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Identifying Individuals at High Risk for HIV and Sexually Transmitted Infections With an Artificial Intelligence–Based Risk Assessment Tool

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Background. We have previously developed an artificial intelligence–based risk assessment tool to identify the individual risk of HIV and sexually transmitted infections (STIs) in a sexual health clinical setting. Based on this tool, this study aims to determine the optimal risk score thresholds to identify individuals at high risk for HIV/STIs.

Methods. Using 2008–2022 data from 216 252 HIV, 227 995 syphilis, 262 599 gonorrhea, and 320 355 chlamydia consultations at a sexual health center, we applied *MySTIRisk* machine learning models to estimate infection risk scores. Optimal cutoffs for determining high-risk individuals were determined using Youden's index.

Results. The HIV risk score cutoff for high risk was 0.56, with 86.0% sensitivity (95% CI, 82.9%–88.7%) and 65.6% specificity (95% CI, 65.4%–65.8%). Thirty-five percent of participants were classified as high risk, which accounted for 86% of HIV cases. The corresponding cutoffs were 0.49 for syphilis (sensitivity, 77.6%; 95% CI, 76.2%–78.9%; specificity, 78.1%; 95% CI, 77.9%–78.3%), 0.52 for gonorrhea (sensitivity, 78.3%; 95% CI, 77.6%–78.9%; specificity, 71.9%; 95% CI, 71.7%–72.0%), and 0.47 for chlamydia (sensitivity, 68.8%; 95% CI, 68.3%–69.4%; specificity, 63.7%; 95% CI, 63.5%–63.8%). High-risk groups identified using these thresholds accounted for 78% of syphilis, 78% of gonorrhea, and 69% of chlamydia cases. The odds of positivity were significantly higher in the high-risk group than otherwise across all infections: 11.4 (95% CI, 9.3–14.8) times for HIV, 12.3 (95% CI, 11.4–13.3) for syphilis, 9.2 (95% CI, 8.8–9.6) for gonorrhea, and 3.9 (95% CI, 3.8–4.0) for chlamydia.

Conclusions. Risk scores generated by the AI-based risk assessment tool *MySTIRisk*, together with Youden's index, are effective in determining high-risk subgroups for HIV/STIs. The thresholds can aid targeted HIV/STI screening and prevention.

Keywords. HIV; machine learning; risk assessment tool; sexually transmitted infections; STIs.

Sexually transmitted infections (STIs) remain a significant public health issue globally, with an estimated 376 million new cases of curable STIs, including chlamydia, gonorrhea, syphilis, and trichomoniasis, occurring annually among sexually active individuals [1]. These STIs can lead to adverse health outcomes and substantial economic costs. Early detection and prompt treatment are crucial in reducing the spread of STIs and their associated health complications [2, 3]. However, many

individuals delay or avoid seeking testing and treatment, often due to a lack of knowledge about their own risk for developing HIV/STIs, limited availability of testing services, and the social stigma attached to them [4–6].

To encourage early testing and diagnosis, risk prediction tools have been developed to help individuals assess their risk of acquiring HIV/STIs and to facilitate informed decisions on testing and treatment [7–9]. However, most available tools like SexPro and San Diego Early Test (SDET) predict HIV risk using logistic regression methodology, rather than providing concurrent assessments for other major STIs with more advanced algorithms [7–9]. Our recently optimized machine learning–based tool, *MySTIRisk*, aims to advance prediction through enhancing model performance for 4 major infections—HIV, syphilis, chlamydia, and gonorrhea—and to conduct extensive user interface testing for effective risk communication [10].

While the development of risk prediction models has shown promise in identifying individuals at higher risk of acquiring HIV/STIs and providing targeted interventions, it is important to determine both the optimal cutoff point for these models and

the appropriate recommendations for those not at high risk. If the cutoff point is set too high, then individuals not deemed to be "high risk" may not be tested, and if the cutoff point is set too low, then health services may be overwhelmed by individuals requesting unnecessary testing. Therefore, determining the cutoff point that achieves the best health expenditure and use of health outcomes is important.

Previous studies have used methods like receiver operating characteristic curves and Youden's index to derive optimal cutoff points [11–16]. However, the most appropriate technique remains uncertain and may depend on the model and population.

We utilized Youden's index to determine the optimal cutoff point for the risk scores generated by *MySTIRisk*, a recently developed machine learning– and web-based tool for HIV, syphilis, gonorrhea, and chlamydia risk prediction [17–19], in a population of individuals seeking STI testing at a community health clinic. We aimed to identify the optimal threshold that balances the trade-off between sensitivity and specificity, allowing for accurate identification of individuals at high risk for HIV/STIs for tailored interventions and prioritization in resource-limited settings.

Our findings will inform the development of a public-facing web application of the *MySTIRisk* tool that can assist individuals in assessing their risk of contracting STIs and encourage early testing and diagnosis. This study also underscores the importance of using risk prediction tools to identify individuals at high risk and tailor interventions to those most at risk of acquiring HIV/STIs.

METHODS

Study Population
We used self-reported demographic and sexual behavioral data and laboratory-confirmed diagnoses from 167 451 individuals who attended the Melbourne Sexual Health Centre (MSHC) between January 2008 and May 2022. The MSHC is Australia's largest public sexual health clinic, which offers free HIV/STI services to the general public [20]. Data were collected through computer-assisted self-interviewing (CASI) at initial and follow-up visits, with follow-up intervals of at least 3 months. CASI employed prestructured questionnaires filled out by participants, ensuring consistency and efficiency in data collection. Infection diagnoses were systematically recorded in the health record database using standardized fields [21].

Data Source
We conducted a retrospective cross-sectional study using data extracted from the electronic records of individuals who visited MSHC during the study period. The data sets for each infection included consultations where individuals were tested for specific infections at that consultation. The data sets for HIV,

syphilis, gonorrhea, and chlamydia consisted of 216 252 (96 309 unique persons), 227 995 (100 230 unique persons), 262 599 (104 865 unique persons), and 320 355 consultations (139 634 unique persons), respectively.

Estimating the Risk Scores of HIV/STIs
We applied a risk prediction tool developed in a previous study to generate risk scores for HIV, syphilis, gonorrhea, and chlamydia [17, 18, 22]. *MySTIRisk* utilizes machine learning models trained on demographic, behavioral, and diagnostic data to estimate the risk scores from 0 to 1, with 1 indicating the highest risk. The original models were trained and tested on 2015–2018 data, with area under the curve (AUC) values ranging from 0.70 to 0.84 across infections [18]. The key predictors included gender, age, country of birth, men who reported having sex with men, presence of STI symptoms, number of partners, condom use, injection drug use, past STIs, contact with STI diagnoses, and sexual partners outside Australia/New Zealand [18].

For the current study, we retrained the models using an expanded data set from January 2008 to May 2022 to improve model performance and ensure optimal results for the planned public website *MySTIRisk* [22]. However, we adhered to the same rigorous data-cleaning procedures to maintain the integrity and reliability of the expanded data set. Similar to the previous study, we utilized a 1-hot encoding scheme for data classification. No imputations were made for missing data; instead, a binary feature vector was employed to indicate the presence of missing values [18]. While detailed model performance metrics, such as AUC values, were not the central focus of this study and can be found in the supplementary tables for interested readers, the primary objective of this study was to determine the optimal risk score thresholds using Youden's index.

Determining the Optimal Threshold for HIV/STIs
The MSHC is currently developing a public-facing web application of the *MySTIRisk* tool [22] to assist individuals in assessing their risk of contracting HIV/STIs and encourage early testing and diagnosis.

To accurately identify individuals at high risk for HIV/STIs, we used Youden's index to determine the optimal threshold for our *MySTIRisk* model. Youden's index is a commonly used metric in medical research for determining the optimal cutoff point in diagnostic tests or risk prediction models [23, 24]. It considers both the sensitivity and specificity of the model, aiming to maximize both metrics simultaneously. The index is calculated as $J = \max(\text{sensitivity} + \text{specificity} - 1)$, where sensitivity is the proportion of true positives correctly identified, and specificity is the proportion of true negatives correctly identified. The optimal cutoff point is then the threshold with the highest Youden's index value. A value of 1 represents a perfect classification model, and a value of 0 represents a model that is no better than chance [23, 24].

To identify the optimal cutoff points, we first calculated the risk scores for each consultation using the *MySTIRisk* models. We then evaluated a range of possible cutoff values at intervals of 0.02 from 0 to 1. For each potential cutoff, we computed the sensitivity, specificity, and Youden's index (sensitivity + specificity − 1). This allowed us to plot the sensitivity and specificity across the spectrum of cutoff values (Figure 1). We selected the risk score threshold that maximized Youden's index as the optimal cutoff point, balancing the trade-off between sensitivity and specificity for each infection. This data-driven approach allowed us to objectively determine the optimal cutoff points for the *MySTIRisk* models in identifying individuals at high risk for HIV/STIs in our clinic population.

Youden's index was utilized as it considers both sensitivity and specificity equally to provide an objective and balanced threshold aligned with the study goal of effectively stratifying high- and average-risk groups based on subsequent positivity rates. Compared with the receiver operating characteristic (ROC) analysis, which focuses on model accuracy, Youden's index aligns more closely with our objective of discriminating between risk levels for targeted screening purposes.

Utilizing Youden's Index for Categorizing Risk Groups

After determining the optimal cutoff point for the machine learning models for HIV/STIs using Youden's index, we categorized the consultations into binary risk groups. Specifically, consultations with predicted risk scores at or above the optimal cutoff point were classified as "high risk" for contracting that infection. Meanwhile, those scoring below the optimal cutoff point were designated "average risk." The proportion of individuals classified as high risk depends on Youden's index value and the distribution of scores in our data set.

Analysis of Risk Groups

We stratified consultations into high-risk and average-risk groups based on their risk scores for each infection. We then calculated the positivity rate within each risk group by determining the proportion of consultations testing positive. We also performed subgroup analyses to calculate positivity rates for specific populations, including men who have sex with men (MSM), heterosexual males, and females. A large contrast in positivity rates between the risk groups would validate the risk classification. Additionally, we compared positivity between consultations for individuals on and not on HIV preexposure prophylaxis (PrEP). We also calculated unadjusted odds ratios comparing positivity rates between the high-risk and average-risk groups overall and between those on and not on PrEP. Unadjusted odds ratios were used for directly evaluating the performance of the risk categorization and matching the intended use of the tool for risk assessment.

All statistical analyses and model training were conducted using Python programming language (version 3.9.12).

Patient Consent

As this was a retrospective analysis of deidentified data, a waiver of informed consent was granted by the Ethics Committee.

Ethical Considerations

The Alfred Hospital Ethics Committee in Melbourne, Australia, granted ethical approval (project number: 124/18). The study was conducted in accordance with pertinent ethical regulations and guidelines.

RESULTS

Demographic Characteristics of the Study Participants

For each of the 4 infection data sets (HIV, syphilis, gonorrhea, and chlamydia), which included all consultations tested for each infection, MSM accounted for the majority of consultations (40%–50%), followed by women (30%–36%) and heterosexual men (15%–25%). The median age for those with each of the 4 infections (interquartile range [IQR]) was 29 (25–36) years. In terms of country of birth, almost half (47%–49%) of the consultations were from participants born overseas, while the remaining consultations were from Australia and New Zealand. Table 1 also displays the sexual risk factors associated with each infection.

Risk Score Distribution for HIV/STI Data Sets

We calculated the median and IQR of the infection risk scores that were predicted for all individuals, which ranged from 0.00 (the lowest) to 1.00 (the highest) for HIV/STIs. The median risk scores and IQRs for all participants were 0.32 (0.15–0.62) for the HIV data set, 0.35 (0.16–0.47) for the syphilis data set, 0.37 (0.12–0.57) for the gonorrhea data set, and 0.42 (0.31–0.55) for the chlamydia data set (Table 2).

The Optimal Threshold for HIV/STIs

We determined the optimal cutoff thresholds for HIV/STIs for each infection by selecting the risk score cutoff points that maximized Youden's index, balancing sensitivity and specificity. We also identified the number of participants with HIV/STIs who had scores above the optimal threshold and alternative thresholds using quintile values (Supplementary Tables 1–4).

For HIV, the optimal cutoff point was at the risk score value of 0.56, which corresponded to a sensitivity of 86.0% (95% CI, 82.9%–88.7%), a specificity of 65.6% (95% CI, 65.4%–65.8%) and a Youden's index of 0.52. The cutoff classified 35% of individuals as high risk, with 86% of HIV infections found in the high-risk group.

For syphilis, the optimal cutoff point was at the risk score value of 0.49, with corresponding sensitivity and specificity values of 77.6% (95% CI, 76.2%–78.9%) and 78.1% (95% CI, 77.9%–78.3%), respectively, with a Youden's index of 0.56. The cutoff classified 23% of individuals as high risk, with 78% of syphilis infections found in the high-risk group.
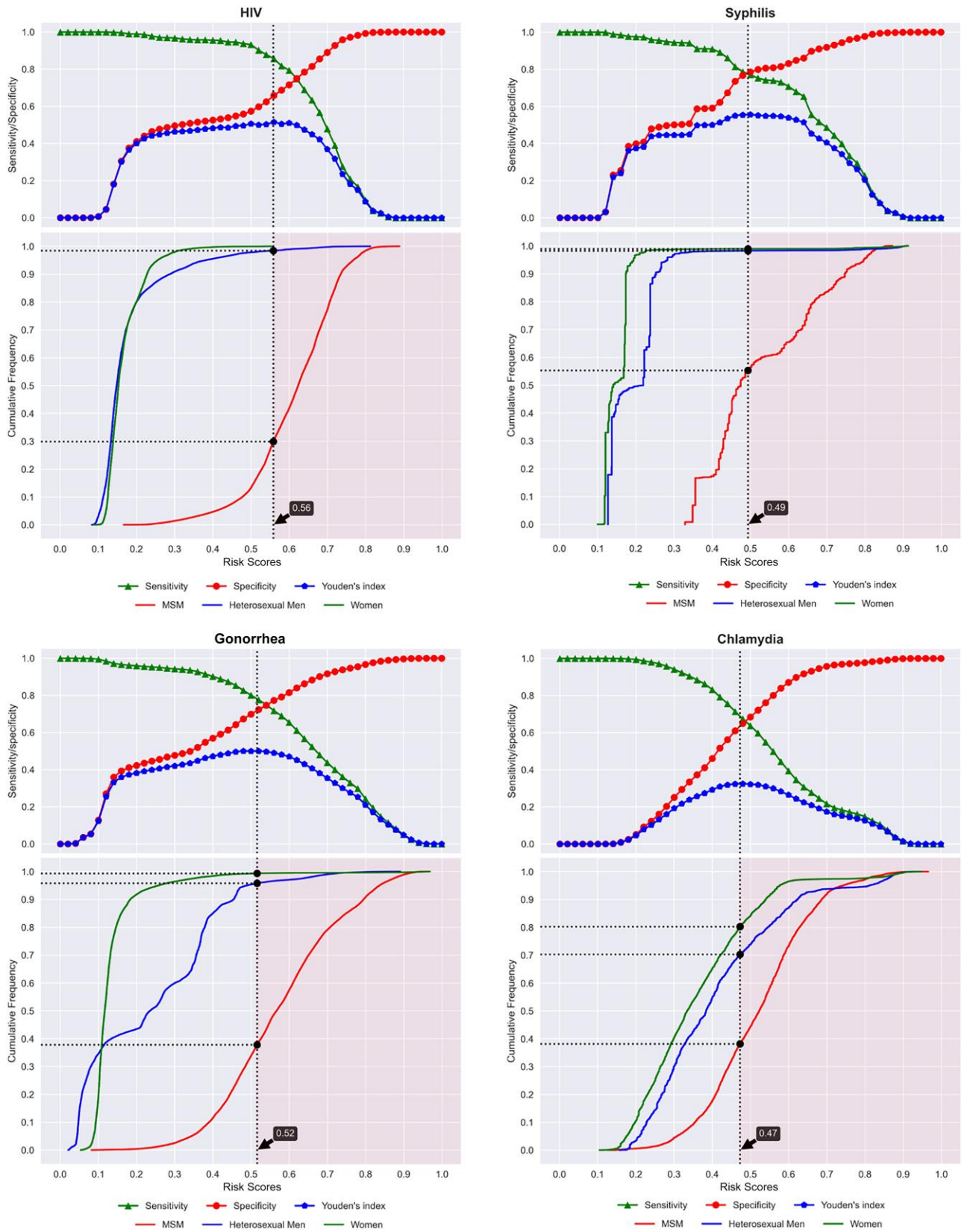
Figure 1. Sensitivity, specificity, and Youden's index with optimal cut-off points for HIV/STIs

Table 1. Characteristics of Clinic Consultations in Individual Data Sets

Predictors	HIV (n = 216 252 Consultations)	Syphilis (n = 227 995 Consultations)	Gonorrhea (n = 262 599 Consultations)	Chlamydia (n = 320 355 Consultations)
Age, median (IQR), y	29 (25–35)	29 (25–36)	29 (25–35)	29 (25–35)
Country of birth, No. (%)				
Australia and New Zealand	102 350 (47.3)	108 755 (47.7)	127 958 (48.7)	155 603 (48.6)
Overseas	104 085 (48.1)	108 965 (47.8)	122 357 (46.6)	149 958 (46.8)
Missing	9817 (4.5)	10 275 (4.5)	12 284 (4.7)	14 794 (4.6)
Population type, No. (%)				
MSM	105 616 (48.8)	113 152 (49.6)	127 500 (48.6)	127 410 (39.8)
Heterosexual male	43 716 (20.2)	45 683 (20)	40 099 (15.3)	78 703 (24.6)
Female	66 920 (30.9)	69 160 (30.3)	95 000 (36.2)	114 242 (35.7)
Condom use with casual male partners, No. (%)				
Always	40 759 (18.8)	42 371 (18.6)	50 959 (19.4)	53 329 (16.6)
Sometimes	90 136 (41.7)	95 076 (41.7)	114 329 (43.5)	127 047 (39.7)
Never	16 289 (7.5)	17 584 (7.7)	23 734 (9)	25 462 (7.9)
Not applicable	3752 (1.7)	3967 (1.7)	4720 (1.8)	4860 (1.5)
Unsure/decline	7896 (3.7)	8966 (3.9)	10 218 (3.9)	10 640 (3.3)
Missing	57 420 (26.6)	60 031 (26.3)	58 639 (22.3)	99 017 (30.9)
Last time injected drugs not prescribed by doctor, No. (%)				
Never	204 029 (94.3)	213 820 (93.8)	245 368 (93.4)	301 328 (94.1)
<3 mo	2588 (1.2)	3070 (1.3)	3535 (1.3)	3785 (1.2)
Within 3–12 mo	908 (0.4)	1054 (0.5)	1211 (0.5)	1329 (0.4)
>12 mo	2453 (1.1)	2707 (1.2)	3134 (1.2)	3707 (1.2)
Decline/unsure	4669 (2.2)	5543 (2.4)	6366 (2.4)	6569 (2.1)
Missing	1605 (0.7)	1801 (0.8)	2985 (1.1)	3637 (1.1)
Having sex overseas, No. (%)				
Yes	67 736 (31.3)	70 411 (30.9)	73 955 (28.2)	98 778 (30.8)
No	131 304 (60.7)	138 757 (60.9)	166 692 (63.5)	197 698 (61.7)
Unsure	10 638 (4.9)	11 335 (5.0)	12 744 (4.9)	13 673 (4.3)
Missing	6574 (3.0)	7492 (3.3)	9208 (3.5)	10 206 (3.2)
Past history of gonorrhea, No. (%)				
Yes	35 939 (16.6)	39 599 (17.4)	46 722 (17.8)	46 193 (14.4)
No	51 906 (24.0)	56 334 (24.7)	67 625 (25.8)	82 874 (25.9)
Unsure	3803 (1.8)	3965 (1.7)	4696 (1.8)	5192 (1.6)
Missing	124 604 (57.6)	128 097 (56.2)	143 556 (54.7)	186 096 (58.1)
Past history of nonspecific urethritis, No. (%)				
Yes	2412 (1.1)	2718 (1.2)	3608 (1.4)	4092 (1.3)
No	85 433 (39.5)	93 215 (40.9)	110 739 (42.2)	124 975 (39.0)
Unsure	3803 (1.8)	3965 (1.7)	4696 (1.8)	5192 (1.6)
Missing	124 604 (57.6)	128 097 (56.2)	143 556 (54.7)	186 096 (58.1)
Past history of syphilis, No. (%)				
Yes	13 149 (6.1)	16 152 (7.1)	17 366 (6.6)	17 232 (5.4)
No	74 696 (34.5)	79 781 (35.0)	96 981 (36.9)	111 835 (34.9)
Unsure	3803 (1.8)	3965 (1.7)	4696 (1.8)	5192 (1.6)
Missing	124 604 (57.6)	128 097 (56.2)	143 556 (54.7)	186 096 (58.1)
Sexual contact with someone diagnosed with gonorrhea, No. (%)				
Yes	4427 (2.0)	4869 (2.1)	6692 (2.5)	6611 (2.1)
No	211 825 (98.0)	223 126 (97.9)	255 907 (97.5)	313 744 (97.9)
Sexual contact with someone diagnosed with chlamydia, No. (%)				
Yes	6852 (3.2)	7333 (3.2)	9900 (3.8)	13 327 (4.2)
No	209 400 (96.8)	220 662 (96.8)	252 699 (96.2)	307 028 (95.8)
Sexual contact with someone diagnosed with syphilis, No. (%)				
Yes	2082 (1.0)	2595 (1.1)	2383 (0.9)	2433 (0.8)
No	214 170 (99.0)	225 400 (98.9)	260 216 (99.1)	317 922 (99.2)

Abbreviations: IQR, interquartile range; MSM, men who have sex with men.

Table 2. Risk Score Distribution for HIV/STIs

	Overall, Median (IQR)	HIV/STI-Positive Consultations, Median (IQR)	HIV/STI-Negative Consultations, Median (IQR)
HIV	0.32 (0.15–0.62)	0.70 (0.62–0.75)	0.31 (0.15–0.62)
Syphilis	0.35 (0.16–0.47)	0.69 (0.53–0.80)	0.30 (0.15–0.47)
Gonorrhea	0.37 (0.12–0.57)	0.67 (0.54–0.80)	0.34 (0.12–0.54)
Chlamydia	0.42 (0.31–0.55)	0.56 (0.44–0.68)	0.41 (0.30–0.54)

Abbreviations: IQR, interquartile range; STI, sexually transmitted infection.

For gonorrhea, the optimal cutoff point was at the risk score value of 0.52, with a sensitivity of 78.3% (95% CI, 77.6%–78.9%), a specificity of 71.9% (95% CI, 71.7%–72%), and a Youden's index of 0.50. The cutoff classified 31% of individuals as high risk, with 78% of gonorrhea infections found in the high-risk group.

For chlamydia, the optimal cutoff point was at the risk score value of 0.47, with a sensitivity of 68.8% (95% CI, 68.3%–69.4%), a specificity of 63.7% (95% CI, 63.5%–63.8%), and a Youden's index of 0.33. The cutoff classified 39% of individuals as high risk, with 69% of chlamydia infections found in the high-risk group.

Positivity Among the High-risk vs Average-risk Group

Overall positivity was highest for chlamydia (8.1%), followed by gonorrhea (5.9%), syphilis (1.7%), and HIV (0.3%). Positivity was highest among MSM across infections, while women had the lowest positivity. Importantly, testing recommendations vary for different groups, which influences overall positivity. The positivity in the high- and average-risk groups is shown in Table 3.

The high-risk group had markedly higher positivity than the average-risk group across all 4 infections. The positivity in the high-risk group for HIV was 0.7%, which was 11.7 (95% CI, 9.3–14.8) higher odds than the average-risk group for HIV. The positivity rate in the high-risk group for syphilis was 5.8%, which was 12.3 (95% CI, 11.4–13.3) higher odds than the average-risk group for syphilis. The positivity rate in the high-risk group for gonorrhea was 14.8%, which was 9.2 (95% CI, 8.8–9.6) higher odds than the average-risk group for gonorrhea. The positivity rate in the high-risk group for chlamydia was 8.1%, which was 3.9 (95% CI, 3.8–4.0) higher odds than the average-risk group for chlamydia.

In the high-risk group, we found that individuals not taking HIV PrEP had 7.4 (95% CI, 4.4–12.4) times higher odds of being infected with HIV than those taking PrEP (0.8% vs 0.1%). Similarly, for syphilis in the high-risk group, we found that individuals not taking HIV PrEP had 1.1 (95% CI, 1.0–1.2) times higher odds of being infected with syphilis than those taking PrEP (6.0% vs 5.3%). For gonorrhea in the high-risk group, we found that individuals not taking HIV PrEP had 0.8 (95%

CI, 0.76–0.8) times lower odds of being infected with gonorrhea than those taking HIV PrEP (14.1% vs 17.2%). For chlamydia in the high-risk group, we found that individuals not taking HIV PrEP had 0.8 (95% CI, 0.8–0.9) times lower odds of being infected with chlamydia than those on PrEP (13.9% vs 16.7%).

In the average-risk group, we found that individuals not on PrEP had 3.2 (95% CI, 0.4–22.9) times higher odds of being infected with HIV than those on PrEP (0.06% vs 0.02%). Similarly, for syphilis in the average-risk group, we found that individuals not on PrEP had 0.3 (95% CI, 0.2–0.6) times lower odds of being infected with syphilis than those on PrEP (0.5% vs 1.5%). For gonorrhea in the average-risk group, we found that individuals not on PrEP had 0.4 (95% CI, 0.3–0.4) times lower odds of being infected with gonorrhea than those on PrEP (1.8% vs 4.8%). For chlamydia in the average-risk group, we found that individuals not on PrEP had 0.6 (95% CI, 0.5–0.7) times lower odds of being infected with chlamydia than those on PrEP (4.1% vs 6.7%).

DISCUSSION

In this study, we utilized Youden's index to determine optimal cutoff points to identify individuals at high or average risk for HIV/STIs. We found substantially higher positivity in the high-risk groups across all 4 infections, indicated by substantially higher odds of positivity. This demonstrates the validity of the risk categorization and its ability to identify individuals based on the underlying risk. Additionally, while HIV positivity was higher in individuals who were not on PrEP compared with PrEP users, syphilis, gonorrhea, and chlamydia positivity showed the opposite pattern. This aligns with existing evidence on the preventive impact of PrEP for HIV vs other STIs [25, 26]. By accurately identifying individuals at high risk for HIV/STIs using a simple tool such as *MySTIRisk*, targeted interventions can be implemented in resource-limited settings, leading to more efficient use of limited resources. Our findings underscore the potential use of the optimized *MySTIRisk* thresholds for targeted sexual health interventions and resource allocation in HIV prevention and management contexts.

Our study identified optimal risk score thresholds that balanced sensitivity and specificity for each infection utilizing Youden's index. With these thresholds, the proportion of consultations that were classified as high risk was 23%–39% across the 4 infections. For all infections, most cases were detected in the high-risk groups, ranging from 69% of chlamydia cases to 86% of HIV cases. This approach allowed for objective determination of customized risk thresholds by finding the trade-off between sensitivity and specificity [23]. Our findings align with previous studies that derived optimal thresholds for STI risk models [11, 27]. Nieuwenburg et al. developed a symptom-based risk score calculator in the Netherlands using

Table 3. Positivity (the Positive Percentage of the HIV/STI Diagnosis) per Total Consultations

Infection Positivity	Overall	High-risk				Average-risk				OR (95% CI) [High-risk vs Average-risk]
		All High-risk	Not on PrEP	On PrEP	OR (95% CI) [No PrEP vs PrEP]	All Average-risk	Not on PrEP	On PrEP	OR (95% CI) [No PrEP vs PrEP]	
HIV										
All	0.27% (593/216 252)	0.68% (510/74 718)	0.81% (495/61 067)	0.11% (15/13 651)	7.43 (4.44–12.42)	0.06% (83/141 534)	0.06% (82/136 248)	0.02% (1/5286)	3.18 (0.44–22.85)	11.71 (9.28–14.77)
Population groups										
MSM	0.52% (548/105 616)	0.67% (498/74 040)	0.8% (483/60 394)	0.11% (15/13 646)	7.33 (4.38–12.26)	0.16% (50/31 576)	0.19% (49/26 373)	0.02% (1/5203)	9.68 (1.34–70.12)	4.27 (3.19–5.71)
Heterosexual male	0.07% (31/43 716)	1.77% (12/678)	1.78% (12/673)	0.00% (0/5)	NA	0.04% (19/43 038)	0.04% (19/42 994)	0.00% (0/44)	NA	40.8 (19.73–84.39)
Female	0.02% (14/66 920)	-	-	-	-	0.02% (14/66 920)	0.02% (14/66 881)	0.00% (0/39)	NA	NA
Syphilis										
All	1.71% (3894/227 995)	5.79% (3020/52 123)	5.93% (2377/40 078)	5.34% (643/12 045)	1.12 (1.02–1.22)	0.50% (874/175 872)	0.45% (747/167 637)	1.54% (127/8235)	0.29 (0.24–0.35)	12.31 (11.41–13.28)
Population groups										
MSM	3.02% (3417/113 152)	5.48% (2773/50 592)	5.53% (2132/38 559)	5.33% (641/12 033)	1.04 (0.95–1.14)	1.03% (644/62 560)	0.95% (518/54 427)	1.55% (126/8133)	0.61 (0.50–0.74)	5.58 (5.12–6.08)
Heterosexual male	0.67% (304/45 683)	18.6% (149/801)	18.49% (147/795)	33.33% (2/6)	0.45 (0.08–2.48)	0.35% (155/44 882)	0.34% (154/44 817)	1.54% (1/65)	0.22 (0.03–1.6)	65.94 (51.99–83.64)
Female	0.25% (173/69 160)	13.42% (98/730)	13.54% (98/724)	0.00% (0/6)	NA	0.11% (75/68 430)	0.11% (75/68 393)	0.00% (0/37)	NA	141.32 (103.58–192.82)
Gonorrhea										
All	5.89% (15 461/262 599)	14.82% (12 099/81 632)	14.14% (8974/63 448)	17.19% (3125/18 184)	0.79 (0.76–0.83)	1.86% (3362/180 967)	1.78% (3129/176 064)	4.75% (233/4903)	0.36 (0.31–0.41)	9.19 (8.84–9.56)
Population groups										
MSM	10.46% (13 338/127 500)	14.60% (11 577/79 315)	13.83% (8455/61 142)	17.18% (3122/18 173)	0.77 (0.74–0.81)	3.65% (1761/48 185)	3.53% (1532/43 391)	4.78% (229/4794)	0.73 (0.63–0.84)	4.51 (4.28–4.75)
Heterosexual male	2.42% (972/40 099)	17.19% (291/1693)	17.12% (288/1682)	27.27% (3/11)	0.55 (0.15–2.09)	1.77% (681/38 406)	1.77% (679/38 349)	3.51% (2/57)	0.50 (0.12–2.05)	11.50 (9.93–13.32)
Female	1.21% (1151/95 000)	37.02% (231/624)	37.02% (231/624)	-	-	0.97% (920/94 376)	0.97% (918/94 324)	3.85% (2/52)	0.25 (0.06–1.03)	59.71 (50.12–71.13)
Chlamydia										
All	8.08% (25 870/320 355)	14.27% (17 811/124 829)	13.85% (14 722/106 269)	16.64% (3089/18 560)	0.81 (0.78–0.85)	4.12% (8059/195 526)	4.07% (7781/191 375)	6.70% (278/4151)	0.59 (0.52–0.67)	3.87 (3.77–3.98)
Population groups										
MSM	10.32% (13 148/127 410)	13.51% (10 649/78 821)	12.55% (7567/60 302)	16.64% (3082/18 519)	0.72 (0.69–0.75)	5.14% (2499/48 589)	4.99% (2223/44 533)	6.80% (276/4056)	0.72 (0.63–0.82)	2.88 (2.75–3.01)
Heterosexual male	7.95% (6257/78 703)	16.66% (3901/23 420)	16.65% (3896/23 395)	20.00% (5/25)	0.80 (0.30–2.13)	4.26% (2356/55 283)	4.26% (2355/55 225)	1.72% (1/58)	2.54 (0.35–18.35)	4.49 (4.26–4.74)
Female	5.66% (6465/114 242)	14.44% (3261/22 588)	14.44% (3259/22 572)	12.5% (2/16)	1.18 (0.27–5.19)	3.50% (3204/91 654)	3.50% (3203/91 617)	2.70% (1/37)	1.30 (0.18–9.48)	4.66 (4.43–4.90)

Abbreviations: MSM, men who have sex with men; OR, odds ratio; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

multivariable logistic regression models for MSM attending the Amsterdam Centre for Sexual Health. They determined the optimal cutoff point for infectious syphilis using Youden's index. Despite strong associations between symptoms and infectious syphilis, the symptom-based risk scores exhibited limited performance, with AUCs ranging from only 0.68 to 0.69, with a corresponding 41% sensitivity, 95% specificity, and Youden's index value of 0.46 [11]. Our optimal thresholds demonstrated improved discrimination compared with the Nieuwenburg et al. syphilis model while balancing the sensitivity and specificity trade-off central to STI screening optimization.

Another study focusing on the development and validation of a risk estimation tool for asymptomatic chlamydia and gonorrhea using multivariable logistic regression reported an AUC of 0.74, with a high sensitivity of 91% but a lower specificity of 32%, highlighting the complexities in optimizing screening tools for STIs. To determine the optimal cutoff point, this study analyzed the screening performance estimates at different cutoff levels of the sum scores, and the cutoff value with a fixed sensitivity of 91% was chosen as the optimal cutoff point [27]. Our study contributes to developing more effective STI screening tools by providing an alternative way to define high-risk populations, which can be used to inform targeted interventions and prioritize resources in clinical settings.

Our study demonstrated that the high-risk group had substantially higher positivity rates than the average-risk group across all 4 STIs, including HIV, syphilis, gonorrhea, and chlamydia. The odds of positivity were found to be 3.9–12.3 times higher in the high-risk group than in the average-risk group. This significant difference in positivity demonstrates the validity of our risk categorization in identifying those most likely to have an infection. Accurately discriminating between high- and average-risk individuals using optimal thresholds is an important advance for targeted STI prevention and care. While all individuals should have access to sexual health services, identifying those at higher risk allows for more intensive interventions and resources to be directed to those who need it most. Our findings support the potential use of the *MySTIRisk* tool in assessing individual risk profiles to guide tailored responses.

Our study also demonstrated notable differences in positivity for HIV and other STIs between individuals using preexposure prophylaxis (PrEP) and those not using PrEP. Specifically, the odds of HIV positivity were 3 times higher among non-PrEP users than among PrEP users, highlighting the effectiveness of PrEP in reducing the risk of HIV infection [28]. In contrast, positivity for syphilis, gonorrhea, and chlamydia was lower among non-PrEP users relative to PrEP users. This finding aligns with existing evidence on the preventive impact of PrEP for HIV vs other STIs [25, 26]. It underscores the importance of comprehensive sexual health strategies that include not only PrEP for HIV prevention but also regular testing and treatment for other STIs. It is crucial for individuals, especially

those at higher risk of acquiring STIs, to be aware of their risk and take appropriate preventive measures, including consistent condom use and regular testing for HIV/STIs.

However, it is important to note that the risk tool developed in this study discriminates risk levels rather than defining absolute risk categories. Therefore, caution should be exercised in interpreting scores below the cutoff, implying no need for testing or prevention. Baseline testing and counseling should be recommended for all individuals in studies such as ours where the source of the individual is a high-risk setting such as an STI center, regardless of their risk score. It highlights the importance of comprehensive sexual health services that go beyond risk prediction models and consider individual circumstances and needs. Furthermore, it should be used to identify higher-risk individuals who may require more frequent or intensive services rather than opt out of services. Individuals with scores above the cutoff point should be considered a high priority for enhanced prevention and testing services due to their greater risk of infection relative to the clinic population. This can help tailor interventions and allocate resources effectively to those most in need.

The findings of our study have important policy implications and provide directions for future research. One significant contribution of this paper is the alternative way it proposes to define the high-risk population. Using machine learning algorithms and the risk scores for each infection, the study identifies individuals in the high-risk group. This information can help policymakers and health care providers improve screening protocols and sexual health guidelines to better identify high-risk subgroups for enhanced testing and preventive interventions. Additional counseling, contact tracing, and treatment escalation can also be directed specifically to those individuals categorized by *MySTIRisk* as higher risk. Such targeted resource allocation and interventions could substantially reduce STI complications and health care costs at the population level by focusing additional testing on the minority of individuals at higher risk.

Future research should focus on investigating the expenses associated with HIV testing and the economic impacts of implementing predictive models like *MySTIRisk*. Understanding cost-effectiveness can further inform resource allocation and budget planning within sexual health programs to guide implementation decisions and policy responses to curb rising STI incidence.

A key strength of our study was the use of Youden's index to identify risk thresholds that effectively differentiated high- and average-risk groups based on their positivity rates. Moreover, we used over 10 years of data from the largest sexual health clinic in Victoria, allowing the model training a significant improvement in sample size, thereby improving the model performance. While providing important insights, our study has several limitations. First, as our study population was limited to a single urban sexual health center, additional validation

of generalizability is warranted through multisite collaboration and access to more diverse demographic data. Comparing performance on external population samples could illuminate variability in predictive factors and optimal thresholds across settings to further optimize *MySTIRisk's* screening capabilities. Furthermore, the risk scores represent relative risk within this population in a sexual health clinic rather than absolute risk categories. The optimal cutoff point may vary depending on the setting, such as the general population or clinic settings. Additionally, the cutoff for routine screening may need to be lower to ensure early detection and prevention efforts, requiring the need for adjustment in routine screenings to represent a broader spectrum of risk levels. Second, sexual orientation was defined based on self-reported sexual practices rather than identity, which may have led to misclassification in some cases. Similarly, while relying on self-reported information, we acknowledge inherent limitations such as recall, nonresponse, and social desirability biases. However, CASI represents best practices for minimizing such biases [29]. Third, comparisons of positivity rates between the high/average-risk groups and PrEP/non-PrEP groups represent unadjusted analyses. Given the potential for confounding by differences in demographic and behavioral characteristics, multivariate analysis adjusting for key covariates is warranted in future studies to confirm the findings. However, the significantly higher positivity rates consistently observed in the high-risk groups across infections are notable even without controlling for potential confounders. Fourth, the data sets only included clients from a sexual health center, who can be considered at higher risk than the general population, which includes lower-risk individuals. Therefore, the generalizability of our findings to the general population could be limited. Nonetheless, our findings demonstrate the utility of Youden's index for objectively balancing sensitivity and specificity to inform user-friendly risk assessment tool development. Further external validation of optimized thresholds across diverse populations and settings remains an important area for future research. Similarly, future implementation research should evaluate the impact of providing *MySTIRisk* risk assessments on testing uptake, treatment adherence, and other outcomes among high-risk groups in real-world settings.

In conclusion, the findings of this study have important implications for policy and practice in sexual health clinics. The alternative way of defining the high-risk population for risk assessment tools for HIV/STIs can guide resource allocation and intervention strategies. Future research should focus on understanding the expenses associated with HIV testing and further refining the risk prediction model to ensure its appropriate use in different settings. It is crucial to remember that the risk tool should be used to identify higher-risk individuals for targeted services, and baseline testing and counseling should be recommended for all individuals, regardless of their risk score.

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