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British association for sexual health and HIV national guideline for the management of anogenital warts in adults (2024)

Diarmuid Nugent[1], Ade Apoola[2], Harry Coleman[3], Cindy Gilmour[1], Mark David Lawton[4], Achyuta Nori[5], Jonathan D C Ross[6], Gary Whitlock[1] and Hannah Yeend-Curd-Trimble[3]

Abstract

This guideline offers recommendations on the diagnosis, treatment and health promotion principles needed for the effective management of human papillomavirus (HPV)-related warts at anogenital sites including the external genitals, vagina, cervix, urethra, perianus and anal canal. The guideline is aimed primarily at patients aged 16 years or older presenting to healthcare professionals working in level 3 sexual health services in the United Kingdom. However, the principles of the recommendations may be applied in other care settings, including in primary care, using locally adapted care pathways where appropriate. The management of HPV-related anogenital dysplasia or warts at other extragenital sites is outside the scope of this guideline.

Keywords

Genital warts < viral disease, HPV (human papillomavirus) < viral disease

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New in the 2023 guideline

- All recommendations are rated according to the GRADE system, including those for the clinical evaluation, treatment and provision of advice for individuals presenting with anogenital warts
- Speculum vaginal examination only required if internal warts are suspected (due to vulvovaginal symptoms or warts which may extend into introitus)
- Recommendations provided for treatments not included in the 2015 guidelines: 5-fluorouracil cream, potassium hydroxide, photodynamic therapy and nitrizinc complex
- Podophyllotoxin solution (0.5%) is preferred over the 0.15% cream formulation where it can be easily applied owing to slightly superior efficacy
- Increased emphasis for patients with an inadequate response to treatment to switch to an alternative option, including a suggested upper limit of four cryotherapy treatment sessions
- We encourage expanded access to treatments with high clearance rates (such as laser, electrosurgery and surgical excision) particularly for patients with difficult to treat warts
- Updated review of evidence for the use of HPV vaccines in individuals with anogenital warts to improve clearance and/or prevent recurrence

Introduction and methodology

Objectives

This guideline offers recommendations on the diagnosis, treatment and health promotion principles needed for the effective management of human papillomavirus (HPV)-related warts at anogenital sites including the external genitals, vagina, cervix, urethra, perianus and anal canal. The guideline is aimed primarily at patients aged 16 years or older presenting to healthcare professionals working in level 3 sexual health services in the United Kingdom. However,

[1] Chelsea & Westminster Hospitals NHS Foundation Trust, London, UK
[2] Derbyshire Community Health Services NHS Foundation Trust, Derby, UK
[3] Central & North West London NHS Foundation Trust, London, UK
[4] Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK
[5] Guy's & St Thomas' NHS Foundation Trust, London, UK
[6] University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Corresponding author:
Diarmuid Nugent, Chelsea & Westminster Hospitals NHS Foundation Trust, 56 Dean Street, Soho, London W1D 6AQ, UK.
Email: diarmuid.nugent@nhs.net

the principles of the recommendations may be applied in other care settings, including in primary care, using locally adapted care pathways where appropriate. The management of HPV-related anogenital dysplasia or warts at other extragenital sites is outside the scope of this guideline.

Methods

This guideline was produced according to specifications set out in the "BASHH 2020 Framework for guideline development and assessment" accessed at https://www.bashhguidelines.org/media/1247/2020-guidelines-framework.pdf

The writing group formulated PICO (Patient/population, Intervention, Comparison, Outcome) questions as detailed in Appendix 1 which formed the basis of the literature search. A literature search for evidence published since drafting of the 2015 guidelines was performed using the search strategy detailed in Appendix 2 via the following databases: MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL). We prioritised evidence from randomised controlled trials (RCTs) and systematic reviews; non-controlled studies, observational studies and case series were considered where evidence from RCTs was limited or absent. Guidelines from the International Union Against STIs (IUSTI-Europe), US Centres for Disease Control and Prevention (CDC) and national guidelines from Germany, Australia, New Zealand and Canada were also reviewed. The GRADE system was used to evaluate evidence and to formulate and rate the strength of recommendations.

Piloting and feedback

The first draft was produced by the writing group and then circulated to BASHH Clinical Effectiveness Group (CEG) for evaluation using the AGREE appraisal tool. The draft was also circulated to current members of the BASHH HPV SIG for expert review. The second draft of the guideline was posted on the BASHH website for wider consultation for 2 months and simultaneously reviewed by the BASHH Public Panel. Following the consultation, the modified draft was piloted in a sample of sexual health clinics.

Aetiology

Anogenital warts (AGW) are caused by the human papillomavirus (HPV) of which over 100 genotypes have been identified but around 90% of warts at the anogenital site are caused by HPV types 6 or 11. The mode of transmission is usually by sexual contact - transmission between sexual partners is common and also occurs in the absence of visible warts.[1] Longitudinal studies suggest that warts develop in 15%–64% of those infected with HPV 6 or 11.[2–4] The time interval between genital HPV infection and the appearance of warts is highly variable but appears to be shorter in women (median 3 months) than men (median 11 months).[2,4]

HPV can be transmitted perinatally and genital lesions resulting from transfer of infection from hand warts (HPV type 2) may also occur.[5] There is no good evidence for transmission via fomites. AGW are benign lesions. Some genital warts may contain additional oncogenic HPV types, but oncogenic HPV most commonly causes anogenital dysplastic lesions and cancers rather than typical warts. HPV infection is very common, but most infections do not result in visible genital tract lesions, and resolve spontaneously within a year.[2–4,6] The estimated annual incidence of genital warts in developed world populations is about 0.15% of the adult population per year[7] with a prevalence of HPV around 3% in adult men in the USA.[8] The prevalence of HPV 6 and 11 in the UK has fallen in vaccinated groups with an associated 35% decline in the number of genital warts diagnosed between 2010–2019.[9] However, genital warts remain common with around 50,000 new cases treated each year in sexual health clinics in England.[9]

Clinical features

AGW are benign epithelial lesions usually up to 5 mm in diameter.[10] Lesions are most often multiple and non-pigmented however different pigment patterns may occur, especially on keratinised skin. Four morphological types are described: condylomata acuminata (flesh-coloured, soft exophytic papillomatous lesions); keratotic warts (thickened horny papules); flat warts (macular lesions) and papular warts.[10] Lesions may be seen anywhere throughout the anogenital skin and mucosa including the vulva, vagina, cervix, urethral meatus and anal canal.[11] Extragenital sites affected by genital HPV subtypes include the lips, oral mucosa, oropharynx, larynx, conjunctivae and nasal cavity. Apart from their presence, most warts are asymptomatic although symptoms such as itching, bleeding or pain can occasionally occur.

Diagnosis

Visual inspection is usually sufficient to diagnose warts although magnification using a colposcope or dermatoscope may be helpful for small lesions.[12] Biopsy may be needed where there is diagnostic uncertainty. Differential diagnosis includes anatomical variants (pearly penile papules, papillomatosis vulvae, Fordyce spots), other sexually transmitted infections (molluscum contagiosum, condylomata lata), benign skin lesions (fibroma, seborrheoic warts, naevi), and pre-malignant and malignant conditions (intraepithelial neoplasia, Bowen's disease, Bowenoid papulosis, carcinoma and malignant melanoma). AGW are by definition benign lesions. However malignant or pre-malignant lesions, such as intra-epithelial neoplasia, may co-exist within wart lesions. Where there are atypical features such as bleeding, ulceration or clinical suspicion of malignancy, urgent biopsy is recommended.

Remote diagnosis through photographs of lesions using telemedicine has significant potential for improving access

to clinical care, but further evidence on accuracy and acceptability is required before the routine use of remote diagnosis can be recommended.[13]

Recommendations

We recommend that individuals presenting with new or recurrent warts are offered careful examination of the entire external anogenital area and urethral meatus with good illumination (1D)

We suggest that speculum examination is offered to those with warts at the introitus where the upper limit cannot be visualised, or in those with external warts and other vulvovaginal symptoms such as irritation, bleeding or discharge (2D)

We suggest that proctoscopy and digital anorectal examination are offered to those with warts at the anal margin where the upper limit cannot be visualised, or in those with external warts and other anal canal symptoms such as irritation, bleeding or discharge (2D)

We recommend that atypical clinical features and/or clinical suspicion of malignancy should prompt urgent biopsy of lesions (1D)

We suggest that biopsy is considered where there is diagnostic uncertainty or non-response to treatment (2D)

General advice

Patients should receive a comprehensive explanation of their condition to include information on the natural history, transmission and treatment of warts. This should be reinforced with up-to-date written advice (see BASHH Patient Information Leaflet). It is important to provide reassurance that AGW are distinct from pre-malignant or malignant lesions and that screening intervals remain unchanged for those eligible for the NHS Cervical Screening Programme. Consistent condom use can reduce onward transmission of HPV and the spread of warts to sexual partners.[14–16] Smoking is associated with increased AGW prevalence and incidence and a reduced clearance of HPV infection; higher AGW recurrence rates have also been shown in current smokers.[17,18] The psychological impact of an AGW diagnosis is well described and may result in significant anxiety, depression and psychosexual dysfunction.[19–21]

Recommendations

We recommend that patients are offered a comprehensive verbal and written explanation of their condition and management options (1D)

We recommend consistent condom use to reduce the risk of onward transmission of warts and HPV to sexual partners (1B)

We recommend provision of smoking cessation advice (1B)

We recommend provision of psychological support to those who experience significant distress related to their AGW diagnosis (1C)

Benefits of treatment

The aims of treatment include the clearance of visible warts, the restoration of the normal appearance of the anogenital skin and/or mucosa and the prevention of wart recurrence. There is no evidence that treatment of warts reduces the risk of onward transmission to sexual partners. As warts may spontaneously regress, deferral of treatment is acceptable if this is the patient's preferred option.[6] All treatments may result in localised skin reactions and/or scarring and therefore it may be preferable to defer treatment for very small lesions and where the diagnosis is unclear.

Choice of treatment

AGW treatments include self-applied (topical) agents and clinician-applied therapies (topical or ablative). The choice of treatment depends on treatment availability, patient preference, volume and location of lesions and the patient's prior experience of and response to treatment. There is no single best treatment for warts and direct comparisons of clearance and recurrence rates between trials are problematic due to differences in study populations and protocols.

Treatment algorithms

The development of a local treatment algorithm has been shown to improve patient outcomes and is recommended, based on local availability of treatment options.[22] A suggested algorithm is shown in Appendix 3 which can be adapted according to availability of treatment options, clinician experience and patient preference.

In choosing between self-applied agents, podophyllotoxin and imiquimod appear broadly equivalent in safety and efficacy.[23–26] However its lower cost, shorter treatment duration and faster mode of action may make podophyllotoxin preferred as a first choice. Sinecatechins have similar clearance rates in trials[27–29] but no randomised head-to-head comparisons with other treatments have been performed and the frequency of dosing (three times daily) may be a barrier to adherence. Current pricing information for recommended self-administered agents is summarised in Table 1 although the cost paid for overlabelled stock procured by sexual health services may differ and vary regionally.

For clinician-applied treatments, the highest clearance rates have been observed for laser, electrosurgery and surgical excision which have also been shown in network meta-analyses comparing multiple treatments to be the most successful approach in clearing warts.[30,31] Fewer treatment sessions are typically required to achieve wart clearance than with cryotherapy or trichloroacetic acid (TCAA). Whilst surgical treatments are likely to be of higher cost and to require specialist equipment and clinical expertise to deliver, their provision may be cost-effective for individuals with recurrent or recalcitrant warts.[32]

Table 1. Current drug tariffs for self-applied treatments for AGW recommended for first-line use (source: British national formulary on-line available at: https://bnf.nice.org.uk/).

Active ingredient	Formulation	Brand name	Manufacturer	Price
Podophyllotoxin	0.5% solution	Warticon®	Phoenix Labs ltd	£14.86 (3 mL)
Podophyllotoxin	0.15% cream	Warticon®	Phoenix Labs ltd	£17.83 (5 g)
Imiquimod	5% cream	Aldara®	Viatris UK healthcare ltd	£48.60 (4-weeks course, 12 × 250 mg sachets) £194.40 (16-weeks course, 48 ×250 mg sachets)
Camelia sinensis (sinecatechins)	10% ointment	Catephen®	Kora healthcare	£39.00 (15 g)

Recurrence

Recurrence of warts following successful clearance can occur after any treatment modality and there is limited evidence that any specific treatment is associated with a reduced recurrence rate following initial clearance of warts.[30] Individuals with lesions at more than one anatomical site may be more likely to experience recurrence.[33] The addition of topical treatment following ablative therapy may reduce the risk of subsequent recurrence; the best evidence is for 4–8 weeks of imiquimod following CO_2 laser.[34] However, evidence is lacking to recommend this strategy following other forms of ablation or using other topical agents.

Recommendations

We recommend that patients are given a full explanation of the strengths and weaknesses of the treatment options available to them and are fully involved in choosing their treatment (1D)

We recommend that a local treatment algorithm is in place to support treatment decisions (1C)

We recommend that individuals with recalcitrant or persistently recurrent warts are prioritised for ablative treatment with laser, electrosurgery or surgical excision (1A)

We suggest that treatment with CO_2 laser can be followed with a 4–8 weeks course of imiquimod to reduce the risk of subsequent recurrence (2A)

Recommended treatments

The following treatments are recommended for the treatment of external AGW.

Self-applied treatments

Imiquimod (1A)

Imiquimod is an immune response modifier which acts via induction of alpha-interferon and other cytokines.[24,25,35–38] In the UK it is available as a 5% cream preparation (Aldara®) supplied in sachets, each containing sufficient cream to cover 20 cm^2 wart area. The cream should be applied three times weekly in a thin layer directly to wart tissue prior to normal sleeping hours and washed off after 6–10 h. Local skin reactions, most commonly erythema, excoriation and erosion, occur 70%–80% of treated individuals and correlate with clinical response. Treatment should be applied until disappearance of warts for a maximum of 16 weeks. It has the potential to exacerbate inflammatory skin conditions and should be used with caution in solid organ transplant recipients and in individuals with autoimmune conditions.

Recommendations. We suggest that where individuals have a <50% reduction in wart volume after 8 weeks' of imiquimod, a switch to an alternative treatment should be considered (2B)

Podophyllotoxin (1A)

Podophyllotoxin is an anti-mitotic agent which arrests mitosis in metaphase leading to epithelial cell death of virally infected cells.[26,39–45] It is available as 0.5% solution or 0.15% cream which should be applied twice daily directly to lesions on three consecutive days, repeated weekly for a maximum of 4 weeks. Recent RCT evidence suggests it can be continued beyond this licensed duration to achieve maximal wart clearance.[26] Although it is not licensed for use on perianal lesions, RCT evidence suggests podophyllotoxin is safe and effective at this site.[26,46,47] The cream preparation is preferable for ease of application at perianal and other difficult to reach sites although has been shown to have slightly inferior efficacy to solution for initial clearance of warts.[24,31] Local skin reactions are common and it may be caustic to normal skin.

Recommendations. We suggest that podophyllotoxin solution should be preferred over the cream formulation at easy to reach sites owing to slightly superior efficacy for initial wart clearance (2A)

We recommend that podophyllotoxin 0.15% cream may be used for the treatment of external perianal warts on an off-license basis (1B)

We recommend that podophyllotoxin can be continued beyond its licensed duration where there is >50% wart clearance following 4 weeks of treatment (1A)

We suggest that petroleum jelly may be applied to healthy skin adjacent to lesions to limit damage from inadvertent contact with podophyllotoxin solution (2D)

Sinecatechins (1A)

Sinecatechins is the extract of *Camellia sinensis* (green tea) plant and contains the active ingredient epigallocatechingallate.[27–29,48] Its mechanism of action is not fully known. It is available in the UK as a 10% ointment (Catephen®) which is applied directly to warts three times daily until clearance, for a maximum duration of 16 weeks. It is not necessary to wash the ointment off the affected area prior to the next application. Mild inflammatory reactions are common following application and correlate with clinical response.

Recommendations. We suggest that where individuals have a <50% reduction in wart volume after 8 weeks' of sinecatechins, switch to an alternative treatment should be considered (2B)

Clinician-applied treatments

Cryotherapy (1A)

Cryotherapy destroys warts by thermal induced cytolysis and is usually available as a liquid nitrogen open spray or, less commonly, closed systems with a cryoprobe opposed directly against the lesion using nitrous oxide or CO_2 cylinders.[49–59] Portable canisters with alternative compressed gas formulations (Norfluorane/Dimethyl ether/propane) have become available more recently. These offer advantages over standard cryotherapy systems in their storage and maintenance, however no safety or efficacy data are yet available to support their use for AGW treatment.

Multiple treatment sessions may be required to achieve wart clearance. Systematic studies on the optimal frequency and application technique for cryotherapy are lacking although retrospective data suggest weekly treatment may reduce the total number of applications required versus longer intervals.[60] Local anaesthetic is not usually required although individuals may experience localised pain, blistering, pigment change or scarring following treatment.

Recommendations. We recommend that cryotherapy is given weekly with one or two freeze-thaw cycles performed per treatment session (1B)

A recommended freeze-thaw cycle should involve cautious application of the cryo-spray in brief bursts to achieve visible freezing of the lesion(s) and 1 mm surrounding halo for up to 20 s followed by visible thawing (1B)

We suggest that where individuals have not achieved complete wart clearance after four cryotherapy sessions, switch to an alternative treatment should be considered (2C)

Laser (1A)

Laser therapy destroys warts by inducing vascular thrombosis in dermal papillary vessels leading to destruction of keratinocytes.[23,30,31,54,61,62] Destruction of the blood vessels results in release of pro-inflammatory cytokines that enhances the cellular immune response which may aid in eradication of HPV. In addition, ablative laser therapy uses longer wavelength laser that is absorbed by water and vaporises keratinocytes.

Four modalities of laser therapy are used for treatment of warts:

(1) Pulsed dye
(2) Neodymium-doped yttrium aluminum garnet (Nd:YAG)
(3) Carbon dioxide (CO_2)
(4) Erbium-doped yttrium aluminum garnet (Er:YAG)

Pulsed dye and Nd:YAG lasers are non-ablative lasers which may be less effective for pigmented lesions and individuals with darker skin. CO_2 and Er:YAG are ablative lasers.

Although comparative studies with other wart treatments are limited, evidence from systematic reviews and network meta-analyses suggest higher clearance rates than standard topical treatments or cryotherapy albeit at higher cost.[23,30,31] Adequate room ventilation and personal protective equipment (PPE) are required due to the potential presence of HPV virions in the smoke plume generated by treatment administration.[63,64]

Recommendations. We recommend that local anaesthetic is administered prior to laser treatment for AGW (1B)

We recommend that exhaust ventilation and PPE including N95 or FFP2/3 particulate respirator are employed during laser treatment of AGW (1A)

Electrosurgery (1A)

Electrosurgery involves the use of electricity to destroy AGW. There are two types:

(1) Electrocautery (thermocautery): A direct current is passed through a wire to generate heat used to destroy tissues. The most common technique is the loop electrosurgical excision procedure (LEEP) where the wire is in the form of a loop used to curette and cauterize tissues. Disposable cautery pens are also available that can be used for treatment of limited (<10) warts.

(2) True electrosurgery: A high frequency alternating current is passed from an electrode through the patient's skin to generate heat. Two techniques are used for treatment of AGW:
   (a) Electrofulguration: The electrode is held 1-2 mm from the surface of the lesion causing an arcing spark resulting in tissue carbonisation and destruction of the AGW with the formation of a thick eschar.
   (b) Electrodessication: The electrode is in contact with the tissue causing heating and dehydration of the superficial epithelium resulting in coagulation of tissue with minimal scarring and pigment loss.

Although comparative studies with other wart treatments are limited, higher clearance rates than cryotherapy have been reported and a single treatment application is usually sufficient.[31,49,59,61,65,66]

Recommendation. We recommend that local anaesthetic is administered prior to any electrosurgery treatment for AGW (1B)

We recommend that exhaust ventilation and PPE including N95 or FFP2/3 particulate respirator are employed during electrosurgery treatment for AGW (1A)

Surgical excision (1B)

Excision can usually be performed under local anaesthetic using scissors, scalpel or curettage.[23,67–69] It may be particularly useful for small numbers of warts and for pedunculated lesions.

Trichloro-acetic acid (1A)

Trichloro-acetic Acid (TCAA) in 80%–90% solution is directly corrosive to tissue.[23,50,52,56,57] It should be applied sparingly to warts by a clinician using a cotton-tip applicator or plastic loop in a single, brief application per treatment session. It is generally administered weekly and multiple treatment sessions are usually required to achieve clearance.

Recommendations. We recommend that TCAA should not be placed on or immediately adjacent to the examining couch to avoid the risk of spillage over the patient (1D)

We recommend that a neutralising agent (eg. Sodium bicarbonate) should be readily available in case of spills during TCAA treatment (1D)

We recommend that a local anaesthetic gel be applied to the treated area after treatment to reduce discomfort (1D)

We suggest that where individuals have achieved <50% wart clearance after four applications of TCAA, switch to an alternative treatment should be considered (1C)

Other treatments

The following treatments may be considered when recommended treatments are unavailable, unsuitable or have failed.

5-Fluorouracil (2A)

Topical 5-fluorouracil is a cytostatic agent licensed for the treatment of malignant and premalignant skin lesions including actinic keratoses and Bowen's disease. It is not licensed for the treatment of AGW but has been shown to be effective in various preparations in clinical trials with similar clearance rates to approved topical agents.[23,70–75] In the UK it is available as a 5% cream preparation which is applied thinly once or twice daily for 3–4 weeks. Treatment response is characterised by inflammation and erosion followed by re-epithelialisation. Animal studies have demonstrated teratogenicity and it should not be used in pregnancy or in individuals attempting to father a child; females of child-bearing potential should use effective contraception during and for 7 months following completion of treatment.

Potassium hydroxide (2A)

Potassium hydroxide 5% is a strong alkali which is caustic to normal skin and has been shown to be effective in treating AGW.[55,72,76] In trials it was self-applied once or twice daily via a cotton tip applicator for up to 12 weeks. In the UK it is available as an over-the-counter treatment for molluscum contagiosum (MolluDab®) but is not licensed for the treatment of AGW.

Photodynamic therapy (2A)

Photodynamic therapy (PDT) involves application of a topical photosensitive agent (eg. 5-aminolaevulinic acid) directly to lesions followed by exposure to a beam of light. This activates the agent resulting in production of free radicals and/or reactive oxygen species which destroy cells. In the UK it is used for the treatment of skin lesions including basal cell carcinoma, actinic keratoses and Bowen's disease. Efficacy and tolerability appear high in clinical trials in which it has been compared favourably to CO_2 laser.[62,77–79]

Nitrizinc complex (2B)

Nitrizinc complex is a clinician-applied topical solution containing nitric acid, organic acids and zinc/copper salts which has a caustic action on warts and has shown similar efficacy to cryotherapy in one RCT among 120 individuals with previously untreated warts of <5 mm diameter on the external genitals or perianal area.[80] Several large case series also support its efficacy and tolerability.[81,82] Marketed in the UK as Verrutop® (Espère Healthcare Ltd), drops of the

solution are applied directly to warts via a capillary tube for up to four treatment sessions at fortnightly intervals.

Treatments not recommended

Interferon applied as a topical gel or intralesional injection have shown benefits over placebo in the clearance of warts.[83] However none are currently available in the UK and they are unlikely to offer significant advantage over other topical immunostimulant therapies. Inosine Pranobex (Imunovir®) is an oral immune stimulant treatment licensed as adjuvant treatment to ablative or topical therapy for AGW taken 1g three times daily for 14-28 days. Several small studies show a marginal benefit in wart clearance but there is insufficient evidence to recommend it for routine use.[84,85]

Warts at internal anatomical sites

Management of internal urethral, cervical, vaginal or anal warts may be challenging as they are often less accessible for clinical evaluation and the application/delivery of local treatments. Moreover, as individuals with internal warts are often excluded from clinical trials, the evidence base for treatments is largely limited to observational studies or case series. Internal warts may be of less cosmetic concern therefore deferral of treatment is an option for asymptomatic lesions. Nonetheless as visualisation of such lesions may be difficult, clinicians should have a low threshold for biopsy where there is any diagnostic uncertainty.

Surgical treatments (laser, electrocautery or excision) are acceptable for internal warts at any site and should be offered first-line where available.[86–88] For urethral warts, cryotherapy may be considered where the base of the wart is clearly visible on meatal eversion.[89] It is therefore important to examine the urethral orifice with a good light source (and meatoscope/otoscope if needed) to determine the size and proximity of lesions to the meatal opening. There is increasing evidence for the effectiveness of PDT for urethral warts.[90,91] Cryotherapy and TCAA may be useful for the treatment of vaginal, cervical or anal warts, although fume extraction is required to maintain visibility of lesions during cryotherapy. Imiquimod, used off-license, appears to be safe and effective when applied internally for anal warts.[92,93]

We recommend the following treatments are suitable for all urethral warts: surgical excision, laser, electrosurgery (1A)

We suggest that cryotherapy may be used for distal urethral warts where the base of the wart is clearly visible on meatal eversion (2C)

We suggest that PDT may be considered for distal urethral warts where clinical provision is available (2A)

We recommend the following treatments for vaginal warts: surgical excision, laser, electrosurgery, cryotherapy or TCAA (1B)

We recommend the following treatments for cervical warts: surgical excision, laser, electrosurgery, cryotherapy or TCAA (1A)

We recommend colposcopy examination of all suspected HPV-related cervical lesions to differentiate between low-grade and high-grade lesions (1C)

We recommend the following treatments for anal warts: surgical excision, laser, electrosurgery, cryotherapy, TCAA or imiquimod (1B)

Pregnancy & breastfeeding

AGW may increase in size and number during pregnancy. As warts may spontaneously resolve in the puerperium, deferral of treatment should be considered where acceptable to the patient. Where treatment is indicated, ablative treatments are preferred with most published data available for cryotherapy and laser.[94,95] TCAA can also used as it is not absorbed systemically although clinical studies to support its use are lacking.

At present, no self-applied topical agent is licensed for use during pregnancy or breastfeeding. Although recent safety data for imiquimod and podophyllotoxin are reassuring,[94,96] there is insufficient evidence to recommend either for routine use given the availability of safe and effective alternatives.

We recommend that the following treatments may be used safely during pregnancy and breastfeeding: cryotherapy, laser, electrosurgery, excision and TCAA (1C)

HPV can be transmitted vertically during delivery and although there is currently no evidence that treatment of HPV-related lesions reduces the risk of transmission, treatment may be considered to reduce the viral burden to the neonate. Caesarean section is not usually indicated to prevent neonatal transmission but may rarely be needed where there is obstruction of the birth canal.[94,97] Juvenile-onset recurrent respiratory papillomatosis (JORRP) is a rare complication of neonatal HPV infection usually caused by types 6 or 11 and estimated to affect 4.3/100,000 births.[98] A history of maternal AGW is a strong risk factor and rates of JORRP incidence are estimated at 6/1000 births from individuals with current or prior AGW.[99] Delivery by caesarean section has not been shown to be protective and is not recommended.

We recommend that individuals with AGW during pregnancy should be reassured of the low absolute risk of significant HPV-related complications in the neonate (1C)

Immunocompromised patients

Immunocompromised individuals, including those living with advanced HIV (CD4 count<200) or organ transplant recipients, are at increased risk of AGW as well as other HPV-related conditions.[100,101] Such individuals may present with

more severe or extensive disease and clinicians should be alert to their higher risk of malignancy, particularly where lesions are atypical in appearance or fail to respond to treatment.[102] Nonetheless in view of the limited trial data for these populations, treatment recommendations do not differ from non-immunocompromised individuals.[103]

Human papillomavirus vaccine

In the UK, HPV preventative vaccination was introduced in 2008 for girls aged 12-13 (with a catch-up programme for those up to 18 years of age) and extended to include boys in 2019. Two HPV vaccines which include coverage against genotypes 6 and 11 are currently licensed, the quadrivalent vaccine Gardasil® and nonavalent Gardasil®9 (Sanofi Pasteur MSD). The quadrivalent vaccine (covering HPV 6/11/16/18) provides protection against the principal causes of both benign and malignant genital HPV disease and was used in the UK vaccine programme from 2012; from 2022 this was replaced by the nonavalent vaccine which offers extended coverage to HPV genotypes 31/33/45/52/58.

HPV vaccine is highly effective for the prevention of AGW when administered prior to coitarche, as demonstrated by the marked reduction in AGW incidence in age-groups offered vaccination via the UK school-based programme.[104] Trials have so far failed to demonstrate a significant therapeutic benefit of vaccine for those with existing warts either for clearance of warts or a reduction in subsequent recurrence.[26,105,106] The use of vaccine for the treatment of warts is therefore not recommended. However, in view of the clear benefits in reducing the risk of HPV-related anogenital intra-epithelial neoplasia and invasive cancer, we recommend that eligible individuals either with or without pre-existing AGW should be offered vaccination, in accordance with national guidance.[107]

Follow-up

Routine follow-up is not required for individuals whose warts have resolved. Follow-up should be arranged for individuals with warts still present at the end of treatment, or at 8 weeks following treatment initiation with imiquimod or sinecatechins.

Contact tracing and treatment

Routine evaluation or notification of sexual partners is not required for individuals with AGW.

Auditable outcomes

Adherence to a locally designed treatment procotol – target >90%

Proportion of individuals receiving cryotherapy completing four or fewer treatments - target >95%

Offer of speculum examination when vulvovaginal symptoms present or external warts at introitus that cannot be fully visualised – target 100%

Offer of proctoscopy and digital anorectal examination when anorectal symptoms present or external warts at anal margin that cannot be fully visualised – target 100%

Provision of patient-focussed written information (as leaflet, weblink or similar) – target >90%

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Editorial independence

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ORCID iDs

Diarmuid Nugent https://orcid.org/0000-0001-7417-8440
Mark David Lawton https://orcid.org/0000-0003-1334-5764
Gary Whitlock https://orcid.org/0000-0003-3070-1281

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Appendix 1

List of PICO questions

(1) What is the incidence of new and recurrent anogenital warts in adults in the UK?
(2) What demographic, behavioural and co-morbidity factors are associated with anogenital warts?
(3) What is the natural history of untreated HPV 6/11 infection?
(4) How are HPV 6/11 and anogenital warts transmitted?
(5) What is the risk of malignancy in patients presenting with anogenital warts?
(6) In individuals with anogenital warts what type of examination will improve clinical outcomes such as wart clearance, identification of alternative or additional diagnoses, and improved patient satisfaction?
(7) In individuals with anogenital warts what investigations will improve clinical outcomes such as wart clearance, identification of alternative or additional diagnoses, and improved patient satisfaction?
(8) In individuals with anogenital warts what type of advice (content and mode of delivery) increases patient understanding and improves well-being?
(9) In partners of individuals with anogenital warts what type of advice (content and mode of delivery) increases understanding and improves well-being?
(10) What treatments are efficacious in the clearance and reduction of recurrence of anogenital warts?
(11) What treatment options are preferred for anogenital warts according to their anatomical site or other clinical features?
(12) In people with anogenital warts who are pregnant or lactating, what treatments are effective and safe?

Appendix 2

Search strategy for literature review

S1	MESH.EXACT.EXPLODE ("Genital Diseases, Female") OR MESH.EXACT.EXPLODE ("Genital Diseases, Male")
S2	ti,ab (anogenital or genitoanal or genito-anal or genital* or anal or perianal or peri-anal or anus or urethra* or penis or penile or vulva* or vagina or vaginal or cervix or cervical or venereal)
S3	S1 OR S2
S4	MESH.EXACT ("Warts")
S5	ti,ab (wart or warts or warty or verruca or verrucas or verrucae)
S6	S4 OR S5
S7	S3 AND S6
S8	ti,ab (condyloma*)
S9	ti,ab (lata or latum)
S10	S8 NOT S9
S11	MESH.EXACT ("Condylomata acuminata")
S12	S10 OR S11
S13	S7 OR S12
S14	MESH.EXACT ("Disease management") or MESH.EXACT ("Treatment outcome")
S15	ti,ab (treat* OR management OR therap* OR outcome*)
S16	S14 OR S15
S17	S13 AND S16
S18	(S17) and (la.exact ("English"))
S19	(S17) and (pd (>20121231)) and (la.exact ("English"))

Appendix 3

Suggested treatment algorithm for external genital warts only in individuals who are not currently pregnant or breastfeeding