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# Enhancing HIV/STI decision-making: challenges and opportunities in leveraging predictive models for individuals, healthcare providers, and policymakers

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## Abstract
The prevention and control of human immunodeficiency virus and sexually transmitted infections (HIV/STI) face challenges worldwide, especially in China. Prediction tools, which analyze medical data and information to make future predictions, were once mainly used in HIV/STI research to help make diagnostic or prognostic decisions, has have now extended to the public as a freely accessible tool. This article provides an overview of the different roles of prediction tools in preventing and controlling HIV/STI from the perspectives of individuals, healthcare providers, and policymakers. For individuals, prediction tools serve as a risk assessment solution that assess their risk and consciously improve risk reception or change risky behaviors. For researchers, prediction tools are powerful for assisting in identifying risk factors and predicting patients' infection risk, which can inform timely and accurate intervention planning in the future. In order to achieve the best performance, current research increasingly underscores the necessity of considering multiple levels of information, such as socio-behavioral data, in developing a robust prediction tool. In addition, it is also crucial to conduct trials in clinical settings to validate the effectiveness of prediction tools. Many studies only use theoretical parameters such as model accuracy to estimate its predictive. If these improvements are made, the application of prediction tools could be a potentially inspiring solution in the prevention and control of HIV/STI, and an opportunity for achieving the World Health Organization's agenda to end the HIV/STI epidemic by 2030.

## Introduction
The strategies of prevention and control of human immunodeficiency virus and sexually transmitted infections (HIV/STI) in China need to be improved. From 2010 to 2019, there was a rise in the prevalence of chlamydia, syphilis, gonorrhea, HIV, and AIDS, yet there is a possibility of significant underdiagnosis and underreporting [1]. Chlamydia infection is the most prevalent STI in China [2]. However, it has not been incorporated as a reportable STI in the national STI surveillance program. It is only addressed in 105 STI surveillance sites, and merely 23.4% of these sites offer nucleic acid amplification tests [3]. In 2021, Gonorrhea was reported as the fourth most common infectious disease in China [4], and its testing rate was also shown to be insufficient [3]. Even HIV testing among key populations is underestimated. Two studies revealed that 25.8% of people who use drugs (PWUD) [5] and 32.6% of female sex workers (FSW) [6]

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has received HIV testing in the past year. Additionally, a national study reported that just 25% of healthcare providers (HPs) offer HIV testing upon patient request [7].

The significant underestimation of HIV/STI underscores the importance of early detection and treatment as essential components of HIV/STI control strategies [8]. In an effort to promote early detection and treatment, prediction tools have been developed to help HPs in identify at-risk groups, and deliver targeted and timely interventions [9–12]. In addition, these tools can support public health system by serving as a prognostic and epidemiological tools to monitor variations in prevalence and risk factors across different regions [13–15], and to access the adherence to the intervention [16, 17] and its outcomes [18]. This comprehension can aid in the development of tailed prevention, control, and resource allocation strategies for diverse regions [19]. The users of prediction tools have gradually shifted from being used only by HPs to being available to the public. The use of such easily accessible prediction tools can enable individuals to assess their risk of reinfection/infection of HIV/STI and recognize the importance of testing and behavior change [20–23].

The purpose of this study is to review the current published HIV/STI prediction tools, and explore their specific roles in assisting individuals, enhancing clinical settings and informing public health strategies. Additionally, this review aims to summarize the limitations in the current research and propose new directions for future HIV/STIs prediction studies.

## Prediction tools for patients

Studies have indicated that a lack of awareness about the risks of HIV/STI and the fear of stigma when seeking healthcare service are significant obstacles for individuals to undergo testing in China [7, 24, 25]. It was pointed out that improving individuals' awareness of HIV will increase the uptake of HIV testing and promote safety behavior [26]. For instance, a survey indicated that after acquiring HIV-related knowledge, 75.2% of patients were motivated to seek healthcare services [27]. Given the current challenges, implementing self-assessment tools could serve as a practical approach to motivate individuals.

Recently, studies have led to the development of HIV/STI risk prediction tools that aid individuals in estimating their current or future risk of HIV/STI infection [12, 20–23, 28]. In 2020, an online HIV risk prediction tool, named SexPro, was developed by Scott et al. [22] with high predictive efficiency. This tool is cater to American men who have sex with men (MSM), especially Black MSM. After the questions related to sexual history have been answered, an HIV risk score of 1–20 will be generated and displayed. More broadly, Xu et al. [21] developed an online tool, MySTIRisk, which is open to the public and based on several machine learning (ML) algorithms to predict the concurrent risk of HIV, syphilis, gonorrhea, and chlamydia within 1 year. Upon completion of a 13-question questionnaire, a report will be generated detailing the risk of acquiring HIV/STI, as well as providing recommendations for risk reduction and testing. Prior to the implementation of such prediction tools in clinical practice, it is essential to conduct clinical validation studies to confirm the effectiveness of these risk prediction tools in behavior changing. Yun et al. [20] conducted a randomized controlled trial (RCT) to reveal the preliminary effects of their online HIV risk prediction tool [23] in reducing the risk of HIV infection and promoting HIV testing among Chinese MSM. The results of the study indicated that the prediction tool had a positive impact on sexual behavior, with higher rates of condom use and fewer male sexual partners among those who used the tool in 3 months compared to those who did not. These findings indicated the potential effectiveness of the prediction tool in promoting safer sexual practices. Further research and validation studies are needed to confirm these results and assess the long-term impact of using such prediction tools. The evidences from other studies supported the idea that internet-based interventions can be effective in helping individuals overcome stigma related to privacy and portability [29]. And these interventions have been shown to improve risk perceptions [30], which can lead to positive changes in behavior. The potential of prediction tools for self-risk assessment and behavior changing is substantial, and it is important to emphasize the need for clinical validation studies to evaluate the effectiveness of these tools when applied in clinical settings.

## Prediction tools for healthcare providers

There are limited healthcare professionals in China who have trained in HIV/STI knowledge and skills to offer appropriated testing and intervention to every patient [7, 24]. Additionally, studies have demonstrated that inadequate testing and high costs are barriers to early detection and treatment, leading to the increased spread of HIV/STI in China [3].

Studies have been conducted in the area of developing prediction tools to prioritize essential groups. Findings from Xia et al. show that using ML algorithms, people living with HIV (PLWH) at high viral loads can be identified, which is the key component of HIV prevention programs to control the transmission [11]. Notably, the authors claimed that when this tool is used in clinical practice, the HPs does not require HIV sequence data to identify PLWH, which is of great benefit in resource-limited settings. It is crucial to inform and ensure that patients undergo regular testing, as recommended by guidelines. Xu et al. developed a ML model to identify individuals who timely attend clinics and undergo HIV/STI testing after receiving reminders. By examining a person's triage reasons, sexual history, and previous reminder methods and frequency, HPs were able to assess the patient's willingness to undergo testing and take immediate action [16]. These models have the potential to be used in routine care, even in resource-limited settings, to efficiently prioritize essential groups. Once more, the clinical effectiveness of using these models requires evaluation.

## Prediction tools for policymakers

### Predicting epidemic trends

In China, rural-to-urban migrants are often considered a high-risk group for HIV/STI infection and transmission [31]. Improved economic prospects entice rural residents to relocate to urban centers, with approximately 385 million migrants [1] typically commuting between urban and rural areas during Chinese major holidays. Due to China's strict household registration system, rural migrants do not have access to all the social and health welfare available in cities [32]. This leads to poor living condition, unstable income, limited access to healthcare services, and inadequate social support. All these contribute to increased vulnerability to HIV/STI in China [31, 32]. A systematic review and meta-analysis found that the risk of HIV infection among migrants was 6.7 times higher than that of the general population. Among female migrants, the risk was even higher, at 12.18 times [33].

The cyclical occurrence of AIDS, gonorrhea and syphilis in China is associated with the migration from rural to urban areas [14]. Zhu et al. [14] utilized time series analysis of the monthly incidence of AIDS, gonorrhea and syphilis over the past decade to forecast the occurrence of these diseases over the next year and five years in China. Their findings suggested that the incidence of HIV/STIs declined significantly to its lowest during the Chinese New Year, but subsequently rose rapidly to a relatively high level after the holiday period. Similarly, Weng et al. [15] developed a time-series prediction model to predict the incidence of chlamydia in Shenzhen, a developed city with large number of migrants in China. The authors also observed that the occurrence of chlamydia varied during the same season. Both of these studies have confirmed the findings of previous studies: a large number of migrants back home and limited health services due to holidays or major events will lead to changes in the incidence of HIV/STI. Ultimately, time-series models can be used to predict the HIV/STI incidence and can serve as a tool for policymakers to rationally allocate health resources and draft HIV/STI prevention and control plans in a timely manner.

### Predicting the effectiveness of government policies

Regulations and policies play a crucial role as structural interventions that can either support or hinder efforts in controlling and preventing HIV/STI. FSWs, who are disproportionately affected by HIV/STI infections, are hesitant to undergo testing due to the illegality of commercial sex, resulting in limited access to HIV prevention services in China [34]. Conversely, the implementation of a free antiretroviral therapy (ART) policy in China resulted in a 0.69% decrease in HIV infection per 100 person-years [31].

Time series prediction models can be utilized to assess the impact of laws and policies on HIV/STI. Ruiz et al. [19] utilized time-series analysis to predict HIV infection in the absence of Syringe exchange program (SEP) and compared it with the actual HIV infection in the presence of SEP. The findings indicate that HIV diagnosis would rise with the implementation of SEP. Consistently, SEP has been demonstrated to be linked to a reduction in bloodborne HIV/AIDS infections among PWUD [35]. As a structural intervention, the risky environment of PWUD is improved to promote their health rather than changing their behavior and social interaction. Likewise, Zhao and colleagues [36] developed a time-series prediction model to predict the anticipated HIV/AIDS cases from 2020 to 2022, excluding the impact of Coronavirus disease. The results showed that an additional 1,314 HIV/AIDS cases would occur every month. Moreover, the lower number of HIV/AIDS cases is hypothesized to be attributed to underdiagnosis, underreporting, and social isolation. The authors emphasized that while lockdown policies help maintain social distancing, they also create distance from healthcare resources, including ART treatment and testing, which could result in a rapid increase in incidence in the future. According to the prediction tool, it is recommended that resource allocation for HIV/AIDS should be prioritized to enable ongoing testing and surveillance during future pandemics.

## Discussion

This review underscores the impact of prediction tools in the prevention and control of HIV/STI, ultimately resulting in improved outcomes for individuals, clinic settings, and public health. Awareness of the potential to use existing information to predict HIV/STIs outcomes is growing rapidly. Recently, the China Center for Disease Control and Prevention (CDC) released guideline for online intervention in HIV, encouraging the development of internet-based HIV risk-assessment tools to identify the risk of HIV infection in the general or specific populations [37]. The crucial importance of utilizing easily accessible, person-centered predictive tools is emphasized.

Research on the effectiveness of predictive models in clinical practice is scarce. Most of the studies evaluated the performance of the model by AUC or accuracy, but these indicators cannot be used to evaluate whether the model is clinically feasible. Of the aforementioned studies, only Yun et al. [23] conducted a RCT to validate the clinical efficacy of the model, which confirmed previous hypothesis that the predictive model could help MSM in improve high-risk behavior. TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) Statement was published in 2015 to help improve the quality of the prediction model research and ensure the reliability and reproducibility of model results [38]. Of the studies mentioned earlier, only Xia et al. [11] developed their model following the TRIPOD guidelines. However, there is a concern that the argument may be overinterpreted. The authors claim that the model is not limit to PLWH with specific characteristics, but also applies to women and heterosexual men with high-risk characteristics, such as high viral load. However, performance for individuals with a high viral load is only 0.56 which means the model has limited ability to discriminate such population. However, this also highlights that following the TRIPOD guidelines can make the findings of such interdisciplinary research more accessible to the audience. Nevertheless, the performance of prediction tools should be interpreted with caution in the absence of clinical validations, otherwise the effectiveness of the model in the clinical settings would be difficult to validate.

The generalizability of prediction tools remains limited. First, some tools are only designed for specific populations, such as MSM [16, 22, 23] and PLWH [17, 18]. MSM are disproportionately affected by HIV/STIs, whom is at higher risk of acquiring HIV/STIs than are heterosexual men and women [39, 40]. However, in 2021, 22% of new HIV infections still occurred among people who reported heterosexual contact in US, while this proportion in China was about 70% [35, 41]. Second, certain tools are designed specifically to predict only HIV [11, 12, 17, 18, 22, 23, 28] or STIs [10, 13, 15] outcomes. It is well established that STIs facilitate HIV transmission by disrupting protective mucosal barriers and recruiting susceptible immune cells to the site of infection [42], and the high prevalence of STIs co-infection among PLWH will impede efforts to prevent HIV transmission using HIV treatment alone [43]. A systematic review revealed that 16.3% of PLWH reported having a STI infection, and co-infection with a STI increases HIV viral shedding and infectiousness [43]. Therefore, focusing solely on awareness and intervention for HIV infection may overlook the risk of STIs. Future studies should incorporate diverse datasets to develop models that can be used in various settings, thereby enhancing the robustness of the model.

The performance of prediction tools varies due to insufficient data. An Australia study sought to develop a ML-based tool to predict chlamydia retesting and reinfection rate over the next 12 months [10]. However, the performance was poor for both outcomes, leading the authors to recommend that future research should not only rely solely on electronic health record (EHR), but should also encompass macro-level data, such as behavioral and social factors [10]. In the aforementioned study, the accuracy of predicting clinic attendance was lacking, promoting the authors to recommend the inclusion of psychological and social characteristics in modeling, as these factors are related to behavior [16]. Controlling and preventing the spread and infection of HIV/STIs involves more than just offering free ART or condoms. Researchers are increasingly acknowledging that the social and structural factors contributing to HIV/STI infection, such as power dynamics within relationships, access to services and transportation, and economic inequalities, also contribute to people being at risk [44]. The US CDC recommends integrating social and behavioral determinants of health into EHR to enhance health outcomes [45], and other reviews have similarly advised that future HIV/STI intervention should consider the relevant factors at various levels, ranging from individual to the structural considerations [31, 44, 46]. In Pakistan, a research took into account behavioral and structural factors including drug use and urbanization, and integrated them with EHR to develop an HIV prediction model that achieved an accuracy of 82% [28]. Similarly, Saldana et al. [12] also integrated socio-demographic factors and Social Vulnerability Index to predict HIV incidence, with good performance for both men and women.

Subsequent clinical validation studies are essential for future research, as they are crucial for maintaining the credibility of prediction tools. In addition, aside from EHR, the inclusion of socio-behavioral information such as Social Vulnerability Index [47], Social Support Rating Scale [48], Sexual Relationship Power Scale [49], etc., should be considered. When socio-behavioral information is lacking, natural language processing (NLP) can be utilized to extract relevant data from EHR, particularly as information such as sexual history is often documented in narrative form within clinical notes. Research has shown that NPL-based EHR can improve the predictive performance in HIV risk assessment [50]. Overall, through the implementation of clinical validation studies and the integration of socio-behavioral information, the value of prediction tools can be significantly enhanced, bringing us closer to achieving the World Health Organization (WHO) 2030 goal of ending AIDS and STI epidemic by 2030 [51].

## Conclusions

Predictive models hold the potential to extract valuable insights from extensive data to aid HIV/STI decision making for individuals, clinical settings, and public health. Emphasizing the inclusion of social and behavior determinants is crucial for developing more precise and applicable models. However, the inadequacy of clinical validation studies has hindered their potential for clinical practice, thereby limiting their effectiveness in reaching the WHO 2030 goal even further.

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