

Epidemiology and predictors of positive serology for syphilis among men attending routine urological consultations

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Objectives: Sexually transmitted infections (STIs) remain a major global public health challenge. Urology consultations often serve as an entry point for men presenting with genitourinary symptoms that may be associated with underlying STIs. This work aims to describe epidemiological characteristics and identify behavioral and clinical predictors associated with self-reported lifetime STIs and laboratory-confirmed syphilis among men attending routine urology consultations in primary healthcare settings.

Methods: This cross-sectional study comprised two analytically independent components of routine urological patients in São Paulo, Brazil. The first included 2582 men aged 34–55 years who completed a standardized sociodemographic and behavioral questionnaire to assess self-reported lifetime STI history. The second included a separate cohort of 1092 men who provided blood samples for serological testing for syphilis. Univariate and multivariate logistic regression models were used to evaluate predictors of STI positivity in each dataset.

Results: In the questionnaire-based analysis, 587 participants (22.7%) reported a prior STI. Independent predictors of lifetime STI history included older age (OR: 1.045; 95% CI: 1.017–1.074), earlier sexual debut (OR: 0.843; 95% CI: 0.805–0.882), lower erectile function (OR: 0.978; 95% CI: 0.958–0.998), absence of prior STI counseling (OR: 1.419; 95% CI: 1.102–1.828), and recreational drug use (OR: 2.163; 95% CI: 1.334–3.509). In the serology-based analysis, 79 of 1092 participants (7.2%) tested positive for syphilis. Age at sexual initiation was the strongest independent predictor of seropositivity (OR: 0.609; 95% CI: 0.470–0.790), with later sexual debut being protective. No other behavioral or clinical variables showed significant associations with syphilis. Syphilis seropositivity was 3 times higher in those with a previous history of STI.

Conclusions: Earlier sexual debut, recreational drug use, lack of STI counseling, and increasing age were key determinants of STI risk. Age at sexual initiation consistently predicted both self-reported and laboratory-confirmed outcomes, emphasizing its role as a robust behavioral marker of vulnerability. Integrating structured sexual-health education, counseling, and preventive strategies into routine urological services may enhance early detection and reduce syphilis transmission.

Key Words: sexually transmitted diseases, syphilis, urology, risk factors, male sexual health

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Introduction

Sexually transmitted infections (STIs) remain a major global public health challenge, including in Brazil, with direct implications for urological practice and

men's health. Urology consultations often serve as an entry point for men presenting with genitourinary symptoms that may be associated with underlying STIs, including syphilis, hepatitis B and C, and HIV. Despite this clinical overlap, few studies have specifically described the epidemiological and clinical characteristics of men screened for STIs within urology-related care settings, particularly in primary healthcare environments.¹

According to the World Health Organization (WHO), more than 1 million curable STIs are acquired every day among individuals aged 15 to 49 years, most of whom remain asymptomatic. In 2020 alone, an estimated 374 million new infections occurred globally, including approximately 7.1 million cases of syphilis. Updated estimates also indicate that in 2022, about 254 million people were living with chronic hepatitis B, contributing to roughly 1.1 million deaths, predominantly from cirrhosis and hepatocellular carcinoma.²

In Brazil, surveillance data underscore the need to implement effective strategies to reduce STI transmission. According to the Epidemiological Bulletins of the Brazilian Ministry of Health, from 2010 to June 2024, 1,538,525 cases of acquired syphilis were reported. Over the same period, 785,571 cases of viral hepatitis were confirmed, including 289,029 cases of hepatitis B (36.8%) and 318,916 cases of hepatitis C (40.6%).³

Understanding the prevalence of positive serologies in this population and identifying predictors of syphilis positivity are crucial steps toward optimizing screening practices, informing targeted prevention strategies, and enhancing clinical outcomes. Age, sexual behavior, comorbidities, and hormonal or metabolic profiles may influence exposure risk and seroconversion; however, these factors remain insufficiently explored in routine urological settings.

This study aims to describe the epidemiological characteristics and identify clinical and laboratory predictors of positive syphilis serology among men attending urology consultations, through an analytical cross-sectional design. By delineating risk profiles in this population, the findings may support the development of more effective screening protocols and promote integrated management strategies in urological care.

Material and Methods

Study design, setting, and participants

This analytical cross-sectional study was conducted after approval by the Research Ethics Committee of

the Faculty of Medical Sciences at the University of Campinas (UNICAMP), approval number 543.095, using medical records of male patients from São Paulo, Brazil.

Participants were recruited from multiple primary healthcare units through routine outpatient urology consultations and completed an anonymous, standardized 22-item questionnaire that assessed sociodemographic and behavioral factors.

The questionnaire assessed self-reported previous history of STI, age, education, occupation, comorbidities, age at sexual initiation (ASI), frequency of sexual activity, masturbation and ejaculation patterns, condom use, presence of a steady partner, prior counseling on STI prevention, legal or illegal drug use, and family history of prostate cancer. Information regarding sexual orientation or partner gender was not collected (**Supplementary File 1**).

STIs were defined for participants in clear, non-technical language as "infections that can be passed from one person to another through sexual contact". Sexual contact was explained to include vaginal, anal, and oral sex. Participants were informed that STIs may or may not cause symptoms and that some infections can remain unnoticed for long periods. Common examples (such as syphilis, gonorrhea, HIV, herpes, and HPV) were provided to facilitate understanding. The term "STI" was used instead of "venereal disease", and no microbiological or clinical terminology was included to ensure comprehension by lay respondents.

The validated International Index of Erectile Function (IIEF) scores were used to measure sexual function,⁴ and the validated International Prostatic Symptoms Score (IPSS) was used to measure urinary symptoms.⁵

Additional biochemical tests included total PSA, free PSA, the free-to-total PSA ratio, total testosterone, and sex hormone-binding globulin (SHBG), which are routinely used in prostate cancer screening and hormonal evaluation. The physical examination data (weight, height, and penile size) were also analyzed.

Data collection occurred between January 2023 and December 2024. A convenience sampling strategy was applied, and all male patients attending urological consultations during the study period were included. The study was authorized to proceed with a waiver of the Informed Consent Form (ICF), as all analyses used anonymized retrospective clinical and laboratory data. All procedures were conducted in accordance with institutional and national ethical regulations, ensuring the full preservation of participant anonymity and confidentiality.

The study comprised two analytically independent cohorts derived from the same underlying source population. The first cohort (A) included 2582 consecutive men who completed the standardized questionnaire and was used exclusively for questionnaire-based analyses. The second cohort (B) included 1092 consecutive men who provided biological samples suitable for serological testing. For syphilis screening, a non-treponemal test (Venereal Disease Research Laboratory [VDRL]) was performed as the initial screening assay. Reactive samples were further evaluated with treponemal serology to confirm exposure to *Treponema pallidum*. Results were interpreted according to standard serologic algorithms, considering both qualitative reactivity and VDRL titers for clinical correlation.

No individual participant contributed data to both analytical models. This design minimizes analytical dependence while allowing complementary inference from behavioral and biological data sources.

(A) Questionnaire-based analysis: previous history of sexually transmitted infection

A total of 2582 patients were classified according to self-reported previous history of STI as “Yes” ($n = 587$, 22.7%) or “No” ($n = 1995$).

(B) Serology-based analysis: syphilis testing

A separate cohort of 1092 patients provided blood samples for serological testing and were categorized according to their syphilis results as positive ($n = 79$, 7.2%) or negative ($n = 1013$). All blood samples were processed at the Men’s Health Hospital in Paulínia County, São Paulo, Brazil, for serological testing for syphilis, following protocols recommended by the Brazilian Ministry of Health.⁶

Statistical analysis

Statistical analyses were performed by the Statistics Service of the Research Chamber at the Faculty of Medical Sciences, UNICAMP, using SAS System for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA). The primary objectives were to identify predictive factors associated with (A) previous history of STI and (B) syphilis seropositivity. For each dataset, univariate and multivariate logistic regression models were used to assess associations among sociodemographic, behavioral, and clinical variables.

Qualitative variables were expressed as absolute and relative frequencies, while quantitative variables were presented as means and standard deviations (SD). Prevalence estimates for STI history were calculated with 95% binomial confidence intervals. A 5% significance level ($p < 0.05$) was adopted.

Results

Previous history of sexually transmitted infection

A total of 2582 male participants completed the questionnaire. Overall, 587 individuals (22.7%) reported a history of STI. The mean age was 51.2 ± 5.7 years, with a median age of 55 years. Educational attainment was predominantly low: 62.2% had completed elementary school, while 9.3% had higher education. Alcohol consumption was infrequent (11.4%), and 5.4% reported recreational drug use. The mean age at sexual debut was 16.9 ± 3.1 years. Most participants reported never using condoms (68.0%) and had not received prior counseling on STIs (62.1%). Manual labor was the most common occupation (56.6%). Descriptive characteristics are summarized in [Table 1](#).

In the univariate analysis, several variables were significantly associated with a prior history of STI. Older age was positively associated with a history of STIs (OR = 1.049; 95% CI, 1.030–1.068; $p < 0.0001$). Conversely, older ASI was inversely associated with STI history (OR = 0.864; 95% CI 0.833–0.895; $p < 0.0001$), indicating that individuals who initiated sexual activity at a younger age had a higher risk of infection. Behavioral factors also contributed: former smokers had increased odds of STI (OR 1.576; 95% CI 1.254–1.980; $p < 0.0001$), and recreational drug users had more than double the risk (OR 2.409; 95% CI 1.683–3.449; $p < 0.0001$).

Moreover, patients without a family history of prostate cancer had a modestly increased risk (OR = 1.307; 95% CI 1.015–1.683; $p = 0.0382$). Participants who did not receive counseling about STIs had a significantly higher likelihood of having had a history of sexually transmitted infection (OR = 1.488; 95% CI = 1.234–1.794; $p < 0.0001$). This finding suggests that the absence of STI-related guidance may be associated with increased vulnerability or reduced access to preventive care.

Additionally, International Index of Erectile Function (IIEF) scores were significantly inversely associated with previous STI positivity (OR = 0.975; 95% CI 0.958–0.992; $p = 0.0051$). SHBG showed no significant association in the univariate model ($p = 0.3954$).

In the full multivariate model ([Table 2](#)), age, age at sexual initiation, erectile function as measured by the IIEF-5 score, absence of prior STI counseling, and recreational drug use remained independently associated with a history of sexually transmitted infection.

Specifically, increasing age was associated with higher odds of having had an STI (OR 1.045; 95%

TABLE 1. Sociodemographic, clinical, and behavioral characteristics according to lifetime STI history

Variable	Yes STI (n = 587)	No STI (n = 1995)	Total (n = 2582)	p-Value
Age, years (Mean $\pm$ SD; Median, min–max)	52.3 $\pm$ 4.8; 55 (34–55) (n = 586)	50.9 $\pm$ 5.9; 55 (34–55) (n = 1994)	51.2 $\pm$ 5.7; 55 (34–55) (n = 2580)	<0.0001 ^a
Penile length (cm). Mean $\pm$ SD/Median (min–max)	13.5 $\pm$ 2.3; 14 (7–19.3) (n = 494)	13.5 $\pm$ 2.3; 14 (4–22) (n = 1721)	13.5 $\pm$ 2.3; 14 (4–22) (n = 2215)	0.8587 ^a
Weight (kg). Mean $\pm$ SD/Median (min–max)	81.3 $\pm$ 14.1; 81 (50.5–133) (n = 566)	82.0 $\pm$ 23.7; 80 (40–850) (n = 1921)	81.8 $\pm$ 21.9; 80 (40–850) (n = 2487)	0.7008 ^a
Height (m). Mean $\pm$ SD/Median (min–max)	1.6 $\pm$ 0.2; 1.7 (1.1–1.9) (n = 582)	1.7 $\pm$ 0.1; 1.7 (1.1–2.0) (n = 1976)	1.7 $\pm$ 0.2; 1.7 (1.1–2.0) (n = 2558)	0.8885 ^a
ASI years Mean $\pm$ SD/Median (min–max)	16.0 $\pm$ 2.7; 16 (9–30) (n = 580)	17.2 $\pm$ 3.2; 17 (5–36) (n = 1949)	16.9 $\pm$ 3.1; 17 (5–36) (n = 2529)	<0.0001 ^a
Sex frequency, monthly Mean $\pm$ SD/Median (min–max)	8.2 $\pm$ 6.0; 8 (0–30) (n = 549)	7.8 $\pm$ 4.8; 8 (0–30) (n = 1865)	7.9 $\pm$ 5.9; 8 (0–30) (n = 2414)	0.2535 ^a
Masturbation frequency, monthly Mean $\pm$ SD/Median (min–max)	1.7 $\pm$ 3.4; 0 (0–20) (n = 498)	1.8 $\pm$ 3.8; 0 (0–60) (n = 1715)	1.7 $\pm$ 3.7; 0 (0–60) (n = 2213)	0.2554 ^a
Alcohol intake, monthly doses. Mean $\pm$ SD/Median (min–max)	6.3 $\pm$ 8.9; 2 (0–30) (n = 58)	7.3 $\pm$ 16.8; 3 (0–196) (n = 174)	7.0 $\pm$ 15.2; 3 (0–196) (n = 232)	0.3865 ^a
IPSS score. Mean $\pm$ SD/Median (min–max)	2.3 $\pm$ 5.0; 0 (0–20) (n = 509)	1.9 $\pm$ 4.4; 0 (0–20) (n = 1699)	2.0 $\pm$ 4.6; 0 (0–20) (n = 2208)	0.2353 ^a
IIEF-5 score. Mean $\pm$ SD/Median (min–max)	17.6 $\pm$ 5.8; 22 (5–22) (n = 472)	18.4 $\pm$ 5.5; 22 (5–22) (n = 1545)	18.2 $\pm$ 5.6; 22 (5–22) (n = 2017)	0.0018 ^a
Total PSA, ng/mL. Mean $\pm$ SD/Median (min–max)	1.5 $\pm$ 1.6; 1.0 (0.1–14.0) (n = 557)	1.3 $\pm$ 1.5; 0.9 (0.1–12.7) (n = 1848)	1.4 $\pm$ 1.4; 0.9 (0.1–14.0) (n = 2405)	0.0646 ^a
Free PSA, ng/mL. Mean $\pm$ SD/Median (min–max)	0.4 $\pm$ 0.5; 0.3 (0–7.7) (n = 481)	0.5 $\pm$ 0.4; 0.3 (0–12.0) (n = 1568)	0.5 $\pm$ 0.5; 0.3 (0–12.0) (n = 2049)	0.2219 ^a
Free/Total PSA ratio (%) Mean $\pm$ SD/Median (min–max)	34.4 $\pm$ 18.0; 30.3 (0.9–100) (n = 479)	34.0 $\pm$ 16.8; 31.6 (1.6–93.8) (n = 1549)	34.1 $\pm$ 17.1; 31.3 (0.9–100) (n = 2028)	0.8464 ^a
Total testosterone, ng/dL. Mean $\pm$ SD/Median (min–max)	483.7 $\pm$ 295.7; 434 (132.4–4704) (n = 520)	467.8 $\pm$ 218.2; 432 (16–2788.5) (n = 1736)	471.5 $\pm$ 238.3; 432 (16–4704) (n = 2256)	0.7341 ^a
Free testosterone, pg/mL. Mean $\pm$ SD/Median (min–max)	46.7 $\pm$ 41.3; 43 (0.7–238) (n = 495)	45.9 $\pm$ 56.8; 34 (0.1–829) (n = 1675)	46.1 $\pm$ 53.7; 37 (0.1–829) (n = 2170)	0.0519 ^a
SHBG, nmol/L. Mean $\pm$ SD/Median (min–max)	46.6 $\pm$ 22.6; 43.1 (8–157.2) (n = 502)	45.4 $\pm$ 27.9; 40.1 (2–464.5) (n = 1692)	45.7 $\pm$ 26.8; 40.8 (2–464.5) (n = 2194)	0.0225 ^a
Education n (%)				0.1890 ^b
– Elementary	367 (65.0%)	1179 (61.4%)	1546 (62.2%)	
– Secondary	144 (25.5%)	565 (29.4%)	709 (28.5%)	
– Higher education	54 (9.6%)	176 (9.2%)	230 (9.3%)	
Occupation n (%)				0.3428 ^b
– Manual labor	313 (54.6%)	1130 (57.2%)	1443 (56.6%)	
– Retired	160 (27.9%)	501 (25.4%)	661 (25.9%)	
– Intellectual	99 (17.3%)	332 (16.8%)	431 (16.9%)	
Comorbidities n (%)				0.5539 ^b
– Diabetes	45 (12.9%)	113 (10.5%)	158 (11.1%)	
– Hypertension	157 (44.9%)	517 (48.0%)	674 (47.2%)	
Steady partner n (%)	483 (86.6%)	1675 (88.8%)	2158 (88.3%)	0.1458 ^b
Condom use n (%)				0.2278 ^b
– Never	373 (68.8%)	1185 (67.8%)	1558 (68.0%)	
– Sometimes	108 (19.9%)	398 (22.8%)	506 (22.1%)	
– Always	61 (11.3%)	165 (9.4%)	226 (9.9%)	
Ejaculation adequate time n (%)	313 (55.4%)	1030 (53.8%)	1343 (54.2%)	0.4991 ^b
STI counseling received n (%)	265 (45.2%)	708 (35.7%)	973 (37.9%)	<0.0001 ^b
Family history of prostate cancer n (%)	89 (15.7%)	373 (19.6%)	462 (18.7%)	0.0378 ^b
Smoking status n (%)				0.0004 ^b
– Former	140 (24.0%)	339 (17.1%)	479 (18.7%)	
– Current	82 (14.1%)	263 (13.3%)	345 (13.5%)	
Alcohol use Yes n (%)	72 (12.3%)	221 (11.2%)	293 (11.4%)	0.4336 ^b
Drug use Yes n (%)	54 (9.5%)	80 (4.2%)	134 (5.4%)	<0.0001 ^b

Note. ^aBased on Mann–Whitney test/^bBased on Chi-square test.

Sexually transmitted infection (STI), age at sexual initiation (ASI), International Prostatic Symptoms Score (IPSS), International Index of Erectile Function (IIEF), sex hormone binding globulin (SHBG), Prostate Specific Antigen (PSA), standard deviation (SD).

TABLE 2. Predictors of reporting a previous STI (“Yes”). Multivariable model including all significant variables from Table 1 (n = 1636)

Factors	OR	95% CI	p-Value*
Age years (continuous)	1.045	1.017–1.074	0.0013
ASI years (continuous)	0.843	0.805–0.882	<0.0001
IIEF-5 (continuous)	0.978	0.958–0.998	0.0328
SHBG nmol/L (continuous)	1.002	0.998–1.006	0.3834
No STI-oriented care	1.419	1.102–1.828	0.0066
Family history of prostate cancer (No)	1.291	0.930–1.792	0.1265
Smoking (former)	1.121	0.839–1.499	0.1819
Smoking (current)	0.769	0.535–1.105	—
Recreational drugs (Yes)	2.163	1.334–3.509	0.0018

Note. *based on multivariable logistic regression.
Age at sexual initiation (ASI), International Index of Erectile Function (IIEF), sex hormone binding globulin (SHBG), sexually transmitted infection (STI), Odds Ratio (OR), Confidence Interval (CI).

TABLE 3. Predictors of reporting a previous STI (“Yes”). Multivariable model using stepwise selection (All variables except monthly dose; n = 427)

Factor	OR	95% CI	p-Value*
ASI years (continuous)	0.862	0.794–0.937	0.0005
SHBG nmol/L (continuous)	1.011	1.001–1.021	0.0316

Note. *based on multivariable logistic regression (stepwise selection).
Age at sexual initiation (ASI), sex hormone binding globulin (SHBG), Odds Ratio (OR), Confidence Interval (CI).

CI 1.017–1.074; $p = 0.0013$), while older age at sexual initiation acted as a protective factor (OR 0.843; 95% CI 0.805–0.882; $p < 0.0001$). Lower IIEF-5 scores were also associated with a history of STIs (OR 0.978; 95% CI 0.958–0.998; $p = 0.0328$). Individuals who had never received STI counseling exhibited increased odds of infection (OR 1.419; 95% CI 1.102–1.828; $p = 0.0066$), and recreational drug use remained a strong independent predictor (OR 2.163; 95% CI 1.334–3.509; $p = 0.0018$). In contrast, family history of prostate cancer and smoking did not retain statistical significance in the adjusted model.

In the reduced model obtained through stepwise selection (Table 3), age at sexual initiation remained a significant protective factor (OR: 0.862; 95% CI: 0.794–0.937; $p = 0.0005$) and SHBG levels showed a modest but statistically significant association (OR 1.011; 95% CI 1.001–1.021; $p = 0.0316$). These findings suggest that both behavioral and biological factors might independently contribute to STI risk, with earlier sexual debut representing a key determinant in this population.

Syphilis serological testing

Among the 1092 patients who underwent serological testing, 79 (7.2%) tested positive for syphilis. In the univariate analysis, individuals with syphilis were significantly older (52.0 ± 5.2 vs. 50.3 ± 5.8 years; $p = 0.0059$), reported an earlier age at sexual initiation (15.6 ± 2.5 vs. 17.1 ± 3.2 years; $p < 0.0001$), and showed higher drug use (5.6% vs. 1.6%; $p = 0.0177$) (Table 4).

No significant differences were observed in penile size, weight, height, frequency of sexual activity or masturbation, PSA levels, testosterone (total or free), or SHBG (all $p > 0.05$). Educational level, occupation, comorbidities, condom use, presence of a steady partner, alcohol use, and STI counseling also showed no significant differences ($p > 0.05$).

Age, age at sexual initiation, and drug use were therefore selected for inclusion in the subsequent multivariate models. In the complete multivariate model (Table 5), both age and age at sexual initiation remained statistically significant predictors of syphilis seropositivity. Increasing age was associated

TABLE 4. Association between baseline clinical/laboratory variables and syphilis status (n = 1092)

Variable	Syphilis—Yes (n = 79)	Syphilis—No (n = 1013)	Total (n = 1092)	p-Value
Age years Mean $\pm$ SD/Median (min–max)	52.0 $\pm$ 5.2/55.0 (35–55)	50.3 $\pm$ 5.8/55.0 (35–55)	50.4 $\pm$ 5.7/55.0 (35–55)	0.0059 ¹
Penile length cm Mean $\pm$ SD/Median (min–max)	14.0 $\pm$ 1.9/14.0 (10–18)	14.2 $\pm$ 1.8/14.0 (7.5–22)	14.2 $\pm$ 1.8/14.0 (7.5–22)	0.3313 ¹
Weight Kg Mean $\pm$ SD/Median (min–max)	83.4 $\pm$ 14.5/82.0 (56–130)	81.5 $\pm$ 16.5/79.5 (40–170)	81.7 $\pm$ 16.3/80.0 (40–170)	0.2755 ¹
Height m Mean $\pm$ SD/Median (min–max)	1.7 $\pm$ 0.1/1.7 (1.5–2.0)	1.7 $\pm$ 0.1/1.7 (1.5–2.0)	1.7 $\pm$ 0.1/1.7 (1.5–2.0)	0.4387 ¹
ASI years Mean $\pm$ SD/Median (min–max)	15.6 $\pm$ 2.5/16.0 (7–22)	17.1 $\pm$ 3.2/17.0 (5–36)	17.0 $\pm$ 3.0/17.0 (5–36)	<0.0001 ¹
Sex frequency per week Mean $\pm$ SD/Median (min–max)	6.0 $\pm$ 6.1/4.0 (0–30)	5.8 $\pm$ 4.6/4.0 (0–30)	5.9 $\pm$ 5.5/4.0 (0–30)	0.7696 ¹
Masturbation frequency per week Mean $\pm$ SD/Median (min–max)	3.1 $\pm$ 5.2/0 (0–20)	2.3 $\pm$ 4.3/0 (0–30)	2.4 $\pm$ 4.4/0 (0–30)	0.1357 ¹
Alcohol doses/month. Mean $\pm$ SD/Median (min–max)	—	11.5 $\pm$ 10.8/8.0 (0–30)	11.5 $\pm$ 10.8/8.0 (0–30)	—
IPSS. Mean $\pm$ SD/Median (min–max)	0.8 $\pm$ 2.4/0 (0–8)	1.5 $\pm$ 4.4/0 (0–20)	1.5 $\pm$ 4.2/0 (0–20)	0.3705 ¹
IIEF-5. Mean $\pm$ SD/Median (min–max)	17.5 $\pm$ 5.8/18.0 (5–22)	18.2 $\pm$ 5.4/22.0 (5–22)	18.1 $\pm$ 5.5/22.0 (5–22)	0.4090 ¹
Total PSA. Mean $\pm$ SD/Median (min–max)	1.5 $\pm$ 1.7/1.0 (0.2–9.4)	1.3 $\pm$ 1.2/0.9 (0.1–12.2)	1.3 $\pm$ 1.3/0.9 (0.1–12.2)	0.4746 ¹
Free PSA. Mean $\pm$ SD/Median (min–max)	0.4 $\pm$ 0.4/0.3 (0.1–1.8)	0.4 $\pm$ 0.3/0.3 (0–3.0)	0.4 $\pm$ 0.3/0.3 (0–3.0)	0.8501 ¹
PSA ratio. Mean $\pm$ SD/Median (min–max)	31.4 $\pm$ 13.8/27.5 (5.1–62.5)	33.9 $\pm$ 15.8/30.9 (2.9–100.0)	33.7 $\pm$ 15.6/30.6 (2.9–100.0)	0.2110 ¹
Total testosterone. Mean $\pm$ SD/Median (min–max)	483.4 $\pm$ 189.1/469.5 (171–1042)	531.0 $\pm$ 237.8/487.8 (16–2788)	526.8 $\pm$ 234.3/486.2 (16–2788)	0.1072 ¹
Free testosterone. Mean $\pm$ SD/Median (min–max)	9.3 $\pm$ 3.4/8.8 (2.8–19.7)	13.1 $\pm$ 46./9.9 (0.3–829)	12.8 $\pm$ 44.2/9.8 (0.3–829)	0.0278 ¹
SHBG. Mean $\pm$ SD/Median (min–max)	39.9 $\pm$ 17.8/38.5 (10–108)	41.7 $\pm$ 25.8/36.7 (9–464)	41.6 $\pm$ 25.2/36.8 (9–464)	0.9407 ¹
Education n (%)				0.2220 ²
Fundamental	50 (67.6%)	452 (57.6%)	502 (58.4%)	
High school	20 (27.0%)	262 (33.4%)	282 (32.8%)	
University	4 (5.4%)	71 (9.0%)	75 (8.7%)	
Occupation n (%)				0.8544 ²
Retired	17 (22.7%)	211 (26.0%)	228 (25.7%)	
Manual labor	45 (60.0%)	478 (58.9%)	523 (59.0%)	
Intellectual	13 (17.3%)	121 (14.9%)	134 (15.1%)	
Other	0 (0.0%)	2 (0.2%)	2 (0.2%)	
Comorbidities n (%)				0.7070 ²
DM	6 (11.3%)	47 (9.8%)	53 (10.0%)	
DM/HAS	8 (15.1%)	90 (18.8%)	98 (18.5%)	
HAS	27 (50.9%)	210 (43.9%)	237 (44.6%)	
Other	12 (22.6%)	131 (27.4%)	143 (26.9%)	
Stable partner				0.2734 ²
No	12 (15.6%)	88 (11.4%)	100 (11.8%)	
Yes	65 (84.4%)	686 (88.6%)	751 (88.2%)	
Condom use				0.8708 ²
Occasional	28 (41.8%)	286 (40.7%)	314 (40.8%)	
Never	30 (44.8%)	334 (47.6%)	364 (47.3%)	
Always	9 (13.4%)	82 (11.7%)	91 (11.8%)	
Premature ejaculation				0.5374 ²
No	41 (55.4%)	448 (59.1%)	489 (58.8%)	
Yes	33 (44.6%)	310 (40.9%)	343 (41.2%)	
STI-oriented care				0.3854 ²
No	20 (26.0%)	173 (21.7%)	193 (22.1%)	
Yes	57 (74.0%)	625 (78.3%)	682 (77.9%)	
Family history of prostate cancer				0.3671 ²
No	63 (80.8%)	613 (76.2%)	676 (76.6%)	
Yes	15 (19.2%)	191 (23.8%)	206 (23.4%)	
Smoking				0.0880 ²
Former	5 (6.3%)	59 (5.9%)	64 (5.9%)	
Never	60 (75.9%)	840 (84.2%)	900 (83.6%)	
Current	14 (17.7%)	99 (9.9%)	113 (10.5%)	
Alcohol use				0.7252 ²
No	78 (98.7%)	978 (98.2%)	1056 (98.2%)	
Yes	1 (1.3%)	18 (1.8%)	19 (1.8%)	
Recreational drugs				0.0177 ²
No	68 (94.4%)	919 (98.4%)	987 (98.1%)	
Yes	4 (5.6%)	15 (1.6%)	19 (1.9%)	

Note. ¹Based on Mann–Whitney test/²Based on Chi-square test

Age at sexual initiation (ASI), International Prostatic Symptoms Score (IPSS), International Index of Erectile Function (IIEF), sex hormone binding globulin (SHBG), sexually transmitted infection (STI), Prostate Specific Antigen (PSA), Standard Deviation (SD).

TABLE 5. Multivariate predictors of syphilis (“Yes” response) (n = 770)

Factor	OR	95% CI	p-Value*
Age years (continuous)	1.094	1.036–1.156	0.0012
ASI years (continuous)	0.818	0.742–0.901	<0.0001
Free testosterone ng/dL (continuous)	0.955	0.894–1.021	0.1803
Recreational drugs (Yes)	2.513	0.732–8.624	0.1429

Note. *based on multivariable logistic regression.
Age at sexual initiation (ASI), Odds Ratio (OR), Confidence Interval (CI).

TABLE 6. Stepwise multivariate predictor of syphilis (“Yes” Response) (n = 185)

Factor	OR	95% CI	p-value*
ASI years (continuous)	0.609	0.470–0.790	0.0002

Note. *based on multivariable logistic regression (stepwise selection).
Age at sexual initiation (ASI), Odds Ratio (OR), Confidence Interval (CI).

with higher odds of infection (OR 1.094; 95% CI 1.036–1.156; $p = 0.0012$), whereas older ASI was protective (OR 0.818; 95% CI 0.742–0.901; $p < 0.0001$).

In the stepwise model (Table 6), age at sexual initiation persisted as the only independent predictor of syphilis, with a strong protective association (OR 0.609; 95% CI 0.470–0.790; $p = 0.0002$). These findings emphasize the central influence of early sexual debut on syphilis risk within this population.

When patients who underwent syphilis serological testing were asked about previous history of STI, the test positivity was significantly higher in those with a previous history of STI (15.1%) compared to those with no history of STI (5.3%), $p < 0.0001$ (Chi-square test).

Discussion

Sexually transmitted infections remain a major public health concern, and the scarcity of male-centered epidemiological data limits the development of effective prevention strategies. In this study, two analytically independent approaches were examined: self-reported lifetime history of STIs and laboratory-confirmed syphilis seropositivity, derived from distinct cohorts. Although these methods assess

different outcomes, their convergence on key predictors enhances the credibility of our findings and emphasizes consistent behavioral risk patterns among middle-aged men attending routine urological services.^{1–3}

From a causal inference perspective, a nested-independent cohort design enables the study to address distinct causal questions while minimizing bias arising from measurement heterogeneity and missing data. The questionnaire-based cohort captures self-reported exposures and outcomes relevant to behavioral and clinical associations, whereas the serology-based cohort enables biologically anchored inference based on objectively measured markers. Restricting each analysis to a single data modality avoids conditioning on post-exposure variables and reduces the risk of collider-stratification bias that could arise if questionnaire and serological data were jointly modeled in a partially observed cohort.

In the questionnaire-based cohort evaluating lifetime STI history, older age was independently associated with increased odds of reporting a previous infection, consistent with international trends of rising STI prevalence among adults over 45 years.^{7,8} Several behavioral and social factors likely contribute, including a greater number of lifetime sexual exposures and inconsistent condom use, although these mechanisms were not directly measured in this study and should therefore be interpreted cautiously.

Across all models, ASI, in particular, earlier sexual debut emerged as a consistent determinant of vulnerability. Later sexual initiation demonstrated a robust protective effect in both analyses, while earlier initiation increased STI risk. This graded effect of ASI supports its interpretation as a continuous behavioral marker of STI risk, aligning with previous studies that show earlier sexual initiation is associated with a higher number of sexual partners and increased engagement in risk behaviors.^{9,10}

Although ASI consistently showed an association across all models, the effect size varied, particularly

in the stepwise regression, where the odds ratio was more pronounced. This variation likely reflects the inherent instability of stepwise model selection, which may inflate effect estimates through variable exclusion and data-driven optimization. Accordingly, while the consistency in direction supports ASI as a relevant behavioral determinant, the absolute effect sizes, especially those derived from reduced models, should be interpreted with caution.

Recreational drug use was independently associated with lifetime STI history, increasing the odds of reporting a previous infection more than twofold. Because drug use did not show a robust association with laboratory-confirmed syphilis, and the number of syphilis-positive individuals reporting drug use was relatively small, this finding should be interpreted specifically within the questionnaire-based cohort.

Family history of prostate cancer was not independently associated with STI history after adjustment, a finding that aligns with previous evidence¹¹ showing that perceived vulnerability linked to family cancer history does not necessarily translate into changes in screening or sexual health behaviors. On the other hand, previous studies have demonstrated that smoking history and alcohol and drug use during sexual activity increase engagement in high-risk behaviors associated with STI acquisition.¹²

A particularly relevant finding was the role of STI counseling. Men who had not received counseling were significantly more likely to report a previous infection, suggesting that lack of guidance reduces awareness of risks and limits adoption of safer sexual practices. This association was observed only for self-reported STI history, not laboratory-confirmed syphilis, highlighting that counseling primarily affects lifetime behavioral risk. Evidence supports the effectiveness of structured educational and risk-reduction interventions in primary care in decreasing vulnerability and improving engagement with testing and follow-up.^{13,14} These results underscore the potential value of integrating structured counseling into routine urological care. Also, in a recent meta-analysis, low-income countries had the highest prevalence of self-reported STIs (5.53%), lower-middle-income countries had a moderate prevalence (5.19%), and upper-middle-income countries had the lowest prevalence among men (1.15%).¹⁵

In the serology-based analysis of syphilis, age and ASI were the only significant predictors of infection, with ASI remaining the sole independent predictor in the stepwise model. No significant associations were

observed for condom use, anthropometric measurements, comorbidities, hormonal parameters, sexual behavior variables, or counseling, consistent with the smaller number of syphilis-positive individuals and the limited statistical power of this cohort.

The consistency of ASI across both datasets reinforces its role as a robust behavioral marker of syphilis risk. On the other hand, the serology-based analysis included a relatively limited number of individuals with positive syphilis serology ($n = 79$), which constrains statistical power, particularly for detecting modest associations. Accordingly, the lack of statistically significant associations between syphilis seropositivity and variables such as prior counseling, condom use, or hormonal parameters should be interpreted with caution. These null findings may reflect insufficient power rather than a true absence of effect, and small to moderate associations cannot be excluded. Larger studies with more seropositive cases are needed to more definitively assess these relationships.

Global evidence also shows that the burden of major STIs, including syphilis, chlamydia, gonorrhea, trichomoniasis, genital herpes, and HPV, has remained high over the last three decades in several regions, including the Middle East and North Africa, despite longstanding public-health initiatives. These trends reflect persistent gaps in prevention, screening, early detection, and sexual-health education. This global pattern is consistent with the present findings, underscoring that insufficient counseling and limited access to preventive services continue to contribute to sustained STI transmission and highlighting the strategic opportunity to leverage urology clinics as critical points of intervention.¹⁶

Although this study is well powered and provides robust estimates of syphilis-associated risk factors, the findings should be interpreted within the geographic and sociocultural context of the study population. All participants were men residing in Brazil, and epidemiological patterns of syphilis, sexual behaviors, access to testing and treatment, and public health responses vary across regions. Consequently, the generalizability of these results to men in other global settings, particularly in Africa and Asia, cannot be assumed. Validation in diverse populations and health system contexts will be necessary to determine the extent to which these associations hold across different regions and epidemiological landscapes.

This study has limitations. Behavioral data relied on self-report and may be affected by recall or social desirability bias. The cross-sectional design

precludes causal inference. The number of syphilis-positive individuals was relatively small, limiting statistical power for some comparisons. Given the modest effect size and the absence of a consistent signal across modeling strategies for some variables (i.e., SHBG), it likely reflects model-dependent effects related to variable selection and shared variance rather than a robust independent association. These findings should be interpreted cautiously and viewed as hypothesis-generating rather than confirmatory. Overall, the result underscores the sensitivity of reduced models to variable selection procedures and reinforces the need to prioritize consistency across analytical approaches when interpreting associations. Furthermore, the cohort represents a specific region of southeastern Brazil and may not fully reflect the diversity of other populations.

Despite these limitations, this study provides consistent evidence that specific demographic and behavioral characteristics shape STI vulnerability among men. The findings highlight a substantial and underrecognized at-risk population within routine urological care, reinforcing the strategic role of these services in delivering targeted prevention, screening, and counseling. Integrating sexual-health assessment into routine urologic practice, especially for older and socially vulnerable men, may enhance early detection, reduce transmission, and strengthen broader public-health efforts to improve male sexual and reproductive health.

Furthermore, the combination of two complementary analytical approaches, one based on self-reported history and one on laboratory confirmation, combined with a large sample size, strengthens the internal validity and interpretability of the findings and highlights patterns that were consistent despite differences between cohorts. Interestingly, syphilis seropositivity was 3 times higher in those with a previous history of STI, indicating that risk behaviors tend to repeat in a specific population.

The present analyses focus on serological evidence of syphilis exposure, and the epidemiological patterns observed should be interpreted considering the infection's diverse and often underrecognized clinical manifestations. Syphilis is increasingly reported at extragenital sites, where presentations may be subtle, atypical, or easily misdiagnosed. Recent evidence highlights the clinical relevance of oropharyngeal syphilis, which may present with nonspecific mucosal lesions or pharyngitis and is frequently overlooked outside otolaryngological settings.¹⁷ Similarly, neurosyphilis remains a diagnostic challenge, with protean neurological manifestations that can

occur at any stage of infection and may mimic other inflammatory or degenerative conditions.¹⁸

In this context, the behavioral and demographic risk factors identified in our study may translate into clinically heterogeneous presentations encountered across specialties, including urology, otolaryngology, neurology, and infectious diseases. These findings reinforce the need for heightened clinical suspicion, comprehensive sexual history-taking, and interdisciplinary collaboration to improve timely diagnosis and management. Integrating epidemiological insights with awareness of site-specific clinical manifestations is essential to address ongoing gaps in syphilis detection and care, particularly as incidence continues to rise in diverse clinical settings.

Finally, our study focused on men attending routine urological consultations, which might explain the relatively high prevalence of a previous history of sexually transmitted infection at 22.7% compared to 4.4 % of STI history among men outside the urological context.¹⁵ Also, the relatively high positivity (7.2%) of syphilis testing in an asymptomatic population might be related to the routine urological scenario and is worth further exploring in future studies that should include data regarding circumcision, though previous studies have shown no significant reduction in risk of acquiring syphilis.¹⁹

Conclusion

This study identified key factors associated with sexually transmitted infections among men and underscored the disproportionate vulnerability of middle-aged patients seen in routine urological care. Earlier sexual initiation, recreational drug use, lack of prior counseling, and increasing age emerged as the most relevant determinants. In contrast, most clinical and hormonal variables showed no consistent association with STI outcomes, reinforcing the predominance of behavioral and demographic influences in this population. These findings highlight the strategic opportunity to incorporate structured sexual-health education, risk-reduction counseling, and preventive guidance into everyday urological practice. Strengthening these services, particularly through proactive, rather than reactive, interventions, may contribute meaningfully to reducing STI transmission and improving sexual and reproductive health outcomes.

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Author Contributions

Leonardo O. Reis: conceptualization; funding and data acquisition; supervision; writing—review of the manuscript. Matheus B. Santos, Caio V. Suartz, Ana Claudia G. de Paula, Gabriela R. Barbosa: data analysis and interpretation; writing original draft, review, and editing. Adriano Cintra, Fabiano A. Simões, Fábio Guimarães, João C. C. Alonso, Ronald F. Rejowski, Walker W. Laranja: data acquisition; writing—review of the manuscript. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

The data that support the findings of this study are available from the authors upon reasonable request and subject to author approval.

Ethics Approval

Research Ethics Committee of the Faculty of Medical Sciences at the University of Campinas (UNICAMP), approval number 543.095. The study was authorized to proceed with a waiver of the Informed Consent Form (ICF), as all analyses used anonymized retrospective clinical and laboratory data.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Materials

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