acetic acid application, or the detection of HPV by laboratory tests. The diagnosis of subclinical genital HPV infection is often not definitive, and no therapy has been identified that eradicates infection. In the presence of coexistent SIL, management should be based on histopathologic findings.

Management of Sex Partners

Examination of sex partners is unnecessary. Most sex partners of infected patients probably are already infected subclinically with HPV. No screening tests for subclinical infection are available. Likewise, whether patients who have subclinical HPV infection are as infectious as patients who have exophytic warts is unknown.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

Throughout the 2002 guideline document, the evidence used as the basis for specific recommendations is discussed briefly. More comprehensive, annotated discussions of such evidence will appear in background papers that will be published in a supplement issue of the journal *Clinical Infectious Diseases*.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate diagnosis, treatment, and management of patients with human papillomavirus (HPV) infection, including external genital warts, vaginal warts, urethral meatus warts, anal warts, oral warts, and subclinical genital HPV infection without exophytic warts.

- Treatment of genital warts can induce wart-free periods and result in the removal of symptomatic warts. If left untreated, visible genital warts may resolve on their own, remain unchanged, or increase in size or number. Determining whether treatment of genital warts will reduce transmission is difficult.

Subgroups Most Likely to Benefit:

Patients who are also pregnant, immunodeficient, or have squamous cell carcinoma in situ

POTENTIAL HARMS

- Complications rarely occur if treatments for warts are employed properly. Patients should be warned that persistent hypopigmentation or hyperpigmentation are common with ablative modalities. Depressed or hypertrophic scars are uncommon but can occur, especially if the patient has had insufficient time to heal between treatments. Rarely, treatment can result in disabling chronic pain syndromes (e.g., vulvodynia or hyperesthesia of the treatment site).
- Most patients using podofilox 0.5% solution or gel experience mild/moderate pain or local irritation after treatment.
- Local inflammatory reactions are common with imiquimod; these reactions usually are mild to moderate.
- With cryotherapy, pain after application of the liquid nitrogen, followed by necrosis and sometimes blistering, is common.
- Over-application or failure to air-dry podophyllin resin can result in local irritation caused by spread of the compound to adjacent areas.
- Trichloroacetic acid (TCA) solutions have low viscosity comparable with that of water and can spread rapidly if applied excessively; thus, they can damage adjacent tissue.
- Interferon therapy is associated with a high frequency of systemic adverse effects.

Subgroups Most Likely to be Harmed:

The safety of podofilox, imiquimod, and podophyllin during pregnancy has not been established.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These recommendations were developed in consultation with public- and private-sector professionals knowledgeable in the treatment of patients with sexually transmitted diseases (STDs). They are applicable to various patient-care settings, including family planning clinics, private physicians' offices, managed care organizations, and other primary-care facilities. When using these guidelines, the disease prevalence and other characteristics of the medical practice setting should be considered. These recommendations should be regarded as a source of clinical guidance and not as standards or inflexible rules. These guidelines focus on the

treatment and counseling of individual patients and do not address other community services and interventions that are important in sexually transmitted disease/human immunodeficiency virus (STD/HIV) prevention.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention. Human papillomavirus infection. Sexually transmitted diseases treatment guidelines. MMWR Recomm Rep 2002 May 10; 51(RR-6):53-7.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1993 (revised 2002 May 10)

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

GUIDELINE DEVELOPER COMMENT

These guidelines for the treatment of patients who have sexually transmitted diseases (STDs) were developed by the Centers for Disease Control and Prevention (CDC) after consultation with a group of professionals knowledgeable in the field of STDs who met in Atlanta on September 26--28, 2000.

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

The information in this report updates the "1998 Sexually Transmitted Diseases Treatment Guidelines" (MMWR 1998; 47[No. RR-1]).

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site:

- [HTML version](#)
- [Portable Document Format \(PDF\)](#)

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Workowski KA, Levine WC, Wasserheit JN. U.S. Centers for Disease Control and Prevention guidelines for the treatment of sexually transmitted diseases: an opportunity to unify clinical and public health practice. *Ann Intern Med.* 2002 Aug 20; 137(4): 255-62. Electronic copies: Available through [Annals of Internal Medicine Online](#).
- Sexually Transmitted Diseases Treatment Guidelines 2002 for PDA or Palm OS. Available from the [CDC National Prevention Information Network \(NPIN\) Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

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