An Empiric Risk Score to Guide Presumptive Treatment of Asymptomatic Anorectal Infections in Men Who Have Sex With Men in Kisumu, Kenya

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Abstract

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Introduction

The World Health Organization (WHO) recommends presumptive therapy (PT) for *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) in asymptomatic MSM who report unprotected receptive anal intercourse in the past 6 months and either multiple sex partners or a partner with an STI. We aimed to identify predictors of asymptomatic anorectal infection in Kenyan MSM and compare performance of an empiric, model-based risk score to that of the WHO PT algorithm.

Methods

Anorectal GC/CT infections were diagnosed at baseline among 698 MSM enrolled in the *Anza Mapema* study in Kisumu, Kenya. Study clinicians conducted and recorded a standardized medical history and physical examination findings (including genital and rectal examination). Rectal swabs for GC and CT screening were obtained by proctoscopy or self-collection. The Abbott RealTime GC/CT NAAT was used to diagnose anorectal infections. Multivariable logistic regression was used to identify associations with asymptomatic anorectal GC/CT infection, after excluding participants with anorectal symptoms. We derived a total risk score (range: 0-5) for each participant using the coefficients of the final multivariable model. Risk score algorithm performance was compared to WHO algorithm performance with respect to sensitivity, specificity, and number needed to treat (NNT).

Results

Asymptomatic anorectal GC/CT infection prevalence was 4.2%. Predictors and corresponding risk scores were: HIV infection (2), age 18-24 years (2), and unprotected anal sex (1). A risk score ≥3 was 83% sensitive and 65% specific in detecting asymptomatic GC/CT anorectal infection. In contrast, the WHO PT algorithm had low sensitivity (25%), but was 84% specific. While 37% of asymptomatic participants met

PT eligibility criteria using a risk score ≥3, only 17% met eligibility by WHO PT criteria. Using our risk score algorithm, 12 participants would need PT to treat one anorectal GC/CT infection, compared to 38 participants by WHO criteria.

Conclusion

An empiric risk score based on age, HIV status, and unprotected anal sex improved both sensitivity and efficiency (i.e., NNT) of identification of asymptomatic anorectal GC/CT infection, compared to the WHO PT algorithm. If validated in other settings, this risk score could improve the management of asymptomatic anorectal GC/CT infections in settings where diagnostic testing is not available.

Introduction

A high prevalence of sexually transmitted infections (STIs) has been reported in men who have sex with men (MSM) across sub-Saharan Africa.[1,2] African studies have estimated that the prevalence of both *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) anorectal infections in MSM ranges between 1% to 15%,[3,4,5] and the majority of these infections are asymptomatic.[6,7] Furthermore, a higher proportion of GC and CT infections in MSM are anorectal.[3] In a study of MSM in Coastal Kenya, anorectal gonorrhea infection in the past 6 months was associated with increased HIV acquisition.[8] Collectively, these studies have drawn attention to the crucial need for effective anorectal STI management in African MSM.

Based on expert consensus, the 2011 WHO guidelines recommend that clinicians in resource-limited settings use syndromic management to treat symptomatic anorectal infections in MSM and presumptive therapy (PT) for asymptomatic MSM reporting unprotected receptive anal intercourse (RAI) and either multiple sex partners or a sex partner with an STI in the past 6 months.[9] To date, the WHO PT algorithm for asymptomatic anorectal infections has only been validated in one small study among male sex workers in Coastal Kenya, in which application of the risk algorithm compared to nucleic acid amplification testing (NAAT) for GC and CT demonstrated 74.1% sensitivity and 45.8% specificity.[10] In the authors' estimation, for every four MSM who qualified for the PT algorithm using WHO guidelines, one asymptomatic infection would be treated.[10]

We conducted an analysis of enrollment data from *Anza Mapema*, an ongoing observational cohort study of 700 MSM in Kisumu, Kenya, with the primary objective to determine GC and CT anorectal infection prevalence and identify predictors of all anorectal GC/CT infections combined and of asymptomatic anorectal infections after excluding symptomatic men. Our secondary objective was to compare the performance of an empiric, model-based risk score to that of the WHO PT algorithm for identifying asymptomatic infections. Our overall goal was to determine how best to identify and treat anorectal infections among MSM in settings where diagnostic testing is not routinely available.

Materials and Methods

Study population. Eligibility criteria for the *Anza Mapema* (Kiswahili for "Start Early") study included the following: male sex at birth, at least one act of oral or anal sexual intercourse with a man in the past 6 months, ≥18 years of age, and resident in Kisumu, Kenya. Men who were already enrolled in an HIV care program and had taken antiretroviral therapy (ART) within the past 3 months were excluded. Recruitment was conducted through peer networks, snowballing, and recruitment at MSM "hotspots," including bars, discos, restaurants, social halls, with the assistance of local lesbian, gay, bisexual, and transgender (LGBT) support groups.

Clinical procedures. All participants, regardless of HIV status, underwent behavioral assessment via audio computer-assisted self-interview (ACASI), a standardized medical history and physical examination (including genital and rectal examinations), and collection of biological samples for STI screening (blood, urine and rectal swabs). The ACASI included the following domains: sociodemographic background, sexual behavior with men and women, alcohol and drug use, experience of discrimination and violence, and current physical symptoms. Only men who reported engaging in anal intercourse were asked about anorectal symptoms. Syndromic STI treatment was provided to symptomatic men at the study visit, while asymptomatic men with STI diagnosed through laboratory testing were offered treatment when results became available. WHO Treatment Guidelines were used for STI management.[11,12]

Rectal swab procedures. Rectal swab specimens were collected by a clinician using proctoscopy or were self-collected if proctoscopy was refused. From August 31, 2015 to January 6, 2016, a single sterile dry Dacron rectal swab was collected for NAAT. From January 7, 2016, two rectal swab specimens were obtained: (1) one swab was collected for NAAT using Abbott's Multi-Collect specimen collection kit and (2) a sterile dry Dacron swab was collected for Gram staining. Rectal swabs for NAAT and Gram stain were each inserted into tubes, stored at 2ºC to 8ºC, and transported to the CDC-KEMRI laboratory within 12 hours of specimen collection.

Laboratory procedures. HIV testing was performed at the clinic using two rapid tests (Determine®, Abbott Laboratories, Abbott Park, Illinois, USA; and First Response®, Premier Medical Corporation, Kachigam, Nani Daman, India), in accordance with Kenyan HIV testing guidelines. The Abbott RealTime CT/NG assay was used to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in rectal swab specimens. Microscopy was used to count leukocytes per high-power field and detect Gram-negative intracellular diplococci on Gram-stained slides of rectal secretions. Gonorrhea culture was not available.

Outcomes. Primary outcomes evaluated were (1) any anorectal GC/CT infection and (2) asymptomatic anorectal GC/CT infection. Any anorectal GC/CT infection was defined as a positive GC and/or CT NAAT result in a study participant, regardless of symptoms. An asymptomatic anorectal infection was determined by a positive GC and/or CT NAAT result in a participant who reported having no anorectal symptoms (i.e., rectal pain, pain with defection, pain while having sex, or rectal discharge) in the past 3 months. For the purposes of this analysis, men who reported no anal sex were included in the group with no reported anorectal symptoms.

Predictors. Potential predictors of anorectal GC/CT infections analyzed included the following: age, education, ever married to a female partner, current cohabitation with male partner, HIV status, prior sex with a female partner, multiple male sex partners, unprotected anal intercourse (receptive or insertive), transactional sex, sexual position during anal intercourse (insertive, receptive, versatile), RAI in past 3 months, treatment for recent STI, disclosure of MSM status to provider, physical violence, sexual violence, alcohol use, any drug use, and injection drug use. Manifestations of anorectal GC/CT infection that were analyzed included: purulent discharge, rectal mucosal erythema, detection of Gram-negative intracellular diplococci (GNID) on rectal Gram Stain, and the presence of leukocytes on rectal Gram Stain. For predictors and manifestations with >5% missing data, a separate category was created for missingness.

Data analysis: prevalence, predictors, and outcomes. 95% confidence intervals were calculated for HIV and GC/CT prevalence estimates using exact binomial distributions. Bivariable logistic regression was used to estimate unadjusted odds ratios (ORs) for potential predictors and the combined anorectal infection outcome (i.e., both symptomatic and asymptomatic infections). A multivariable logistic regression model was then tested, including HIV status *a priori* plus any other variable associated with the outcome at $p<0.2$ in bivariable analysis. After exclusion of men with symptomatic anorectal infections, bivariable logistic regression was then used to estimate unadjusted odds ratios (ORs) for potential predictors and the asymptomatic anorectal infection outcome. Finally, all predictors associated with asymptomatic anorectal infection in the multivariable logistic regression model were included in a final multivariable model and non-significant predictors were removed.

D*ata analysis: manifestations and outcomes.* Chi-square and Fisher's exact tests were used to explore associations between clinical and laboratory manifestations of infection including anorectal signs (purulent discharge or mucosal erythema) and rectal Gram Stain results (presence of leukocytes or GNID compatible with *Neisseria gonorrhoeae* infection), and the asymptomatic anorectal infection outcome.

Predictor scores and score cut points. A predictor score was derived from each predictor's beta coefficient in the final multivariable model, rounded to the nearest integer. A total risk score was calculated for each participant at baseline by summing the predictor scores for each predictor present. The receiver operating characteristics curve was examined to determine the optimal cut point of the calculated risk score.

WHO algorithm performance. The sensitivity, specificity, and number needed to treat (NNT) one true GC/CT anorectal infection were calculated for the WHO PT algorithm. Based on expert consensus, the WHO guidelines recommend that clinicians in resource-limited settings use PT for asymptomatic MSM who report having unprotected RAI and either multiple sex partners or a sex partner with an STI in the past 6 months. This latter variable (i.e., partner with an STI in the past 6 months) was not collected at *Anza Mapema*, so instead we used the variable "treated for any STI symptom in the last 3 months" as a proxy for recent STI exposure. Performance of the current WHO algorithm was compared to performance of the risk score algorithm at different cut-points, with respect to sensitivity, specificity, and NNT. Stata 14.1 software was used for statistical analyses.

Results

Population. Between September 2015 and August 2016, 700 MSM enrolled in *Anza Mapema*, of whom 698 had stored samples available for GC/CT NAAT testing. Of the 698 participants with enrollment samples available, the median age was 23 (interquartile range, 21-28) and most were single (73% had never been married to a woman). Most participants reported completing secondary education or higher (79%). Overall, HIV-1 prevalence was 11% (95% CI: 8.4% – 13.1%).

Anorectal GC and CT Prevalence and Risk Factors. At enrollment, 36 participants (5.2%) were positive for any anorectal GC/CT infection. Seventeen participants (47%) were positive for GC only, nine (25%) for CT only, and ten (28%) for both infections. In bivariable analyses, the following predictors were associated with increased odds of anorectal GC/CT infection at p<0.2: being 18-24 years of age, HIV positive serostatus, unprotected anal intercourse in past 3 months, any RAI in past 3 months, being the receptive partner during anal intercourse, and versatile sexual positioning. The following predictors were associated with decreased odds of anorectal GC/CT infection at p<0.2 in bivariable analyses: any drug use in the past year, transactional sex, and prior sex with a female. In the multivariable model, HIV positive serostatus (adjusted OR [aOR]=10.38; 95% CI, 4.39-10.55), being 18-24 years of age (aOR=3.74; 95% CI, 1.49-9.39), unprotected anal intercourse (aOR=4.71; 95% CI, 1.57-14.13), and engaging in RAI (aOR= 3.25; 95% CI, 1.31-8.07) were associated with increased odds of anorectal GC/CT infection, while transactional sex (aOR=0.39; 95% CI, 0.18-0.84) was associated with a decreased odds of anorectal GC/CT infection (Table 1). Because of collinearity, the variable “sexual position” was dropped from the multivariable model.

Risk Factors for Asymptomatic GC/CT anorectal infection. Of 36 participants with anorectal GC/CT infections, 24 (67%) were asymptomatic. In bivariable analyses excluding the 12 men with symptomatic infection, the following predictors were associated with increased odds of asymptomatic anorectal GC/CT infection at p<0.2: being 18-24 years of age, HIV positive serostatus, unprotected anal intercourse, and any RAI in the past 3 months. In bivariable analyses, the following predictors were associated with decreased odds of asymptomatic anorectal GC/CT infection at p<0.2: prior marriage to a female, cohabitation with male partner, and prior sex with a female. In the multivariable model, the following predictors were associated with increased odds of asymptomatic anorectal GC/CT infection: being 18-24 years of age (aOR=6.40; 95% CI, 1.82-22.51), HIV positive serostatus (aOR=8.61; 95% CI, 3.21-23.10), and unprotected anal intercourse (aOR=3.80; 95% CI, 1.23-11.75; Table 2).

Exam and laboratory findings. Among 401 (70%) asymptomatic men who underwent proctoscopy, there were no men with anorectal erythema among those with anorectal GC/CT infection and there was one man with anorectal erythema among those without anorectal GC/CT infection (0.3%). Anorectal erythema was not associated with anorectal GC/CT infection (Fisher's exact p=1.0). There were no asymptomatic men in the cohort who were found to have anorectal discharge on proctoscopy. There were 535 (93%) asymptomatic men for whom rectal Gram stain results were available. Seven men had leukocytes on rectal Gram stain among those with anorectal GC/CT infection (32%) compared to 72 men who had leukocytes on rectal Gram stain among those without anorectal GC/CT infection (14%). Four men had GNID on rectal Gram stain among those with anorectal GC/CT infection (18%) compared to 24 men who had GNID on rectal Gram stain among those without anorectal GC/CT infection (5%). The presence of leukocytes on rectal Gram stain was associated with asymptomatic anorectal GC/CT infection (X^2=5.30, p=0.02). Likewise, GNID on rectal Gram stain was associated with asymptomatic anorectal infection (Fisher's exact=0.02).

Predictor scores and score cut points. The final, combined model for asymptomatic anorectal GC/CT infections included the following carried forward from the multivariable model: HIV positive serostatus (risk score = 2), being 18-24 years of age (risk score = 2), and unprotected anal sex in the past 3 months (risk score = 1, Table 2). Risk-score algorithm performance is shown in Figure 1. With a risk score cut-off of 2, 88% of cases would be treated; however, presumptive therapy would be provided to 62% of participants and 22 participants would need to receive PT to prevent one anorectal GC/CT infection. With a risk score cut-off of 3, 83% of cases would be treated, but presumptive therapy would be provided to fewer participants (37%). Given the negative consequences of antibiotic overuse, a risk score of 3 would achieve the most favorable balance between sensitivity and specificity, and would reduce the NNT to 12 men treated with presumptive therapy in order to treat one true anorectal GC/CT infection.

WHO PT algorithm performance. The WHO PT algorithm had low sensitivity (25%), but was 84% specific when applied to the *Anza Mapema* cohort. Only 17% of participants met eligibility for PT by WHO criteria and 38 participants would need to receive PT to prevent one anorectal GC/CT infection using this approach.

Discussion

In this cohort of MSM in Kisumu, Kenya, we found a low overall prevalence (5.2%) of anorectal GC/CT infections, of which 67% were asymptomatic. Several sociodemographic and sexual behavioral risk factors were associated with increased odds of any (symptomatic and asymptomatic) anorectal GC/CT infection, including the following: HIV-positive serostatus, younger age (18-24 compared to >24 years of age), unprotected anal intercourse, RAI, and versatile sexual position. Transactional sex was inversely associated with having any anorectal GC/CT infection. After excluding symptomatic infections, significant predictors of asymptomatic anorectal GC/CT infection in our cohort were HIV-positive serostatus, younger age (18-24 compared to >24 years of age), and unprotected anal intercourse in the past 3 months, all of which were included in our final risk score algorithm. The algorithm performed most favorably at a risk score cut-off of 3, at which 83% of cases would be treated and 12 men would need to be treated with presumptive therapy to treat one true anorectal GC/CT infection. If this risk score algorithm approach was applied in this cohort, 37% of participants would have received presumptive therapy.

Prior studies have described associations between anorectal GC/CT infections and the predictors found to be significant in the *Anza Mapema* study including HIV-positive serostatus, unprotected anal intercourse, sexual position, and younger age. For example, in a study of anorectal GC/CT infections among Thai MSM, HIV infection was an independent risk factor for rectal GC (aOR=2.0, 95% CI: 1.3-3.1) and rectal CT (aOR=2.4, 95% CI: 1.2-4.7).[13] HIV-positive serostatus was also found to be associated with STIs combined (rectal/urethral GC/CT and syphilis) in a Ugandan study of 257 MSM (aOR=3.46; 95% CI: 1.03-11.64).[4] Unprotected RAI is a known risk factor for rectal GC/CT in MSM.[14,15] In a Tanzanian study, having RAI without a condom with a recent partner was associated with having anorectal GC/CT infection

(X^2=10.5, p=0.001) and was a significant predictor (aOR= 3.69, 95% CI: 1.47-9.25) for any STI (including GC/CT at any site and syphilis).[3] Younger age has been associated with increased risk for STIs, including anorectal GC/CT infections. In a cohort of asymptomatic HIV-infected MSM in the United States, older age was protective for having an incident STI, including anorectal GC/CT infections (per 10 years; OR=0.55, 95% CI: 0.37-0.83).[16] In a study of Nigerian MSM and transgender women (n=862), age greater than 30 years old was found to be protective for rectal and urethral GC/CT infections (aRR=0.48, 95% CI: 0.29-0.82).[17]

This is the first study to evaluate the burden of anorectal GC and CT infections among MSM in Kisumu, Kenya. The overall anorectal GC/CT infection prevalence (5.2%, 95% CI: 3.6%, 7.1%) in the *Anza Mapema* cohort was somewhat lower compared to prior studies of anorectal GC/CT infections among Kenyan MSM. Anorectal GC/CT infection prevalence may be different across Kenyan studies due to variations in sexual behavior, especially reported RAI. In a study conducted in Coastal Kenya in which 75% of 147 MSM reported RAI (compared to 45% in the last 3 months among all men in this study), anorectal GC/CT infection prevalence was estimated at 18.4% (95% CI: 12.5%, 25.6%).[10] In a study of 563 MSM in Nairobi, in which 45.5% reported one or more male partners with whom they had had receptive anal intercourse, the estimated anorectal GC/CT infection prevalence was 8.5% (95% CI: 6.4%, 11.1%).[5] The confidence interval for this estimate overlaps with our estimate from the *Anza Mapema* cohort. Reported transactional sex varied across these studies (from 75% in Coastal Kenya, 48% in Nairobi, and 63% in *Anza Mapema*), and was found to be protective, possibly due to higher condom use with clients compared to non-clients, as has been reported in other populations.[18-20] There were also differences in HIV prevalence in these study populations (40% in Coastal Kenya, 26% in Nairobi, and only 11% in the *Anza Mapema* cohort, which excluded men with a previous HIV diagnosis who were already linked to care and on treatment).[5,10]

The majority of anorectal GC/CT infections in the *Anza Mapema* cohort were asymptomatic (67%), which is consistent with prior studies of anorectal GC/CT among MSM in sub-Saharan Africa.[6,7,10,17] This is the second study that we are aware of that has specifically looked at predictors of asymptomatic anorectal GC/CT infections in MSM, which is crucial to understanding the impact of PT guidelines in settings where the syndromic approach to STI treatment is used. In the study by Sanders *et* *al* to evaluate performance of the WHO PT algorithm, no risk factors (including HIV serostatus, age, and unprotected RAI) were predictive of asymptomatic anorectal GC/CT infections.[10] However, this study was limited by a small sample size (n=147). We could identify no other studies evaluating the WHO PT algorithm for MSM in resource-limited settings.

The WHO PT algorithm is the current recommended strategy for identifying and treating men at risk for asymptomatic anorectal GC/CT infection in settings where diagnostic testing is not routinely available. In the Kenyan study which validated the WHO PT algorithm, 33% of participants were eligible to receive PT based on risk factors, the sensitivity was 74%, and number needed to treat was 4.[10] By applying the WHO PT algorithm to the *Anza Mapema* cohort, only 17% of participants would be eligible for PT, reflecting the lower prevalence of RAI. The WHO PT algorithm had very low sensitivity (25%) in this population, and 38 participants would need to receive PT to prevent one anorectal GC/CT infection. Our analyses included the sexual risk factors used in the WHO PT algorithm such as multiple sex partners, unprotected anal intercourse, and RAI, while substituting history of a recent STI as proxy for having a partner with a recent STI. Only unprotected anal intercourse was an independent predictor in the final multivariable model and was therefore included in our risk score. It is possible that risk factors requiring patient recall, such as personal history of a recent STI, number of sex partners, or partner treatment information, were subject to reporting or recall bias. More importantly, since even symptomatic anorectal infections and other STIs are often not diagnosed or treated in Kenya due to lack of diagnostic capacity, most men would not be aware that they or their partners have had a recent infection. For this reason, identifying at-risk men based on a prior STI diagnosis may not be of great utility in resource-limited settings.

This is the first study to develop a risk score algorithm for the prediction of asymptomatic anorectal GC/CT infections in MSM to guide PT. At a risk score cut-off of 3, which translates to meeting any 2 of the 3 criteria in our risk score, a high proportion (83%) of anorectal GC/CT infection cases would be treated, although 258 participants, or 37% of the cohort, would meet criteria and need to receive PT. PT for STIs has been utilized in several public health settings, including for sex partners of STI index cases and for periodic presumptive therapy in female sex workers.[21] Periodic presumptive therapy (PPT) for female sex workers has been shown to reduce the burden of GC and/or CT infection in targeted populations. This intervention is recommended by the WHO as part of a package of services to rapidly reduce STI prevalence in sex work settings.[21] While high cure rates can be achieved with PT, concerns about overtreatment remain, including increased antibiotic resistance, particularly in GC. In a meta-analysis of PPT use in female sex workers, there were no reports of increased antibiotic resistance, although few studies monitored for this and existing surveillance is inadequate.[21] When PPT is used as a strategy, antimicrobial susceptibility should be monitored to ensure that appropriate regimens are utilized and high cure rates are maintained in the target population. In settings that lack access to alternative methods for diagnosing and treating GC/CT infections, PT remains a strategy of considerable importance for preventing infectious sequelae and reducing HIV acquisition and transmission risk.

In addition to surveillance for antibiotic resistance, affordable and effective STI diagnostic tests are greatly needed in resource-limited settings both to target therapy more efficiently and reduce time to treatment. Based on our results, microscopy findings could be helpful for diagnosing asymptomatic anorectal GC/CT infections in clinics, depending on laboratory capabilities and available trained workforce. The limited lab data in our study showed that the presence of leukocytes on rectal Gram stain and GNID on rectal Gram stain were each associated with asymptomatic anorectal GC/CT infection in bivariable analyses. However, both of these variables were not independent predictors of asymptomatic anorectal infection when included in the multivariable analysis.

The *Anza Mapema* study is one of the largest cohorts of MSM in sub-Saharan Africa, which strengthened our ability to evaluate associations between behavioral and sociodemographic risk factors and anorectal GC/CT infections. Additionally, research funding enabled us to use highly sensitive and specific NAAT diagnostics to detect cases. However, our study is subject to several limitations. First, our study population was composed of MSM attending one of two urban research sites in western Kenya. Most MSM in Kenya are hidden and difficult to access, such that the *Anza Mapema* study cohort population may differ in some important aspects compared to the entire population of Kenyan MSM or to MSM in other sub-Saharan African countries. Therefore, the study results may not be generalizable to other MSM communities and caution should be exercised in interpreting results. Second, there may be information bias due to participant hesitation to report sexual risk and other behaviors. We tried to limit bias by the use of ACASI to enhance reporting of sensitive data. We also used a relatively short recall period (3 months) to reduce recall bias. Third, we were limited in our ability to determine how frequently PT should be given due to the cross-sectional design. As treatment was provided in the *Anza Mapema* cohort based on NAAT results, we were unable to use longitudinal data to test the efficacy of PT. PPT has been shown to be effective at decreasing GC and CT prevalence when given to high risk populations at monthly intervals, though the optimal frequency of PT administration remains unknown.[22] Fourth, an additional limitation of our study was that men who denied engaging in any anal sex were not asked if they had any anorectal symptoms. Of the 24 cases of asymptomatic anorectal GC/CT infection in the *Anza Mapema* cohort, 33% of the individuals had reported not engaging in any anal sex and were not asked for the presence of anorectal symptoms. Therefore, it is possible that some of the asymptomatic GC/CT cases may have actually been symptomatic and we may be overestimating the prevalence of asymptomatic anorectal GC/CT infections. However, this is likely similar to actual clinical practice where most clinicians would not ask for the presence of anorectal symptoms if a patient denied engaging in anal sex. Finally, the study questionnaire protocol was developed by a multidisciplinary team to address a number of data collection objectives, but by necessity had to be limited in length. Therefore, not all questions we would like to have asked are represented in the data (e.g., partner STI diagnosis, serosorting).

In conclusion, our empiric risk score to guide PT of asymptomatic anorectal GC/CT infections in MSM outperformed the WHO PT algorithm. Our risk score algorithm requires further validation in different MSM populations in sub-Saharan Africa, as risk factors for anorectal GC/CT infections may vary in different settings and populations. PT should be considered as a strategy to treat anorectal GC/CT infections in MSM and to decrease the burden of anorectal GC/CT disease in settings where diagnostic testing is not widely available. Our findings highlight the importance of developing effective low-cost diagnostic tests for use in vulnerable high-risk populations in resource-limited settings.

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Table 1. Factors associated with combined symptomatic and asymptomatic GC/CT anorectal infections at enrollment among 698 MSM

Characteristics and Behaviors	*GC/CT Cases, Proportion (%)*	*Bivariate Analysis*		*Multivariate Analysis*	
		OR (95% CI)	*P-value*	*aOR (95% CI)*	*P-value*
Age group			0.01		0.005
> 25 year	8/304 (2.6)	Reference		Reference	
18-24 year	28/394 (7.1)	2.83 (1.27, 6.30)		3.73 (1.48, 9.38)	
Education			0.48		
Secondary	16/348 (4.6)	Reference			
Primary or less	8/149 (5.4)	1.18 (0.49, 2.82)			
Higher/tertiary	12/201 (6.0)	1.32 (0.61, 2.85)			
Ever married to female partner			0.89		
No	26/511 (5.1)	Reference			
Yes	10/187 (5.3)	1.05 (0.50, 2.23)			
Living with male partner			0.25		
No	26/440 (5.9)	Reference			
Yes	10/258 (3.9)	0.64 (0.30, 1.35)			
HIV seropositive			<0.001		<0.001
No	21/624 (3.4)	Reference		Reference	
Yes	15/74 (20.3)	7.30 (3.57, 14.92)		10.29 (4.36, 24.25)	
Ever had sex with female partner			0.03		0.08
No	16/198 (8.1)	Reference		Reference	
Yes	20/500 (4.0)	0.47 (0.24, 0.94)		0.52 (0.25, 1.08)	
Multiple sex partners			0.52		

No	18/323 (5.6)	Reference			
Yes	16/356 (4.5)	0.80 (0.40, 1.59)			
Unprotected anal sex, past 3 months			0.01		0.006
No	5/251 (2.0)	Reference		Reference	
Yes	31/447 (6.9)	3.67 (1.41, 9.56)		4.73 (1.55, 14.43)	
Transactional sex, past 3 months			0.12		0.02
No	17/245 (6.9)	Reference		Reference	
Yes	19/453 (4.2)	0.59 (0.30, 1.15)		0.39 (0.18, 0.84)	
Usual sexual position, anal sex[a]			0.004		
Inserting partner	10/380 (2.6)	Reference			
Receiving partner	14/150 (9.3)	3.81 (1.65, 8.78)			
Versatile	12/155 (7.7)	3.10 (1.31, 7.35)			
RAI, past 3 months			0.001		0.01
No	10/380 (2.6)	Reference		Reference	
Yes	26/305 (8.5)	3.45 (1.63, 7.27)		2.79 (1.26, 6.19)	
Treated for any STI, last 3 months			0.47		
No	33/613 (5.4)	Reference			
Yes	3/85 (3.5)	0.64 (0.19, 2.15)			
Disclosure of MSM status at last STI treatment			0.47		
No	29/525 (5.5)	Reference			
Yes	7/162 (4.3)	0.64 (0.19, 2.15)			

Physical violence, past 3 months			0.56		
No physical assault	28/509 (5.5)	Reference			
Physically assaulted	6/141 (4.3)	0.76 (0.31, 1.88)			
Missing	2/48 (4.2)	0.75 (0.17, 3.24)			
Sexual assault, past 3 months			0.33		
No sexual assault	30/529 (5.7)	Reference			
Sexually assaulted	4/117 (3.4)	0.59 (0.20, 1.71)			
Missing	2/52 (3.8)	0.67 (0.15, 2.87)			
Any alcohol use, past year			0.60		
No	14/243 (5.8)	Reference			
Yes	22/455 (4.8)	0.83 (0.42, 1.66)			
Any drug use, past year			0.08		0.17
No	26/405 (6.4)	Reference		Reference	
Yes	10/293 (3.4)	0.52 (0.24, 1.09)		0.56 (0.25, 1.29)	
Injection drug use, past year			0.89		
No	34/614 (5.3)	Reference			
Yes	0/44 (0)	1			
Missing	2/40 (2.9)	0.90 (0.21, 3.88)			

GC indicated *Neisseria gonorrhoeae*; CT, *Chlamydia trachomatis*; MSM, men who have sex with men; HIV, human immunodeficiency virus; RAI, receptive anal intercourse; CI, confidence interval; OR, odds ratio; aOR, adjusted odds ratio

[a] "Usual sexual position, anal sex" was dropped from the multivariable model due to collinearity with the variable RAI

Table 2. Factors associated with asymptomatic GC/CT anorectal infections at enrollment among 576 MSM

Characteristics and Behaviors	*GC/CT Cases, Proportion (%)*	*Bivariate Analysis*		*Multivariate Analysis*		*Final, Combined Model*		*Predictor Score*[a]
		OR (95% CI)	*P-value*	*aOR (95% CI)*	*P-value*	*aOR (95% CI)*	*P-value*	
Age group			0.01		0.02		0.004	2
> 25 year	4/249 (1.6)	Reference		Reference		Reference		
18-24 year	20/327 (6.1)	3.99 (1.34, 11.84)		4.39 (1.24, 15.49)		6.40 (1.82, 22.51)		
Education			0.33					
Secondary	11/289 (3.8)	Reference						
Primary or less	3/114 (2.6)	0.68 (0.19, 2.50)						
Higher/tertiary	10/173 (5.8)	1.55 (0.64, 3.73)						
Ever married to a female			0.14		0.29			
No	21/426 (4.9)	Reference		Reference				
Yes	3/150 (2.0)	0.39 (0.12, 1.34)		0.48 (0.12, 1.88)				
Living with male partner			0.16		0.06			
No	19/378 (5.0)	Reference		Reference				
Yes	5/198 (2.5)	0.49 (0.18, 1.33)		0.38 (0.14, 1.04)				
HIV seropositive			<0.001		<0.001		<0.001	2
No	15/522 (2.9)	Reference		Reference				
Yes	9/54 (16.7)	6.76 (2.80, 16.32)		9.46 (3.38, 26.50)		8.61 (3.21, 23.10)		
Ever had sex with a female			0.09		0.15			
No	10/153 (6.5)	Reference		Reference				
Yes	14/423 (3.3)	0.49 (0.21, 1.13)		0.54 (0.24, 1.23)				

Multiple sex partners			0.83					
No	12/280 (4.3)	Reference						
Yes	11/281 (3.9)	0.91 (0.39, 2.10)						
Unprotected anal sex, past 3 months			0.04		0.01		0.02	1
No	4/219 (1.8)	Reference		Reference		Reference		
Yes	20/357 (5.6)	3.19 (1.07, 9.47)		4.31 (1.43, 12.98)		3.80 (1.23, 11.75)		
Transactional sex, past 3 months			0.21					
Never	12/217 (5.5)	Reference						
Yes	12/359 (3.3)	0.59 (0.26, 1.34)						
Usual sexual position, anal sex			0.21					
Inserting partner	10/333 (3.0)	Reference						
Receiving partner	6/107 (5.6)	1.92 (0.68, 5.41)						
Versatile	8/124 (6.5)	2.23 (0.86, 5.79)						
RAI, past 3 months			0.08		0.31			
Never	10/333 (3.0)	Reference		Reference				
Yes	14/231 (6.1)	2.08 (0.91, 4.78)		1.57 (0.66, 3.73)				
Treated for any STI, last 3 months			0.79					
No	22/519 (4.2)	Reference						
Yes	2/57 (3.5)	0.82 (0.19, 3.59)						
Disclosure of MSM status at last STI treatment			0.25					
No	21/439 (4.8)	Reference						
Yes	3/126 (2.4)	0.49 (0.14, 1.66)						

Physical violence, past 3 months			0.43
No physical assault	21/440 (4.8)	Reference	
Physically assaulted	2/102 (2.0)	0.40 (0.09, 1.73)	
Missing	1/34 (2.9)	0.60 (0.08, 4.64)	
Sexual assault, past 3 months			0.58
No sexual assault	21/454 (4.6)	Reference	
Sexually assaulted	2/83 (2.4)	0.51 (0.12, 2.22)	
Missing	1/39 (2.6)	0.54 (0.07, 4.15)	
Any alcohol use, past year			0.43
No	10/197 (5.1)	Reference	
Yes	14/379 (3.7)	0.72 (0.31, 1.65)	
Any drug use, past year			0.37
No	16/333 (4.8)	Reference	
Yes	8/243 (3.3)	0.67 (0.28, 1.60)	
Injection drug use, past year			0.71
No	22/504 (4.4)	Reference	
Yes	0/37 (0)	1	
Missing	2/35 (5.7)	1.33 (0.30, 5.90)	

GC indicated *Neisseria gonorrhoeae*; CT, *Chlamydia trachomatis*; MSM, men who have sex with men; HIV, human immunodeficiency virus; RAI, receptive anal intercourse; CI, confidence interval; OR, odds ratio; aOR, adjusted odds ratio

[a]Predictor score is the natural log (i.e., the unexponentiated coefficient) of the adjusted odds ratio in the final model, rounded to the nearest integer (see Methods section).

Figure 1. Sensitivity, specificity, and proportion offered presumptive therapy. The horizontal axis displays all risk score cut-offs that could be chosen for the presumptive therapy algorithm. The risk scores correspond to the range of risk scores observed across study participants, based on participant risk factors. In a situation where diagnostic testing was unavailable, all men with risk scores at or above a chosen cut-off would receive presumptive therapy. The vertical axis displays the proportion of *Anza Mapema* participants who would have been offered presumptive therapy at a given risk score cut-off, had diagnostic testing been unavailable. Sensitivity refers to the proportion of GC/CT cases with risk scores at or above a given cut-off. Specificity refers to the proportion of participants without GC/CT anorectal infections with risk scores lower than a given cut-off, who would receive presumptive therapy in the absence of infection.