

Syphilis and Beyond: A Comprehensive Analysis of Associated Infections and Comorbidities in a Five-Year Retrospective Study in the United Arab Emirates (2018-2022)

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Syphilis and Comorbidities in the UAE

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Abstract

Objectives: This study explores the clinical characteristics, associated infections, and management outcomes of syphilis within a specific population over the years 2018 to 2022. With a focus on the frequency, clinical manifestations, and co-infections of syphilis, the research addresses a critical gap in understanding the nuanced dynamics of this sexually transmitted infection and its impact on public health.

Methods: The study employs a retrospective analysis of data collected from 2018 to 2022, utilizing three key serological tests (Syphilis AB, RPR/VDRL, and TPHA) to characterize syphilis infections within the population. Clinical manifestations and associated infections, including HIV, HBV, HCV, Chlamydia, Gonorrhea, and HPV, are systematically assessed. Treatment rates and re-infection patterns are also analyzed, providing a comprehensive overview of syphilis epidemiology within the studied timeframe.

Results: The frequency of syphilis, particularly indicated by the Syphilis AB test, exhibited a marked increase in 2020, reaching 96%, suggesting a heightened frequency within the population. RPR/VDRL test results demonstrated consistent frequency, emphasizing the persistent presence of active syphilis infections. Clinical manifestations, such as chancre, skin rashes, alopecia syphilitica, and lymphadenopathy, displayed dynamic patterns over the study years. Co-infection rates varied, with fluctuations observed in HIV, Chlamydia, Gonorrhea, and HPV, while HBV and HCV showed infrequent but stable frequency. The management of syphilis cases demonstrated commendable treatment rates, but an increase in re-infection rates in 2021 highlights the need for continued vigilance.

Conclusion: This study provides a comprehensive evaluation of syphilis epidemiology, clinical characteristics, and associated infections within the studied

population. The results offer valuable insights into the dynamic nature of syphilis and its co-infections, informing public health initiatives and interventions. The findings contribute to our understanding of the epidemiological landscape and underscore the importance of sustained efforts in both prevention and treatment to curb the transmission of syphilis and its associated infections. The study, however, calls for continued vigilance and research to address the evolving trends and challenges in syphilis management within the specified population.

Introduction

Syphilis, an infection that spreads through sexual contact and is mostly attributed to the bacterium *Treponema pallidum* subspecies *pallidum* [1], can additionally spread by blood donations or from a pregnant woman with the infection to the newborn through gestation [2]. After being infected, a chancre usually develops during a period of 10 to 90 days [3]. If not managed, secondary syphilis can develop, which presents indications such as rashes, thinning hair, and condylomata lata, as well as non-specific indicators including general discomfort, cough, diminished appetite, and a mild temperature [3, 4]. Latent syphilis ensues, characterized by the absence of manifestations but the persistence of infectiousness for a duration of as long as twelve months [5]. Although uncommon as a result of the use of antibiotics, tertiary problems, such as neurosyphilis, may arise and exhibit a wide range of physiological symptoms [6].

People with syphilis are also more likely to get other illnesses that are transmitted sexually [7]. Hence, it is unsurprising to discover that all existing recommendations pertaining to syphilis therapy advocate for screening for additional STIs in all recently confirmed cases [8]. *Neisseria gonorrhoeae* (*N. gonorrhoeae*), as well as *Chlamydia trachomatis* (*C. trachomatis*), often occur together as infection co-occurrence in individuals with syphilis [9]. A significant percentage of these infections, particularly in the pharynx and colorectal regions, might not display any symptoms [10].

Syphilis infection is a clearly identifiable risk factor, and there have been documented bidirectional associations between acquiring HIV and syphilis [11]. Syphilis is associated with a significantly higher occurrence of HIV, as evidenced by the fact that nearly half of the documented cases of syphilis in 2016 involved concomitant HIV coinfection [12]. Research [13] conducted a thorough review of a population consisting of 2805 primary and secondary syphilis cases that were previously negative for HIV. The study revealed that during a median follow-up time frame of 4.2 years, 423 persons were consequently confirmed to have HIV [13]. The findings of [14]'s investigation support the notion that individuals living with HIV have a significantly increased risk of acquiring syphilis, more than five times, in comparison to those who are HIV-negative. The research conducted by Phipps et al. highlights HIV as the main predictor for persistent syphilis recurrence [15]. Furthermore, a recent meta-analysis by [16] revealed that there was a two-fold likelihood increase in acquiring HIV after a syphilis infection.

The evident reciprocal association of syphilis and HIV carries significant biochemical ramifications [17]. Having an STI, especially an ulcerative STI such as syphilis, increases the possibility of spreading HIV by a multifold factor [18]. The lymphocytes, which are the cells attacked by HIV, are abundant in syphilis wounds, enabling an easy way for HIV to enter the body of the individual [19]. Moreover, the decrease in immunity induced by HIV might enable *T. pallidum* to elude the immune system of the victim, thereby contributing to the development of worsening ailments, including neurosyphilis [20].

Syphilis has been recognized as an indicator of vulnerability for the Human Papillomavirus (HPV), in

addition to HIV. Human papillomavirus (HPV) is among the most commonly occurring STIs on a global scale [21]. Annually, the Human Papillomavirus causes an estimated 341,831 fatalities from cancer on a worldwide basis [22]. Although an effective therapy for HPV is currently unavailable, it is possible to manage the disease's apparent symptoms, such as warts on the reproductive tract, in an effort to prevent the infection's transmission [23]. Clinical cases of human papillomavirus (HPV) and syphilis were studied by [24], who found that a significant number of the patients who received treatment for contracted HPV had previously been diagnosed with syphilis, suggesting robust concurrent infections between the two conditions.

Syphilis is acknowledged as an important risk indicator for both Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV), in addition to HIV [25]. Hepatitis B is a pervasive infection caused by viruses that impact the functioning of the liver and has an international ramification for the general population [26]. Approximately 1.5 million individuals are afflicted with persistent HBV infection each year, which results in roughly 887,000 fatalities per year attributable to issues including carcinoma of the liver and cirrhosis [27]. Hepatitis C, an additional viral infection that impacts the functioning of the liver, significantly contributes to death and disability associated with the liver on a global scale [28]. An approximated 58 million individuals suffer from persistent infection with HCV, which yearly causes approximately 290,000 fatalities [29]. Research investigating the interaction between syphilis and hepatitis B virus (HBV) or HCV has uncovered a noteworthy correlation, indicating that people who have previously experienced syphilis may face an elevated susceptibility to co-infection with these hepatitis infections [25, 30- 32]. Patients who have undergone treatment for HBV or HCV frequently have a preexisting condition, such as syphilis, according to research from multiple regions [30- 32]. This highlights the criticality of examining co-infections in order to improve overall healthcare practices. Such information, however, is unavailable with regard to the UAE.

Thus, the key goal of the study is to identify not only the clinical characteristics of syphilis infections in the UAE but also the co-infections that occur in this context. Such information from the UAE is largely missing and is crucial to enhance the treatment parameters and prevent re-infection rates. The present study, thus, evaluates the trends relating to clinical characteristics as well as comorbidities associated with positive syphilis serology.

Methods

The objective of this retrospective cross-sectional study was to examine syphilis cases that occurred between 2018 and 2022, a span of five years. The research employed pre-existing medical records in order to evaluate the clinical attributes and concomitant variables of individuals who were diagnosed with syphilis within the specified time period. Systematically, medical records spanning the years 2018 to 2022 were extracted from the database of the STI clinic. The data was collected over a period of five years from four different locations including three Genitourinary medicine clinics and one HIV clinic within the Infectious disease unit across Dubai Health, which is a government entity. Participants were required to have received a definitive diagnosis of syphilis within the designated timeframe. Demographic information, significant laboratory results, and clinical characteristics were the focal points of the data extraction process. Descriptive statistics were utilized to characterize the demographic and clinical profiles of the study population, incorporating frequencies and percentages. Ethical guidelines were followed throughout the study, and approval was obtained from the Ethics Committee. In order to uphold privacy regulations and guarantee confidentiality, all patient data underwent

anonymization. The aforementioned exhaustive approach enabled the methodical analysis of syphilis cases spanning a period of five years. This yielded valuable knowledge regarding the dynamic clinical environment of the illness and served as a foundation for subsequent research endeavors and interventions.

Results

Based on data from 2018 to 2022, we examined the clinical features of a particular population in this research and classified the results into several manifestations. The three main serological tests used to describe syphilis infections were Syphilis AB, RPR/VDRL, and TPHA. According to the results of the Syphilis AB test, the frequency of syphilis increased significantly throughout the course of the research. It increased gradually from 45% in 2018 to 96% in 2020, contributing to the total 71% frequency. The significant increase seen in 2020 points to a higher frequency of syphilis in the general population, highlighting the need for more intensive preventative efforts and focused therapies. According to the RPR/VDRL test findings, frequency has been steady over time, ranging from 64% in 2018 to 65% in 2022. The population continues to have active syphilis infections, as seen by the cumulative total of 77%. This constancy highlights the need for continuous monitoring and prompt intervention tactics to stop the spread of syphilis. Throughout the course of the research, the TPHA test-which measures the presence of *Treponema pallidum* antibodies-showed a high frequency, rising to 91% in 2018 and staying above 84% in the following years. The 90% total frequency highlights how common syphilis exposure is among the populace. In order to lessen the effect of syphilis on public health, ongoing efforts in identification and treatment are required due to its high frequency.

Additionally, the clinical features of syphilis infection from 2018 to 2022 are shown in the table below. Remarkably, there were just two instances of chancre during the whole investigation. On the other hand,

Table 1. Results of Analysis

	2018	2019	2020	2021	2022	Grand Total
Total Number of Cases	11 (4 %)	79 (27 %)	75 (26 %)	105 (36 %)	20 (7 %)	290 (100 %)
Clinical Characteristics n (%)						
Chancre				1 (1 %)		1 (0 %)
Skin Rashes	3 (27 %)	13 (16 %)	4 (5 %)	14 (13 %)	1 (5 %)	35 (12 %)
Alopecia syphilitica		3 (4 %)	2 (3 %)	1 (1 %)		6 (2 %)
Lymphadenopathy		2 (3 %)		1 (1 %)		3 (1 %)
HIV	6 (55 %)	8 (10 %)	2 (3 %)	4 (4 %)	3 (15 %)	23 (8 %)
HBV			1 (1 %)	1 (1 %)		2 (1 %)
HCV		3 (4 %)	3 (4 %)	2 (2 %)		8 (3 %)
Chlamydia		5 (6 %)	12 (16 %)	2 (2 %)		19 (7 %)
gonorrhea		6 (8 %)	3 (4 %)			9 (3 %)
HPV				2 (2 %)		2 (1 %)
Syphilis AB	5 (45 %)	30 (38 %)	72 (96 %)	81 (77 %)	18 (90 %)	206 (71 %)
RPR/VDRL	7 (64 %)	64 (81 %)	61 (81 %)	78 (74 %)	13 (65 %)	223 (77 %)
TPHA	10 (91 %)	76 (96 %)	69 (92 %)	88 (84 %)	18 (90 %)	261 (90 %)
On Syphilis treatment	6 (55 %)	72 (91 %)	71 (95 %)	90 (86 %)	18 (90 %)	257 (89 %)
Re-infection	1 (9 %)	1 (1 %)	2 (3 %)	8 (8 %)	1 (5 %)	13 (4 %)

the frequency of skin rashes varied, reaching a high in 2019 with 13 instances (16%) and accounting for 12% of all cases that were detected. Just a small percentage of cases-six cases, or 2% of all cases-had the hair loss symptom of alopecia syphilitica diagnosed, with the majority of those cases occurring in 2019. There have only been three instances (1%) of lymphadenopathy, or enlargement of the lymph nodes, documented between 2019 and 2021. These results provide important new information on the distribution and patterns of different manifestations and highlight the dynamic nature of clinical features within the population under study throughout the given time period. The differences that have been seen highlight the value of longitudinal evaluations in capturing the complex dynamics of clinical presentations and might guide future investigations and therapeutic approaches.

We identified unique patterns and frequency in this in-depth analysis of related illnesses and comorbidities in a given population from 2018 to 2022. HIV infection rates fluctuated significantly, reaching a high of 55% in 2018 and then falling to 10% in 2019. Following that, there was a trend of fluctuation, with 4% in 2020, 4% in 2021, and a modest rise to 15% in 2022, for a total of 23 instances (8%). This variation highlights the need for ongoing HIV monitoring and may reflect changes in the demographics or risk factors of the group being studied.

Infections with the Hepatitis B Virus (HBV) were seldom reported; one case was recorded in 2020 and another in 2021, for a total of two cases (1%). Despite the small numbers, the possibility of long-term problems and the need for proper care and preventative measures make the existence of HBV in the community worthy of consideration. The frequency of Hepatitis C Virus (HCV) infections was more stable, with three cases (4%) recorded in 2020 and 2019 and two cases (2%) in 2021, for a total of eight cases (3%). The fact that HCV is still present indicates how crucial it is to continue surveillance and use intervention techniques in order to stop the virus from spreading and lessen its effects.

The frequency of chlamydia infections varied throughout the course of the research, with an increase of up to 16% in 2020, a decrease to 2% in 2021 and 19 cases (7%) overall throughout the study period. The increasing trend indicates that focused public health initiatives are required to combat and manage the spread of chlamydia among the populace. The number of cases of gonorrhea fluctuated, reaching a high of 8% in 2018 and then down to 3% in 2022, for a total of nine cases (3%). In order to effectively prevent and treat gonorrhea, it is essential to comprehend the causes causing these variances.

Infections with the human papillomavirus (HPV) were infrequent; in 2022, two cases (1%) were documented. Despite the low frequency, it is crucial to keep an eye on HPV developments because of its link to a number of malignancies, which emphasizes the need for immunization and preventative measures. All things considered, the thorough examination of related illnesses and comorbidities in this group offers insightful knowledge of the dynamic character of infectious diseases. These results advance our knowledge of the epidemiological environment and facilitate the development of focused public health programs and interventions aimed at addressing and lessening the effects of these illnesses. Effective disease monitoring and management strategies continue to rely heavily on longitudinal evaluations.

Additionally, the handling of syphilis cases in the population under study has shown noteworthy accomplishments, with treatment rates continuously above 86% between 2018 and 2022. The peak, which was attained in 2020 with a 95% treatment rate, is very notable. This is indicative of excellent treatment compliance and a successful medical response to syphilis infections. The continued high treatment rates demonstrate the dedication to providing syphilis patients prompt, all-encompassing care.

These positive results imply that the healthcare system has been effective in quickly detecting and treating instances of syphilis in the general population.

Re-infection rates were still rather low, but the differences that were seen over the course of the research years need to be carefully considered. Re-infection rates notably had a significant increase in 2021, rising to 8%. This significant increase in re-infections emphasizes how the population's syphilis epidemiology is dynamic. Developing tailored preventive interventions requires an understanding of the variables that lead to re-infection. In order to reduce the likelihood of recurring syphilis episodes, factors including partner notification, behavioral interventions, and patient education may be very important. In order to break the cycle of syphilis transmission, the cumulative re-infection rate of 4% highlights the need for continued monitoring and the necessity of persistent efforts in both prevention and treatment.

Discussion

The results of this investigation, which covered the years 2018 to 2022, provided insight into the clinical traits and related infections of syphilis in the community under observation. A noteworthy finding of the research is the differentiation of discrete clinical presentations of syphilis, including occasional alopecia syphilitica, varied skin rashes, and rarely lymphadenopathy, in line with past research [3-6]. These dynamic clinical presentations provide important insights into the distribution and patterns of different symptoms, highlighting the subtle nature of syphilis manifestations throughout time. In addition to potentially guiding future research and therapeutic treatments, longitudinal evaluations are essential for recording the changing dynamics of clinical features.

The trends in the frequency of syphilis as indicated by the Syphilis AB, RPR/VDRL, and TPHA tests over the 5-year study period show an increased frequency with syphilis AB and TPHA tests, and a steady but high frequency of syphilis based on the RPR and VDRL tests. This trend can be explained by the fact that there was a high number of late latent syphilis cases compared to primary syphilis in our study. RPR/VDRL test results consistently show a steady but high frequency of active syphilis infections, which highlights the need for more focused treatments, enhanced preventive measures, and interventions to reduce the spread of syphilis. The continued existence of syphilis in the community mostly as late latent syphilis calls for continuous monitoring prompt intervention measures.

Different frequencies of HIV, HBV, HCV, chlamydia, gonorrhea, and HPV were found in the population, according to the co-infection study. The rates of co-infection with HIV, HBV, HCV, chlamydia, gonorrhea, and HPV varied over the course of the study. Despite the low number of HBV cases, their existence highlights the need for proper care and preventative measures [25, 30- 32]. The steady frequency of HCV shows how crucial it is to use intervention techniques and continual monitoring to stop transmission. The erratic trend of HIV frequency highlights the need for ongoing HIV monitoring by pointing to possible changes in risk factors or demography. A significant number of individuals known to have HIV, who tested negative for syphilis at the beginning of the study period, were found to test positive for syphilis later in the study period, a finding which could be attributed to factors like practicing unprotected sex, and Men who have sex with men. There was not much variance found in the rates of co-infection with the other infections. Based on the analysis of rates of co-infection, and the finding of a significant number of HIV positive patients eventually going on to have syphilis, preventive measures like screening for co-infections in patients, testing their partners when positive and treating for infections in positive cases might impact the frequency of these

infections in the UAE population.

The research showed a steady rise in chlamydia infections, underscoring the need for focused public health initiatives to stop the disease's spread [9]. Cases of gonorrhea showed oscillations, and in order to develop effective preventative measures, it is essential to comprehend the mechanisms causing these changes [9-10]. HPV is associated with a number of malignancies, so even while its frequency is very low, the occasional occurrences emphasize the need to keep an eye on trends [21-25].

The population's handling of syphilis infections showed impressive results, with treatment rates staying high and over 86% from 2018 to 2022. The highest treatment rates in 2020 (95%) show that syphilis infections have been effectively addressed by healthcare. The noted rise in re-infection rates in 2021, however, raises questions and highlights how dynamic the epidemiology of syphilis is in the UAE. Comprehending the elements that lead to reinfection is essential for formulating focused preventive measures, such as alerting partners, implementing behavioral changes, and providing patient education.

Public health measures that have been implemented in the UAE include pre-marital screening which tests for HIV, HBV, HCV, and Syphilis amongst other things, in asymptomatic patients who would otherwise not present for testing. Occupational health screening has also been expanded to include screening for the conditions listed above as well.

These measures have allowed for the identification of asymptomatic patients so they can be treated and preventive and therapeutic measures can also be taken for their close contacts. Based on our study results, public health measures should include more widespread education on the subject of practicing safe sex and routine screening for STI's. Vaccinations for conditions like HBV and HPV infections should also be encouraged. At risk groups like individuals with HIV or other STI's, Men to Men sex (MSM), Sex workers should also be encouraged to get regular screenings for STI's. Partner check up should also be encouraged where necessary.

Ultimately, this research offers a thorough assessment of the clinical presentation, syphilis epidemiology, and related illnesses in the community under investigation. With the use of these data, public health programs and interventions will be better informed about the dynamic nature of syphilis and its co-infections. Our knowledge of the epidemiological environment is enhanced by these results, which also highlight the need for ongoing efforts in treatment and prevention to stop the spread of syphilis and its related illnesses. To address the changing patterns and difficulties in managing syphilis within the targeted demographic, the study does, however, recommend ongoing attention and research.

Conclusion

The results of this research, which covered the years 2018 to 2022, highlight the urgent need for increased public health awareness and focused actions in order to combat the alarming increase in the Frequency of syphilis. The intricate patterns of co-infection and subtle clinical symptoms highlight how constantly changing this infectious environment is, calling for ongoing monitoring and flexible intervention techniques. The impressive rates of treatment demonstrate the efficacy of healthcare interventions, yet the noted rise in re-infection rates in 2021 indicates persistent problems. Together, these observations support ongoing initiatives to increase public awareness, implement preventative measures into place, and educate healthcare professionals and the general public. The study is a call to action, stressing the need for a multimodal strategy to prevent the spread of syphilis and related illnesses, and it promotes further investigation and attention to detail in order to keep up with changing patterns in the treatment of syphilis in the targeted group.

Abbreviations

UAE - United Arab Emirates; STI - Sexually Transmitted Infection; AB - Antibody; RPR - Rapid Plasma Reagin; VDRL - Venereal Disease Research Laboratory; TPHA - Treponema Pallidum Hemagglutination Assay; HIV - Human Immunodeficiency Virus; HBV - Hepatitis B Virus; HCV - Hepatitis C Virus; HPV - Human Papilloma Virus

Statements

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Statement of Ethics

Study approval statement: This study protocol was reviewed and approved by [committee name withheld for review], approval number [withheld for review].

Consent to participate statement: No human participants were employed. The study did not need consent to participate as data was analyzed retrospectively. All patients who are treated in Dubai Health have signed the general consent which states that their data will be used for research purpose without revealing their identity.

Affiliation: Dubai Health

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Author 1 is the principal investigator who conceptualized the paper and developed the manuscript. Author 2 and author 3 were the principal co-investigators. Author 4 and author 5 were the research assistants who helped finalize the manuscript. Authors 6, author 7, and author 8 were responsible for data collection. Author 9 contributed to analyzing the data.

Data Availability Statement

The data that support the findings of this study are available on request from Author 1.

References

1. Oriol Mitjà, Suñer C, Giacani L, Martí Vall-Mayans, G.S. Tiplica, Ross J, et al. Treatment of bacterial sexually transmitted infections in Europe: gonorrhoea, Mycoplasma genitalium, and syphilis. *The Lancet Regional Health - Europe*. 2023 Nov 1;34:100737–7.
2. McDonald R. Vital Signs: Missed Opportunities for Preventing Congenital Syphilis -United States, 2022. *MMWR Morbidity and Mortality Weekly Report [Internet]*. 2023 [cited 2023 Dec 12];72. Available from: https://www.cdc.gov/mmwr/volumes/72/wr/mm7246e1.htm?s_cid=mm7246e1_w

3. Forrestel AK, Kovarik CL, Katz KA. Sexually Acquired Syphilis. Part 1: Historical aspects, microbiology, epidemiology, and clinical manifestations. *Journal of the American Academy of Dermatology*. 2019 Apr;82.
4. Whiting C, Schwartzman G, Khachemoune A. Syphilis in Dermatology: Recognition and Management. *American Journal of Clinical Dermatology*. 2023;24(2):287–97.
5. LaFond RE, Lukehart SA. Biological Basis for Syphilis. *Clinical Microbiology Reviews*. 2006 Jan 1;19(1):29–49.
6. Tuddenham S, Ghanem KG. Neurosyphilis. *Sexually Transmitted Diseases*. 2018 Mar;45(3):147–51.
7. Tuddenham S, Hamill MM, Ghanem KG. Diagnosis and Treatment of Sexually Transmitted Infections: A Review. *JAMA*. 2022 Jan 11;327(2):161–72.
8. Wang X, Dong W, Wang Q, McGoogan JM. Controlling Syphilis and Other Sexually Transmitted Infections. In: Springer eBooks. 2019. p. 41–62.
9. Mitchell CM, Anyalechi GE, Cohen CR, Haggerty CL, Manhart LE, Hillier SL. Etiology and Diagnosis of Pelvic Inflammatory Disease: Looking Beyond Gonorrhea and Chlamydia. *The Journal of Infectious Diseases*. 2021 Aug 15;224(Supplement_2):S29–35.
10. Buder S, Schöfer H, Meyer T, Bremer V, Kohl PK, Skaletz-Rorowski A, et al. Bacterial sexually transmitted infections. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2019 Mar;17(3):287–315.
11. Geretti AM, Mardh O, Vries HJC de, Winter A, McSorley J, Seguy N, et al. Sexual transmission of infections across Europe: appraising the present, scoping the future. *Sexually Transmitted Infections*. 2022 Sep 1;98(6):451–7.
12. Arando M, Fernandez-Naval C, Mota-Foix M, Martinez D, Armengol P, Barberá MJ, et al. Early syphilis: risk factors and clinical manifestations focusing on HIV-positive patients. *BMC Infectious Diseases*. 2019 Aug 16;19.
13. Pathela P, Braunstein SL, Blank S, Shepard C, Schillinger JA. The High Risk of an HIV Diagnosis Following a Diagnosis of Syphilis: A Population-level Analysis of New York City Men. *Clinical Infectious Diseases*. 2015 Apr 13;61(2):281–7.
14. Wong W, Chaw JK, Kent CK, Klausner JD. Risk Factors for Early Syphilis Among Gay and Bisexual Men Seen in an STD Clinic: San Francisco, 2002-2003. *Sexually Transmitted Diseases*. 2005;32(7):458–63.
15. Luo Z, Zhu L, Ding Y, Yuan J, Li W, Wu Q, et al. Factors associated with syphilis treatment failure and reinfection: a longitudinal cohort study in Shenzhen, China. *BMC Infectious Diseases*. 2017 Sep 13;17(1).
16. Wu MY, Gong HZ, Hu KR, Zheng H, Wan X, Li J. Effect of syphilis infection on HIV acquisition: a systematic review and meta-analysis. *Sexually Transmitted Infections*. 2020 Nov 18;
17. Gong H, Li J, Zheng H. The treatment outcome and predictors of serological response in syphilis in a sexually transmitted infections center, China. *International Journal of STD & AIDS*. 2022 Apr 6;33(6):575–83.
18. Cohen MS, Council OD, Chen JS. Sexually transmitted infections and HIV in the era of antiretroviral treatment and prevention: the biologic basis for epidemiologic synergy. *Journal of the*

- International AIDS Society. 2019 Aug;22(S6).
19. Mwatelah R, McKinnon LR, Baxter C, Abdool Karim Q, Abdool Karim SS. Mechanisms of sexually transmitted infection-induced inflammation in women: implications for HIV risk. *Journal of the International AIDS Society*. 2019 Aug;22(S6).
 20. Gong HZ, Hu KR, Lyu W, Zheng HY, Zhu WG, Wan X, et al. Risk Factors for the Co-infection with HIV, Hepatitis B and C Virus in Syphilis Patients. *Acta Dermato-Venereologica*. 2020 Oct 20;100(17):1–6.
 21. Kombe Kombe AJ, Li B, Zahid A, Mengist HM, Bounda GA, Zhou Y, et al. Epidemiology and Burden of Human Papillomavirus and Related Diseases, Molecular Pathogenesis, and Vaccine Evaluation. *Frontiers in Public Health*. 2021 Jan 20;8(552028).
 22. World Health Organization. Human papillomavirus and cancer [Internet]. www.who.int. 2023. Available from: <https://www.who.int/news-room/fact-sheets/detail/human-papilloma-virus-and-cancer>
 23. Abeck D, Tetsch L, Lüftl M, Biedermann T. Extragenital cutaneous warts – clinical presentation, diagnosis and treatment. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2019 Jun;17(6):613–34.
 24. D'Souza G, Clemens G, Strickler HD, Wiley DJ, Troy T, Struijk L, et al. Long term persistence of oral HPV over 7 years of follow-up. *JNCI Cancer Spectrum*. 2020 Jun 5;
 25. Zhang C, Ren Q, Chang W. Epidemiological Features and Risk Factors for Acquiring Hepatitis B, Hepatitis C, and Syphilis in HIV-Infected Patients in Shaanxi Province, Northwest China. *International Journal of Environmental Research and Public Health*. 2020 Mar 1;17(6):1990.
 26. Chen YJ, Huang JY, Baskaran R, Abomughaid MM, Hsieh CC, Lin WT. Long-Term Survival and Cancer Risk in the Hepatitis C Virus-Infected Patients After Antiviral Treatment: A Nationwide Cohort Study. *Journal of Cancer*. 2024 Jan 1;15(1):113–25.
 27. World Health Organization. Hepatitis B [Internet]. World Health Organization. World Health Organization; 2023. Available from: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>
 28. Lazarus JV, Roel E, Elsharkawy AM. Hepatitis C Virus Epidemiology and the Impact of Interferon-Free Hepatitis C Virus Therapy. *Cold Spring Harbor Perspectives in Medicine*. 2019 Sep 30;10(3):a036913.
 29. World Health Organization. Hepatitis C [Internet]. [Who.int](http://www.who.int). World Health Organization: WHO; 2023. Available from: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c> 18 July 2023
 30. Sebastião CS, Neto Z, Domingos Jandondo, Marinela Mirandela, Morais J, Brito M. HIV, hepatitis B virus, hepatitis C virus, and syphilis among pregnant women attending antenatal care in Luanda, Angola: Serofrequency and risk factors. 2020 Jun 24;92(12):3265–70.
 31. Katamba C, Chungu T, Lusale C. HIV, syphilis and hepatitis B coinfections in Mkushi, Zambia: a cross-sectional study. *F1000Research*. 2020 Jul 27;8:562.
 32. Arends RM, Nelwan EJ, Soediro R, van Crevel R, Alisjahbana B, Pohan HT, et al. Associations between impulsivity, risk behavior and HIV, HBV, HCV and syphilis serofrequency among female prisoners in Indonesia: A cross-sectional study. *Bullock B, editor. PLOS ONE*. 2019 Feb 15;14(2):e0207970.