

Perspective

New Perspectives on Cutaneous and Sexually Transmitted Infections: Clinical, Epidemiological, and Therapeutic Updates

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Abstract

Sexually transmitted infections (STIs) remain a global health burden. Beyond classical pathogens, dermatophytes are increasingly identified within sexually linked transmission networks. Genital dermatophytosis is a superficial fungal infection of the genital area, primarily caused by anthropophilic and zoophilic dermatophytes. Recently, *Trichophyton mentagrophytes* genotype VII and *Trichophyton indotineae* have emerged as clinically significant dermatophytes, increasingly linked to human-to-human and sexually associated transmission within highly interconnected sexual networks. These infections are often marked by inflammatory, persistent, and treatment-refractory presentations, with prominent genital involvement and rising antifungal resistance—particularly to terbinafine—posing growing diagnostic and therapeutic challenges. Doxycycline post-exposure prophylaxis (Doxy-PEP) has recently emerged as a novel preventive strategy for bacterial STIs, involving the administration of 200 mg doxycycline within 24–72 h after activities associated with increased infection exposure, particularly among men who have sex with men (MSM) and transgender women. While effective in reducing infections such as syphilis and chlamydia, its broader implementation raises concerns regarding antimicrobial resistance. Chemsex is an increasingly prevalent behavioural phenomenon, defined as the intentional use of psychoactive substances during sexual activity to enhance or prolong the experience, particularly among MSM. It is associated with multiple adverse effects, including increased STI transmission, substance dependence, drug toxicity, psychological disturbances, and significant challenges in treatment adherence and healthcare engagement. This review aims to provide a comprehensive and clinically oriented overview of emerging trends in STIs, with a particular focus on dermatophyte infections as pathogens with potential sexually associated transmission, alongside evolving prevention strategies and behavioral factors influencing transmission.

Keywords: sexually transmitted infections; dermatophytes; *Trichophyton mentagrophytes*; *Trichophyton indotineae*; genital dermatophytosis; doxycycline post-exposure prophylaxis; doxy-PEP; chemsex; antimicrobial resistance; MSM



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1. Introduction

1.1. Global Sexually Transmitted Infections (STIs) Burden

Sexually transmitted infections (STIs) still constitute a major and growing public health burden worldwide. The most clinically relevant STIs include bacterial infections such as chlamydia, gonorrhea, and syphilis; viral infections such as human immunodeficiency virus (HIV), human papillomavirus (HPV), and herpes simplex virus (HSV); as well as parasitic infections such as *Trichomonas vaginalis*. In recent years, dermatophytes are increasingly reported in sexually associated transmission networks, defining a novel and still under-recognized clinical entity. This observation challenges the traditional classification of STIs and suggests a broader, evolving spectrum of pathogens involved in sexually associated transmission. Despite growing evidence on emerging pathogens and changing transmission dynamics, the integration of these developments into a unified clinical framework remains limited, particularly regarding the role of dermatophytes as agents with sexually associated transmission.

STIs are primarily transmitted through sexual contact, including vaginal, anal, and oral intercourse, but they may also spread through direct skin contact or vertical transmission. According to the World Health Organization, more than 1 million sexually transmitted infections are acquired every day worldwide, corresponding to an estimated 374 million new cases annually of the four most common curable STIs—chlamydia, gonorrhea, syphilis, and trichomoniasis [1]. The burden is greatest in low socio-demographic regions and among young and middle-aged populations. From 1990 to 2021, incidence trends showed marked geographic variability, with stabilization or decline in high-income countries and substantial increases in low- and middle-income settings, reflecting persistent disparities in healthcare access, screening, and sexual health education [2].

1.2. European/Italian Trends in STIs

A 2025 European Centre for Disease Prevention and Control (ECDC) report confirms increasing STI trends, underscoring the need to update prevention strategies, reduce testing barriers, and strengthen surveillance systems [3]. Data from the Italian National Institute of Health demonstrate a progressive increase in STI notifications over time, with a particularly marked rise among men who have sex with men (MSM), who account for the largest contribution to recent trends. A temporary decline around 2020, during the COVID-19 pandemic, was followed by a sharp rebound, likely reflecting both behavioral changes and improved testing and reporting. In 2023, in Italy, STI notifications increased markedly compared with 2021, with the most substantial rise observed for gonorrhea (+83.2%), followed by primary and secondary syphilis (+25.5%) and chlamydia (+21.4%). Conversely, anogenital warts declined (−21.4%), likely reflecting the beneficial impact of HPV vaccination [4].

1.3. Clinical and Psychological Impact

Importantly, STIs may impact the patient's physical, psychological and sexual health and negatively influence their Quality of Life (QoL). A recent study showed that symptoms of depression were more common and severe in STIs patients compared with patients affected by other chronic diseases involving the ano-genital area, such as the chronic inflammatory bowel diseases (IBD). Sexual functioning is also slightly worse in STIs patients than in IBD patients. Therefore, physicians dealing with STIs should keep in mind the possible psychological consequences of these diseases [5].

1.4. Emerging Themes in STIs

These epidemiological changes are also influenced by evolving sexual behaviors and interconnected transmission networks, including phenomena such as chemsex, which further complicate prevention and management strategies.

This review aims to offer a comprehensive and clinically relevant overview of recent advances in cutaneous infections and STIs, with particular emphasis on emerging pathogens, evolving transmission patterns, and contemporary strategies for prevention and management. Therefore, the article focuses on synthesizing the most recent evidence on STIs from both clinical and behavioral perspectives. Indeed, novel STIs risk behaviors, such as chemsex, which involves the intake of a range of drugs (e.g., synthetic cathinones, gamma-hydroxybutyric acid/gamma-butyrolactone, ketamine, and occasionally a few other molecules) to enhance and prolong sexual experiences, are closely linked to the emergence of treatment-resistant infections, driving the clinical need for updated recommendations [6].

2. Emerging Cutaneous Dermatophyte Infections

Dermatophytoses are superficial fungal infections affecting keratinized tissues, including the skin, hair, and nails. Dermatophytes are ubiquitous filamentous fungi capable of colonizing and degrading these structures, leading to infection. The main genera involved in human infections are *Trichophyton*, *Epidermophyton*, and *Microsporum*. Dermatophytes are categorized according to their primary reservoir and mode of transmission into anthropophilic (human), zoophilic (animal), and geophilic (soil) species.

Genital dermatophytosis is a superficial fungal infection of the genital area, mainly caused by anthropophilic and zoophilic strains. It is more prevalent in tropical regions, and additional predisposing factors include HIV, diabetes mellitus, immunosuppression, and atopic dermatitis. Although classically transmitted through autoinoculation from tinea pedis or onychomycosis, increasing evidence suggests that sexual transmission may also occur. Another contributing factor is the inappropriate use of potent corticosteroids, whether administered topically or systemically [7,8].

Historically, *Trichophyton rubrum*, an anthropophilic species, has been the predominant dermatophyte implicated in human infections. A significant epidemiological shift in dermatophyte distribution has been observed in recent years, with a transition from *Trichophyton rubrum* to *Trichophyton mentagrophytes*, a pattern also observed in genital infections. Nenoff et al., in a large study conducted in India on patients with chronic and recalcitrant dermatophytosis, reported that *T. mentagrophytes* accounted for up to 93% of isolates, whereas *T. rubrum* was identified in only a small proportion of cases [9]. These infections were frequently characterized by extensive, inflammatory, and refractory lesions, often involving multiple body sites and showing a tendency toward chronicity and recurrence.

Several factors have been proposed to explain this shift, including the widespread misuse of topical combination creams containing corticosteroids, antifungals, and antibiotics, as well as inappropriate or incomplete antifungal therapy and self-medication practices. Environmental conditions in tropical and subtropical regions further facilitate fungal proliferation, while increased global travel and migration have contributed to the dissemination of these strains beyond endemic areas, ultimately leading to the emergence of more persistent infections.

Although *Trichophyton mentagrophytes* has traditionally been considered a zoophilic dermatophyte, emerging evidence indicates predominantly human-to-human transmission in the absence of a clear animal reservoir, suggesting an adaptive shift toward increased human tropism. Genotyping may be required to distinguish zoophilic from anthropophilic

strains, as certain genotypes—such as *T. mentagrophytes* genotypes VII and VIII—have demonstrated the capacity for sustained human-to-human transmission (Table 1).

Table 1. Key characteristics of emerging dermatophytes associated with sexually related transmission.

Feature	<i>Trichophyton mentagrophytes</i> Genotype VII (TMVII)	<i>Trichophyton indotineae</i> (<i>Trichophyton mentagrophytes</i> Genotype VIII)
Epidemiology	Initially reported in Southeast Asia; now emerging in Europe and the USA	Originated in South Asia; rapidly spreading globally
Transmission	Human-to-human, sexually associated (MSM)	Human-to-human, sexually associated; possible fomites
Population	Predominantly MSM; frequent STI co-infections	Mainly adults; immunocompetent; MSM cases reported
Clinical Presentation	Inflammatory lesions; (genital, gluteal, facial); may mimic bacterial infections	Persistent, extensive plaques (genital/inguinal); often refractory
Diagnosis	PCR-based identification	PCR-based identification
Treatment	Terbinafine generally effective (↓ susceptibility reported)	Terbinafine resistance; itraconazole often used
Key issue	Misdiagnosis and delayed treatment	Antifungal resistance and therapeutic failure

Abbreviations: MSM, men who have sex with men; PCR, polymerase chain reaction; ↓, reduction.

The revised taxonomy of dermatophytes proposed by de Hoog et al. distinguishes *Trichophyton interdigitale* from its closely related species *Trichophyton mentagrophytes*, which were previously grouped within the same species complex, and recognizes them as separate species. This classification is based on the inability of *T. interdigitale* isolates to produce fertile offspring with *T. mentagrophytes* reference strains, as well as on their distinct clinical presentations [10].

T. mentagrophytes genotype VII (TMVII) represents an emerging dermatophyte predominantly affecting adults and associated with anthropophilic and sexual transmission. First described in travelers returning from Thailand after sexual contact with sex workers [11], TMVII has more recently been reported among MSM populations in Europe, particularly in countries such as Germany and Switzerland [12]. More recently, its detection in the United States suggests the transition from imported infections to early local transmission [11]. The anthropophilic nature of TMVII is supported by the absence of zoonotic exposure, the identification of human-to-human transmission clusters, and molecular evidence of a clonal lineage, collectively indicating adaptation to human hosts and continued spread within sexual networks.

The incubation period of dermatophyte infections typically ranges from 4 to 14 days. Clinically, TMVII infections are often characterized by inflammatory and occasionally ulcerative lesions, reflecting transmission through close skin-to-skin contact. They typically present as erythematous, papulo-pustular, and nodular plaques, frequently involving the genital, gluteal, and facial regions. In some cases, they may also present with associated lymphadenopathy [11,13,14].

In a recent case series of 32 TMVII infections, predominantly affecting MSM, the authors described severe inflammatory presentations, including two cases of beard kerion that were initially misdiagnosed as bacterial infections. Such diagnostic pitfalls may lead to

inappropriate antibiotic use and delayed antifungal treatment, with potential consequences including scarring and secondary bacterial infection [15,16]. Zhang et al. (2025) [14] reported that, in a review of 124 cases of *T. mentagrophytes* genotype VII infection, the most common presentations were tinea faciei/barbae/capitis (51.7%) and tinea genitalis (36.7%). Infections predominantly affected MSM (64%), with high rates of co-infection, particularly gonorrhea (42.6%) and HIV (29.6%) [14].

Direct microscopy cannot distinguish dermatophyte species and fungal culture is time-consuming. Therefore, diagnosis relies on molecular techniques such as polymerase chain reaction (PCR), which enable accurate identification of the genotype. Oral terbinafine is typically recommended, with treatment duration extending up to 3 months depending on clinical response. Topical treatment showed limited efficacy and was occasionally associated with clinical worsening, even in localized cases, thus supporting the initiation of systemic therapy from the onset.

Prolonged culture positivity during treatment, reported up to 8 weeks in some cases, indicates that patients may remain contagious for several weeks, underscoring the importance of considering this factor in transmission prevention [13]. Of particular concern is the increasing detection of strains with reduced susceptibility or resistance to terbinafine, complicating therapeutic management. Furthermore, limited clinical awareness among clinicians may contribute to diagnostic challenges and difficulties in the appropriate management of TMVII infections.

Trichophyton indotineae (formerly *Trichophyton mentagrophytes* genotype VIII) has recently emerged as a novel terbinafine-resistant pathogen, first described in South Asia and now increasingly reported worldwide. Current evidence suggests that *T. indotineae* may have evolved as an anthropophilic clonal lineage from zoophilic *T. mentagrophytes*, potentially as a consequence of the inappropriate use of over-the-counter corticosteroid–antifungal combinations, promoting the persistence and spread of resistant strains. It was formally recognized as a distinct species in 2020. Definitive identification requires molecular diagnostic methods, since culture-based approaches do not allow reliable distinction between *T. indotineae* and other *Trichophyton* species [17].

In the past decade, India has seen a significant rise in *T. indotineae* infections, with recent surveys indicating that this species accounts for approximately 78% of all dermatophyte cases [18]. Its global spread has been facilitated by travel and migration, extending beyond endemic regions. A recent study from Ontario, Canada, reported cases of dermatophytosis caused by *T. indotineae*, underscoring its emergence as a growing public health concern. Most cases were identified between 2022 and 2023, coinciding with the pathogen's global spread and the resumption of international travel following the COVID-19 pandemic. Infections predominantly affected adults and were characterized primarily by skin involvement (tinea corporis and cruris), with limited nail involvement. Genomic analysis showed that isolates clustered closely with strains from endemic regions such as India and Iran, suggesting that most cases were likely imported, although limited local transmission cannot be excluded [19].

Similarly, European data highlight a rising number of cases, often underdiagnosed and associated with therapeutic failure, particularly due to terbinafine resistance [20]. A recent whole-genome sequencing (WGS) study analyzing 103 clinical *Trichophyton* isolates from multiple countries, including Canada, Ireland, the UK, France, and India, provided important insights into the genetic basis of antifungal resistance and the population structure of *T. indotineae* [21]. Genomic analysis revealed a high degree of genetic similarity among isolates, supporting a largely clonal and globally distributed population without clear geographic clustering; however, evidence of local clustering within specific countries suggests limited regional transmission alongside widespread international dissemination.

Transmission of *T. indotineae* occurs mainly through direct human-to-human contact, including close physical and sexually associated exposure, while indirect transmission via fomites may also occur. Clinical criteria that may raise suspicion of sexual transmission include the presence of genital lesions in individuals with highly interconnected sexual networks, in the absence of concomitant involvement of the feet or nails, lack of contact with infected animals, and the presence of similar lesions in sexual partners.

A key feature of this pathogen is its resistance to terbinafine, primarily driven by mutations in the squalene epoxidase (SQLE) gene, such as Phe397Leu (F397L) and Leu393Phe (L393F). These mutations impair terbinafine binding, allowing continued ergosterol synthesis—essential for fungal cell membrane integrity—and thereby reducing treatment efficacy [22,23]. Additionally, mechanisms of reduced susceptibility to azoles, including CYP51B gene duplications, have been identified, potentially limiting treatment efficacy. Although itraconazole is generally effective for *T. indotineae* infections, emerging resistance to azoles, along with issues related to absorption, drug–drug interactions, and the need for prolonged high-dose therapy (e.g., 200 mg twice daily), may complicate its use [24].

From a clinical perspective, *T. indotineae* cutaneous infection is characterized by inflammatory, erythematous plaques with clear borders, predominantly involving the genital region, frequently raising suspicion for close-contact or sexually associated transmission. These lesions may resemble classical dermatophytosis; however, they often display a more persistent and progressive course, with incomplete response to standard antifungal therapy [25]. Consistently, additional reports, including cases among Italian MSM, have described similar patterns with genital and gluteal involvement linked to direct skin-to-skin contact [26].

A recent systematic review by De Marco et al. (2025) [27], including 30 studies and 64 patients, reinforces these findings. Most cases of *T. indotineae* infections originated from South Asia, with a mean age of 36 years, and predominantly affected immunocompetent individuals. Transmission was largely human-to-human, with minimal evidence of zoonotic exposure and occasional reports of sexually associated spread. Clinically, infections were often extensive and multifocal, involving the lower limbs, inguinal and gluteal regions, and trunk, with potential progression to widespread dermatophytosis. Consistently, terbinafine demonstrated limited efficacy, whereas itraconazole (200 mg/day) was associated with higher rates of clinical response, although recurrences were frequently observed [27].

These findings highlight *T. indotineae* as an emerging and clinically challenging dermatophyte, characterized by efficient human-to-human transmission, expanding global dissemination, and increasing antifungal resistance. Its atypical clinical presentation, frequent genital involvement, and poor response to first-line therapies contribute to diagnostic delay and suboptimal management. The reduced susceptibility to conventional antifungals described for these dermatophytes, especially for *Trichophyton indotineae* (Table 1), emphasizes the clinical necessity of performing antifungal susceptibility testing before treatment initiation and prompt reassessment in non-responsive patients, as suggested by the current literature [26,27].

3. Doxycycline Post-Exposure Prophylaxis (Doxy-PEP)

Prevention of bacterial STIs remains challenging, given the absence of effective vaccines and the limited availability of chemoprophylactic interventions. Post-exposure prophylaxis (PEP) involves the administration of medication after a suspected exposure to reduce the risk of infection and is commonly employed in the prevention of HIV and other infectious diseases. Unlike pre-exposure prophylaxis (PrEP), which is taken before exposure, PEP is initiated after the exposure has occurred. Alongside recent developments

regarding emerging pathogens, important advances in the field of sexually transmitted infection prevention have arisen over the past two years [28].

Doxycycline post-exposure prophylaxis (Doxy-PEP) has recently been recommended in the 2024 guidelines of the Centers for Disease Control and Prevention (CDC) for selected communities experiencing a high burden of STIs [28]. Doxycycline is a broad-spectrum tetracycline antibiotic characterized by good oral absorption, favorable tolerability, and an elimination half-life of approximately 12 h [29]. Doxycycline is a first-line treatment for chlamydia and an alternative for syphilis in selected patients [30], while its use in gonorrhea is limited by resistance.

This strategy involves the administration of doxycycline shortly after potential exposure to reduce the risk of bacterial STIs, including syphilis, chlamydia, and gonorrhea.

As based on an antibiotic drug, doxy-PEP does not, as expected, prevent dermatophyte infections. Evidence from three randomized controlled trials in MSM and transgender women (TGW), both HIV-positive and HIV-negative, has demonstrated a significant reduction in STI incidence. Specifically, gay, bisexual, and other MSM and TGW with a history of bacterial STIs within the previous 12 months should be counseled on the use of doxycycline 200 mg, taken ideally within 24 h but no later than 72 h after condomless anal, oral, or vaginal sex. The maximum dose corresponds to 200 mg of doxycycline every 24 h. Evidence supporting the use of doxy-PEP in populations other than MSM and TGW remains insufficient. HIV screening should be performed for HIV-negative MSM and TGW according to current recommendations [31].

Counseling is essential and should include discussion of potential adverse effects, such as photosensitivity, gastrointestinal intolerance, and esophagitis, as well as strategies to mitigate these risks. Attention should also be given to potential drug interactions, particularly with retinoids. Patients should be advised to separate doxycycline administration by at least 2 h from dairy products, antacids, and supplements containing calcium, iron, magnesium, or sodium bicarbonate. The medication should be taken with adequate water, and patients should avoid lying down immediately after ingestion.

A major concern regarding Doxy-PEP is its potential to promote antimicrobial resistance, both in sexually transmitted pathogens and in commensal or opportunistic bacteria such as *Staphylococcus aureus*. The 2024 position statement of the European branch of the International Union against Sexually Transmitted Infections (IUSTI Europe) indicates that Doxy-PEP can reduce the risk of certain bacterial STIs at the individual level, particularly syphilis and chlamydia, while showing limited efficacy against gonorrhea due to prevalent antimicrobial resistance. Doxy-PEP should be implemented through shared decision-making and reassessed periodically, typically every 3–6 months [32].

Follow-up data from Doxy-PEP studies showed a reduction in overall *S. aureus* carriage, but an increase in tetracycline-resistant strains among colonized individuals. Similarly, although data on *Neisseria gonorrhoeae* are limited, some studies reported higher proportions of tetracycline-resistant isolates in the doxy-PEP group compared with standard care, while others found high baseline resistance levels regardless of prophylaxis. In contrast, no significant changes in resistance patterns were observed for *Chlamydia trachomatis*, Methicillin-resistant *Staphylococcus aureus*, or Extended-Spectrum Beta-Lactamase-producing *E. coli*. Data on long-term microbiome effects are lacking, highlighting the need for ongoing surveillance.

A recent cross-sectional survey among Italian dermatologists revealed high levels of awareness but limited clinical implementation, with only a minority of clinicians reporting direct prescribing experience [33]. Importantly, key concerns were consistently highlighted, particularly regarding antimicrobial resistance—especially in *Neisseria gonorrhoeae*—as well as potential microbiome disruption. MSM were consistently identified as the main target

population, particularly in the setting of recent situations with a higher probability of infection exposure, including chemsex and multiple sexual partners.

4. Chemsex

Lastly, chemsex represents another emerging and highly relevant area within the landscape of sexually transmitted infections.

The term “chemsex,” derived from “chemical sex,” describes the intentional use of selected psychoactive and non-psychoactive substances during sexual activity to facilitate or enhance the experience, particularly among MSM [5]. “Slamming” refers to the practice of injecting drugs intravenously during sexual activity as part of chemsex [34]. It is an increasingly prevalent phenomenon in Europe, with estimates ranging from 9% to 21% among MSM populations, and is now recognized as a growing global public health concern [35–38]. A concerning pattern is the higher prevalence of chemsex among MSM living with HIV compared with HIV-negative individuals, suggesting a complex interplay between risk perception, treatment status, and sexualized drug use [39].

Chemsex typically occurs in private settings, often involving prolonged sessions lasting hours to days, with multiple partners. The substances most commonly involved are crystallised methamphetamine, mephedrone, γ -butyrolactone (GBL) and gamma-hydroxybutyric acid (GHB). Mephedrone and crystal meth are stimulant drugs that increase heart rate and blood pressure, while also producing feelings of euphoria and enhancing sexual desire. In contrast, GHB (and its precursor GBL) mainly acts on the brain by reducing psychological inhibitions and has a mild anesthetic effect. Some United Kingdom-based reports and small qualitative studies suggest that individuals engaging in chemsex often perceive improved sexual experiences, as these substances reduce inhibitions, enhance pleasure, promote prolonged arousal, and may also be used to cope with negative feelings such as low confidence, poor self-esteem, internalized homophobia, or stigma related to HIV status.

These substances are associated with a range of side effects and varying degrees of toxicity. In particular, GHB is associated with central nervous system depression, while methamphetamine is linked to neurotoxicity, cardiotoxicity and hepatic and renal damage. Mephedrone and crystal meth can lead to strong psychological dependence, whereas GHB/GBL is associated with a significant risk of physical dependence [40].

Partner recruitment is largely facilitated by digital platforms and social applications, further expanding sexual networks. The typical profile includes MSM or bisexual men aged 32–42 years, living in urban settings, with higher educational attainment and stable employment [41,42]. Recent data from an Italian STI/HIV center confirm that individuals engaging in chemsex exhibit higher-risk sexual behaviors, including a greater number of partners, more frequent group sex, and less consistent condom use, alongside a higher prevalence of prior STIs, reflecting greater exposure and ongoing transmission within interconnected sexual networks [43]. Consequently, because it involves prolonged intercourse and microtrauma, extensive skin-to-skin contact, the sharing of spaces and objects, and an altered perception of risk, the practice of chemsex is associated with a high risk of acquiring infections from both classic and emerging pathogens, such as the aforementioned dermatophytes.

Data from a Milan cohort provide further insight into the relationship between chemsex, substance use, and sexual health pathways. Chemsex was reported in 16% of participants and was more prevalent among people living with HIV compared with PrEP users. Substance use was common, with a high prevalence of chemsex-associated drugs, and polydrug use was observed in 57% of individuals. Notably, 37% did not disclose drug use to healthcare providers, highlighting a gap between clinical assessment and real-life behav-

iors. The study population was predominantly composed of MSM (86.7%), supporting the concentration of chemsex within highly interconnected sexual networks [44].

Chemsex-related harm is multifactorial, involving infectious, pharmacological, psychological, and behavioral components [40]. Some forensic reports have documented fatalities [45]. It is associated with an increased risk of STI transmission, driven by practices with higher potential for transmission such as a higher number of sexual partners, unprotected sex, prolonged sexual activity, and injecting drug use, often facilitated by substance use. The use of multiple psychoactive substances introduces challenges such as drug–drug interactions and adherence issues, particularly in individuals receiving antiretroviral therapy or PrEP. The greatest interaction risk involves boosted antiretrovirals (e.g., ritonavir, cobicistat), which strongly inhibit CYP450, while non-nucleoside reverse transcriptase inhibitors pose a lesser risk and nucleoside-based agents have minimal interaction potential [46].

Psychological vulnerability—including anxiety, depression, stress and loneliness—also plays a significant role, with chemsex often functioning as a maladaptive coping strategy [47,48]. Chemsex is strongly linked to social isolation, with some individuals reporting problems at work, progressive distancing from friends, and reduced willingness to engage in social activities outside of chemsex. Furthermore, chemsex is associated with a risk of psychiatric decompensation, including an increased likelihood of developing psychosis, as reported by Moreno-Gómez et al. [49]. A key challenge for addiction treatment professionals is that individuals engaging in chemsex often do not identify as drug users or perceive their substance use as problematic, which makes them less likely to seek conventional medical care.

These overlapping dimensions highlight the complexity of chemsex as both a behavioral and clinical phenomenon. Overall, chemsex represents an evolving public health challenge that requires a multidisciplinary approach, integrating infectious risk reduction (e.g., PrEP, vaccination, harm reduction strategies), appropriate care services with psychological and social support, and improved access to accurate information regarding substance use and sexual health.

5. Conclusions

In conclusion, these evolving trends highlight several key priorities for clinicians. Early recognition of emerging pathogens and atypical presentations of classic diseases [50], particularly dermatophyte infections with possible sexually associated transmission, is essential, alongside the timely use of appropriate diagnostic tools, including molecular methods. The emergence of antifungal-resistant dermatophytes and the expanding role of unconventional sexually transmitted pathogens call for a redefinition of current STI paradigms, integrating dermatological and infectious disease perspectives.

Clinicians should routinely assess sexual behaviors and substance use, including chemsex, in a nonjudgmental manner to better identify individuals at increased risk. Targeted prevention strategies, such as vaccination, PrEP, and when appropriate Doxy-PEP, should be actively considered in populations with increased exposure potential. Particular attention must be paid to potential drug–drug interactions and treatment adherence, especially in patients receiving antiretroviral therapy.

Overall, a collaborative, patient-centered approach is essential to improve outcomes and reduce the global burden of STIs.

Future Perspectives and Research Priorities

Given the alarming rise of global antifungal resistance, innovative and multidisciplinary strategies are urgently needed to mitigate the problem and offer viable clinical solutions for multidrug-resistant infections [26,27].

Doxy-PEP represents a major advancement in bacterial STI prevention among MSM and transgender women with recent STI history. However, close surveillance of clinical outcomes, antimicrobial resistance patterns, and patient-related factors (adherence and individual pharmacokinetics) is crucial. Further research in additional populations remains essential to optimize the long-term public health impact of this prevention strategy [33].

Finally, future research should focus on understanding the pathways into chemsex, identifying how and when it becomes problematic, and determining how best to support individuals when this practice is intertwined with typical issues of polysubstance misuse [35–38].

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Abbreviations

The following abbreviations are used in this manuscript:

CDC	Centers for Disease Control and Prevention
Doxy-PEP	Doxycycline post-exposure prophylaxis
ECDC	European Centre for Disease Prevention and Control
GBL	Gamma-butyrolactone
GHB	Gamma-hydroxybutyric acid
HIV	Human immunodeficiency virus
HSV	Herpes simplex virus
IBD	Inflammatory bowel disease
IUSTI	International Union against Sexually Transmitted Infections
MSM	Men who have sex with men
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PrEP	Pre-exposure prophylaxis
QOL	Quality of life
SQLE	Squalene epoxidase
STIs	Sexually transmitted infections
TMVII	Trichophyton mentagrophytes genotype VII
TGW	Transgender women
WGS	Whole-genome sequencing

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