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SPECIAL ARTICLE

New advances and challenges in sexually transmitted infections in the adolescent population. Document of the Working Group on HIV and STIs of the Spanish Society of Pediatric Infectious Diseases (SEIP)

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Received 30 January 2026; accepted 2 February 2026
Available online 15 May 2026

KEYWORDS
Sexually transmitted infections;
Adolescents;
Challenges and progress;
Prevention

Abstract Sexually transmitted infections (STIs) constitute a significant public health concern, with an increasing incidence in recent years. The management of these infections among the adolescent population represents a current challenge and should be based in comprehensive educational interventions (such as access to comprehensive sexuality education from early childhood and specialized training in sexual health for health care professionals), preventive strategies (including access to vaccination, implementation of pre- and post-exposure prophylaxis programs, and organized STI screening initiatives), and ensuring free, confidential access to public health care services for adolescents. This approach facilitates timely and appropriate

DOI of original article:
https://doi.org/10.1016/j.anpedi.2026.504172
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diagnosis and treatment, thereby preventing complications and reducing the stigma associated with these infections. This document describes the main advances in the management of sexually transmitted infections in the adolescent population, with an analysis of the specific characteristics of this vulnerable group.
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PALABRAS CLAVE
Infección transmisión sexual;
Adolescente;
Retos y avances;
Prevención

Nuevos avances y retos en infecciones de transmisión sexual en la población adolescente. Documento de Grupo de trabajo de VIH e ITS de la SEIP

Resumen Las infecciones de transmisión sexual son un problema de salud pública con una incidencia creciente en los últimos años. El manejo de estas infecciones en población adolescente es un reto urgente y actual, que debe basarse en intervenciones educativas (como el acceso a una educación sexual integral desde primera infancia y la formación en salud sexual de profesionales sanitarios), estrategias preventivas (acceso a vacunación, ofreciendo programas de profilaxis pre y post-exposición y programas de cribado de ITS), y garantizar el acceso libre y confidencial a los servicios sanitarios públicos a la población adolescente que permita un diagnóstico y tratamiento adecuado y precoz, evitando complicaciones y reduciendo el estigma asociado a estas infecciones. En este documento se describen los principales avances en cuanto a la atención de las infecciones de transmisión sexual en población adolescente, analizando las peculiaridades de esta población vulnerable.
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Introduction

Addressing sexually transmitted infections (STIs) among adolescents today is a topical, essential, and urgent matter. Adolescence is a stage of life in which individuals undergo significant changes—physical, psychological, and social. These changes make adolescents vulnerable, as they begin to rely less on their guardians and role models to manage their leisure time and may lack risk awareness. The increasingly early onset of sexual activity, coupled with the inconsistent use of barrier methods, an increase in the number of sexual partners, the normalization of risky sexual practices, difficulty accessing the health care system, easy access to pornography, and absence of early and comprehensive sexuality and emotional education in school curricula have contributed to an alarming increase in STIs among adolescents.

In this context, contracting an STI during adolescence can have significant health consequences not only in the short term, but also in the medium and long term, including unintended pregnancies, reproductive complications, vertical transmission and transmission among peers, a deleterious psychosocial impact, and stigmatization.

For all these reasons, it is essential to raise awareness of this reality among professionals who care for adolescents. The purpose of this document is to outline current epidemiological trends and recent advances in the prevention, diagnosis, and treatment of STIs among adolescents, in addition to highlighting existing challenges in providing care for this highly vulnerable population.

Current epidemiology of STIs among adolescents

Sexually transmitted infections (STIs) constitute a public health problem due to their increasing incidence and the complications that can develop if left untreated. There are eight pathogens responsible for the majority of STI cases: *Chlamydia trachomatis* (CT), *Trichomonas vaginalis* (TV), *Neisseria gonorrhoeae* (NG), *Treponema pallidum* (TP), herpes simplex virus (HSV), human papillomavirus (HPV), hepatitis B virus (HBV) and human immunodeficiency virus (VIH).[1]

Globally, it is estimated that more than one million people aged 15–49 years contract a curable STI each day, corresponding to an annual incidence of approximately 376 million new cases. These figures reflect the magnitude of the problem and its persistence in spite of advances in diagnosis and treatment. This has motivated an increase in STI screenings with the aim of detecting them earlier, and better diagnostic tests—such as molecular biology techniques—are now available, which together have contributed to an increase in the number of newly diagnosed cases. The reason notwithstanding, the overall increase in STIs is a reality, and the disease burden is particularly high among adolescents due to a combination of biological and behavioral risk factors.[1]

In Europe, epidemiological surveillance systems have shown a significant increase in STIs in recent years. In 2023, there was a 31% increase in gonorrhea cases and a 13% increase in syphilis cases compared to the previous year, with a cumulative increase of 300% and 200%, respectively,

compared to 2014. That same year, approximately 230 000 cases of CT infection were reported, making it the most frequently diagnosed bacterial STI.

In Spain, trends are similar to the global trends in Europe. The incidence of gonorrhea has nearly tripled over the past five years and is currently more than eleven times higher than in 2014. The incidence of chlamydia infection also continues to increase. The 15- to 24-year-old age group accounts for a significant proportion of new cases, with notable differences by sex. In this age group, the incidence of chlamydia is greater in women, which can be partly explained by biological factors and a higher probability of screening compared to men.[2]

These figures must be interpreted taking into account that many STIs are asymptomatic, especially in women, which leads to underdiagnosis and an underestimation of the actual incidence. This underscores the importance of systematic screening strategies for sexually active adolescents.

Associated factors: biological, behavioral, social, and structural

Cervical ectropion, a common condition among adolescents, and the composition of the cervical and vaginal microbiota appear to increase the risk of STIs.[3]

Behavioral factors include an earlier age of sexual debut (16.5 years in 2023),[4] an increase in the number of sexual partners, inadequate use of condoms (77% among adolescents aged 15–19 year),[4] and engagement in sexual activity under the influence of alcohol and other substances.

The lack of formal comprehensive sexuality education for children and adolescents, combined with early exposure to pornography, promotes risky sexual behavior.[3]

It is essential to ensure that adolescents have easy access to health services while safeguarding their privacy.[3]

Recent advances

Advances in diagnosis

In recent years, there have been significant advances in the diagnosis of STIs, with a particularly significant impact on the adolescent population. The latest updates to national and international guidelines recommend screening for chlamydia and gonorrhea at least once a year for sexually active women aged less than 25 years and men who have sex with men, as well as testing for HIV and syphilis from age 15 years, with varying frequency depending on specific sexual practices.[3,5] For CT and NG screening, self-administered vaginal swabs should be considered for sample collection in adolescents with a vagina, and first-void urine collection for adolescents with a penis, as these methods offer a high sensitivity and improve acceptability, in addition to pharyngeal and rectal swabs as applicable based on the individual's sexual practices.[3–6]

Molecular techniques are recommended for the detection of STIs such as chlamydia (CT) or gonorrhea (NG), and point-of-care (POC) tests—which take 90 min in Spain and 30 min with techniques available in the United States—facilitate not only targeted treatment, which limits the development of antimicrobial resistance, but also a reduction in the number of adolescents with STIs who do not receive treatment.[6,7] Fourth- and fifth-generation HIV tests, which detect antibodies and antigens, can shorten the window period to between 15 and 45 days.[8]

Advances in treatment

The treatment of STIs offers benefits both for individuals and in terms of public health, and it should be considered an essential preventive strategy, especially given the barriers to advances in vaccines. For adolescents, presumptive treatment based on the clinical manifestations is recommended if rapid diagnostic tests are not available, as follow-up is often challenging.[5,6]

Adherence to treatment is one of the major challenges in the adolescent population. Consequently, short treatment regimens (a single 1 g dose of azithromycin) for CT and simplified dosing (one tablet every 24 h) are recommended; or, in the case of HIV infection, long-acting medications (cabotegravir-rilpivirine injections every 2 months).[5–9]

Table 1 summarizes the treatment recommendations.

Advances in prevention

Comprehensive sex education starting in childhood is essential for preventing STIs and should cover not only STIs but also mental health, respect, and sexual pleasure. Age-appropriate information should be provided, and using a variety of formats (web, apps) can be helpful, especially for adolescents.[6]

In addition to vaccines against three viral STIs (HBV, HAV, and HPV, with boys now included in HPV vaccination programs) the mpox vaccine is available for individuals aged 12 and older. Although it is not approved for this indication, the 4CMenB meningococcal vaccine has been found to reduce gonococcal infections by 30%, particularly among adolescents.[6,7]

Pre-exposure prophylaxis (PrEP) is highly effective in reducing new HIV infections and is approved in Spain for individuals aged 16 and older. The difficulty of adhering to a daily oral regimen is one of the major limitations to the effectiveness of PrEP, and alternative strategies based on injectable drugs given every 2 (cabotegravir) or every 6 months (lenacapavir) have proven efficacious, although they are not yet available in Spain.[8]

In addition to post-exposure prophylaxis (PEP) for HIV, whose effectiveness is well known, PEP with doxycycline, known as Doxy PEP (200 mg within 72 h of high-risk sexual exposure) is now also available to reduce the risk of infection by CT and syphilis, and to a somewhat lesser extent gonorrhea, in selected populations with a higher predisposition to STIs (not investigated in adolescents).[7,8]

Successful programs

Recent interventions to address STIs in adolescents seek to facilitate access to preventive care, diagno-

Table 1 Empiric antibiotic treatment treatments based on the clinical presentation and treatment regimens for specific infections in adolescents.

Clinical presentation	Treatment	Comments
Urethritis/Cervicitis/Proctitis	Ceftriaxone 500 mg IM as a single dose AND Azithromycin 1 g PO as a single dose (preferred to ensure adherence) O Ceftriaxone 500 mg IM as a single dose AND Doxycycline 100 mg PO every 12 h for 7 days (most effective for rectal chlamydia infection)	In cases of proctitis, extend the course of doxycycline to 21 days if LGV is confirmed or suspected
First clinical episode of genital herpes	Acyclovir 400 mg PO every 8 h for 7—10 days OR Valacyclovir 1 g PO every 12 h for 7—10 days	Treatment should be initiated within 5 days of onset, or as long as new lesions develop or systemic symptoms persist
Episodic therapy for recurrent genital herpes	Acyclovir 800 mg PO every 12 h for 5 days OR Acyclovir 800 mg PO every 8 h for 2 days OR Valacyclovir 500 mg PO every 12 h for 3 days OR Valacyclovir 1 g PO every 24 h for 5 days	Episodic therapy for recurrent herpes is most effective if treatment is started within one day of the appearance of the lesion or during the prodromal phase
Microorganism	**Treatment**	**Comments**
Neisseria gonorrhoeae	Ceftriaxone 500 mg IM as a single dose	Perform test of cure 14 days after treatment in cases of pharyngeal infection
Chlamydia trachomatis	Azithromycin 1 g PO as a single dose (preferred to ensure adherence)) OR Doxycycline 100 mg PO every 12 h for 7 days (most effective for rectal chlamydia infection)	Perform test of cure after treatment if doxycycline is not used
Primary, secondary, and early latent syphilis	Penicillin G benzathine 2.4 million units IM as a single dose OR 50 000 IU/kg, up to a maximum of 2.4 million units	
Late latent syphilis, indeterminate syphilis, and tertiary syphilis with normal CSF findings	Penicillin G benzathine, 7.2 million units in total, administered in 3 doses of 2.4 million units IM (or 50 000 IU/kg, up to a maximum of 2.4 million units) each, at one-week intervals	
Neurosyphilis, ocular syphilis, and otosyphilis	Penicillin G sodium, 18–24 million units per day, administered in doses of 3–4 million units IV every 4 h for 10–14 days (or 200 000—300 000 IU/kg with a maximum of 2.4 million units every 4 h for 10–14 days)	

Abbreviations: CSF, cerebrospinal fluid; IM, intramuscular; IV, intravenous; LGV. lymphogranuloma venereum.

sis, and treatment, and the evidence shows that these efforts have improved health outcomes. Some of the features shared by these interventions are free access, confidentiality, absence of administrative barriers, and adaptation to the needs of young people. For example, in France, individuals younger than 26 years have free access to testing that does not require prior referral by a doctor. There are also some programs in Spain that provide free access to care without prior appointment in specialized youth or STI clinics, currently limited to large cities, which may allow ordering tests or checking results through online platforms like Drassanes Exprés (https://drassanesexpres.vallhebron.com/pacientes) or TÉSTATE (https://testate.org), available in Catalonia.

Current challenges

Despite the aforementioned advances, certain challenges and unique issues remain in providing care for STIs in the adolescent population, including those specific to this age group.

First, *access to health care is more complicated* compared to the adult population due to the need (or the belief that there is a need) for parental consent and notification, concerns about confidentiality, a lack of information on how to access health care services, and a shortage of specialized providers,[9,10] There are also geographical differences in the availability of resources in urban versus rural settings. Furthermore, it is important to note that, starting at age 12, the concept of the ''mature minor'' applies, allowing a physician to assess whether a minor has sufficient maturity to make a specific medical decision.[11] Making services accessible involves ensuring confidentiality (informing users about confidentiality and its limits) and offering services at convenient hours. In any case, adolescents must be allowed to access counseling and guidance without the consent of their parents or guardians, regardless of their age.

In this regard, another outstanding challenge in the management of STIs among adolescents is the implementation of *comprehensive sexuality education* in primary and secondary education and teacher training curricula. A recent study on the inclusion of sex education in the curricula of teacher education programs in the Spanish public university system found that there is still insufficient coverage of this area in basic teacher training curricula.[12] With regard to primary and secondary education curricula, the Ministry of Education, Vocational Training and Sports, the Ministry of Health, and the Working Group on Health-Promoting Schools support the proposal to include sexuality and emotional education in the curriculum; however, they note that each school has the autonomy to adapt this proposal to the specific circumstances of the local community and student body, as well as to the needs of its students and teachers,[13] which severely limits its enforceability and actual implementation.

Another current challenge in sexuality and emotional education is the fact that many adolescents turn to the internet as their primary source of information about sexuality. While they may find valuable resources online, it is also common for them to encounter misinformation or inappropriate content. A recent study examining the sources of sexual health information on TikTok demonstrated that content on social media lacks reliable sources.[14]

Compared with heterosexual and cisgender youth, youth who belong to sexual and gender minorities report lower rates of condom use in their most recent sexual encounter, earlier sexual debut (before age 13), and a higher number of sexual partners over their lifetime in association with various factors,[15] which may result in an increased incidence of STIs.[16] In addition, they have greater difficulty accessing health services due to non-inclusive cultures in health care systems or settings.[16] Pediatricians should be familiar with the concepts of sexual and gender minority and be aware that sexual identity is a characteristic of the individual that develops throughout childhood and adolescence.[17]

Finally, although it is not exclusive to adolescence, the *emergence of resistance to commonly used antimicrobials* is a global cause for concern in the field of STIs, particularly in relation to NG and *Mycoplasma genitalium* (MG).[18]

Future outlook

At present, the main lines of research on STIs, in both the general and adolescent populations, focus on several key areas.[19]

Prevention

Vaccine

With regard to NG, observational and case-control studies suggest that the 4-valent meningococcal B vaccine (4CMenB), originally designed for the prevention of meningococcal B disease, could reduce the incidence of gonorrhea by as much as 31%–47% in young people.[20] Although this has not been confirmed in the only randomized trial conducted in men who have sex with men[21] and no specific data on the adolescent population are available, its efficacy is to be determined in studies currently underway. The development of vaccines specifically targeting NG is in the preclinical and early clinical phases.[22]

For CT, there are vaccine candidates that have been found to be safe and immunogenic in phase I clinical trials in adult women.[23] Despite these advances, no vaccine against CT has been approved for clinical use in either adolescents or adults.

With regard to HSV, clinical trials have begun for two mRNA-based vaccines in young adults, with potential for preventive and therapeutic use in adolescents in the future.[24]

Multipurpose prevention technologies

Multipurpose prevention technologies (MPTs) are products designed to simultaneously prevent unintended pregnancy and STIs. They are being developed at a rapid pace and encompass various formulations and routes of administration. Contraceptive products currently under investigation include oral pills, vaginal rings, implants, injectables, vaginal films, and patches. Oral products and vaginal rings are in more advanced phases of development and are of particular interest to adolescents on account of their potential to foster high adherence and autonomy.[25]

Educational strategies

Recent evaluations of interventions that integrate digital resources (which can be implemented in clinical or community-based settings) have demonstrated their effectiveness in reducing risky behaviors and increasing STI testing rates, although the evidence regarding their impact on the prevalence of STIs is limited.[26]

These novel interventions must align with the ways in which adolescents seek and share information.[27] This requires involving them in the design of these strategies to undertand the digital channels they use regularly, integrate content into the platforms where they develop new emotional and sexual connections, and maintain rapid-response systems capable of countering myths that can spread at great speed.

Table 2 Recommended vaccinations for the prevention of STIs in adolescents.

	Pauta	Comments
Hepatitis A	Two doses (at 0 and 6 months)	If already vaccinated, serological testing is recommended to confirm an adequate immune response
Hepatitis B	Three doses (at 0, 1, and 6 months)	
Human papillomavirus	Single dose	
Mpox	Adolescents aged more than 12 years. • Pre-exposure: two doses (at 0 and 1 month) • Post-exposure: single dose (0.5 ml subcutaneously)	Pre-exposure: adolescents with repeated risky sexual behavior Post-exposure: following close contact, ideally within the first four days (though it can be administered up to 14 days later)
NG and 4CMenB	Two doses (at 0 and 1 month) if not vaccinated as a child Single dose (if vaccinated as a child)	Studies have shown that vaccination against meningococcal B disease with the 4CMenB vaccine reduces the risk of contracting gonorrhea; therefore, its use should be considered for adolescents at risk of STIs[38]

Diagnosis

Beyond rapid, low-cost point-of-care (POC) diagnostic techniques, the development of single-use molecular devices holds particular promise for routine clinical use, as they enable simultaneous detection of NG, CT, and TV in self-collected specimens, with results in under 30 min and accuracy comparable to that of conventional laboratory tests.[28] In addition, tests based on loop-mediated isothermal amplification (LAMP) have been validated that also allow rapid detection of multiple pathogens in less than one hour.[7]

This type of technology enables immediate diagnosis and therapeutic decisions in a single visit, which is particularly relevant in adolescents, given the high rates of loss to follow-up and premature treatment discontinuation in this population.

Treatment

Innovations in treatment include novel antibiotics, resistance-guided therapy (RGT) for MG and expeditive partner treatment (EPT).

Gepotidacin, zoliflodacin, and lefamulin are newly developed antimicrobials currently undergoing clinical trials for treatment of gonococcal infection in adults and adolescents.[29]

Resistance-guided therapy (RGT) for MG uses molecular techniques to identify genotypic resistance to macrolides and fluoroquinolones. In this approach, doxycycline is administered for 7 days while awaiting results, after which treatment can be targeted to the identified resistance profile.[30]

Expeditive partner treatment, which allows sexual partners to be treated without a prior medical evaluation, is endorsed by organizations in the United States such as the Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics,[31,32] but is not currently contemplated in European guidelines. The risks and benefits of this strategy must be evaluated, and steps taken to implement it if the balance is considered favorable.

Recommendations from the Working Group on HIV and STIs of the SEIP

- All children and adolescents have the right to receive comprehensive sexuality education starting in early childhood. This education should be provided in health care, school, and community-based settings. The information must be age-appropriate and delivered in clear, inclusive, and understandable language, and should provide tools that enable them to experience their sexuality in a positive way. Topics such as emotional well-being, sexuality, gender, sexual orientation, consent, and violence must be covered. In addition, training should include information on prevention methods, recognizing signs and symptoms associated with STIs, and the importance of appropriate treatment and contact tracing.[33]
- Similarly, we believe that training in sexual health is essential for health care professionals who work with children and adolescents (especially in the field of pediatrics) so that they can adopt an up-to-date, comprehensive, and destigmatizing approach.
- Free, easy, and confidential access to public health services must be guaranteed for adolescents, with delivery of comprehensive, high-quality care tailored to this population.[34] In Spain, the age of medical consent is set at 16, but it is important to note that between the ages of 12 and 15, a pediatrician may determine that a child is sufficiently mature (''mature minor'') to consent to tests and treatments and to decide whether or not to inform the child's family.[35]
- Free and unrestricted access to various barrier methods (such as condoms) and lubricants must also be ensured through health care, school, and community-based settings.
- Vaccination is one of the most effective tools for preventing infectious diseases, including STIs. Providers should review the current approved vaccination schedule and recommend the vaccines listed in Table 2.[36,37]
- In adolescents, screening should be conducted before they become sexually active and made accessible through

self-sampling. In children, screening should be conducted whenever sexual abuse is suspected.

- It is important to ensure follow-up and delivery of test results, as well as access to treatment if needed. If there are concerns about adherence to treatment, short-course, single-dose regimens should be offered and administered in the same visit to ensure they are taken correctly.
- It is important to conduct contact tracing in order to reach asymptomatic individuals who could spread STIs within the community.
- Providers should be aware of HIV pre- and post-exposure prophylaxis programs and facilitate access to them. Pre-exposure prophylaxis has been shown to be effective and safe and is approved in Spain for adolescents from age 16 years.[39]
- Sexually transmitted infections (STIs) reduce quality of life due to their potential complications (such as infertility) and the stigma associated with STIs, which makes it difficult to have a fulfilling sex life. Therefore, it is essential to monitor quality of life by integrating tools for its evaluation into routine clinical practice, to promote the psychosocial health of adolescents, and to work toward eliminating social and legal barriers and reducing stigma.[40]

Funding

Biomedical Research Networking Center for Infectious Diseases (CIBERINFEC), Instituto de Salud Carlos III (CB21/13/00077).

Declaration of competing interest

The authors have no conflicts of interest to declare.

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