Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

HHS Public Access
Author manuscript
Sex Transm Dis. Author manuscript; available in PMC 2020 February 01.

Published in final edited form as:
Sex Transm Dis. 2019 February ; 46(2): 80–85. doi:10.1097/OLQ.0000000000000910.

Ocular syphilis and HIV coinfection among syphilis patients in North Carolina, 2014-2016

Anna B. Cope, PhD[1,2], **Victoria L. Mobley, MD**[2], **Sara E. Oliver, MD**[1], **Mara Larson, MPH**[2], **Nicole Dzialowy, MSc**[2], **Jason Maxwell, BS**[2], **Jessica L. Rinsky, PhD**[1,2], **Thomas A. Peterman, MD**[1], **Aaron Fleischauer, PhD**[1,2], and **Erika Samoff, PhD**[2]

[1]Centers for Disease Control and Prevention, Atlanta, GA

[2]North Carolina Division of Public Health, Department of Health and Human Services, Raleigh, NC

Abstract

Background: Ocular syphilis (OS) has been associated with HIV coinfection previously. We compared demographic and clinical characteristics of syphilis patients with and without HIV to identify risk factors for developing OS.

Methods: We reviewed all syphilis cases (early and late) reported to the North Carolina (NC) Division of Public Health during 2014-2016 and categorized HIV status (positive, negative, unknown) and OS status based on report of ocular symptoms with no other defined etiology. We estimated prevalence ratios (PR) and 95% confidence intervals (CI) for OS by HIV status. Among syphilis patients with HIV, we compared viral loads and CD4 cell counts by OS status. We compared symptom resolution by HIV status for a subset of OS patients.

Results: Among 7,123 confirmed syphilis cases, 2,846 (39.9%) were living with HIV, 109 (1.5%) had OS, and 59 (0.8%) had both. OS was more prevalent in syphilis patients with HIV compared to HIV-negative/unknown-status patients (PR: 1.8; 95% CI: 1.2, 2.6). Compared to other patients with HIV, the prevalence of OS was higher in patients with viral loads >200 copies/mL (1.7; 1.0, 2.8) and in patients with a CD4 count ≤200 cells/mL (2.3; 1.3, 4.2). Among 11 patients with severe OS, 9 (81.8%) were HIV-positive. Among 39 interviewed OS patients, OS symptom resolution was similar for HIV-positive (70.0%) and HIV-negative/unknown-status (68.4%) patients.

Conclusion: Syphilis patients with HIV were nearly twice as likely to report OS symptoms as were patients without documented HIV. HIV-related immunodeficiency possibly increases the risk of OS development in co-infected patients.

Short Summary:

Corresponding Author: Anna B. Cope, Division of Public Health, Department of Health and Human Services, 1902 Mail Service Center, Raleigh, NC 27699-1902, USA, anna.cope@dhhs.nc.gov, Telephone: 919-546-1624. Fax: 919-715-7540.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflict of Interest: None of the authors have any conflicts of interest to report.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Ocular syphilis is more prevalent in syphilis patients with HIV, particularly those with unsuppressed viral loads or low CD4 counts. Complaints of ocular symptoms may help detect previously undiagnosed HIV.

Keywords

Treponema pallidum; uveitis; vision loss; viral load; CD4

Introduction

Untreated syphilis can result in complications involving the eye (e.g., uveitis, retinitis, optic neuritis, retinal detachment) collectively referred to as ocular syphilis (OS). In some patients, OS leads to vision loss [1]. Although the proportion of syphilis cases with ocular manifestations remains small, reports of OS have increased with rising syphilis rates in the United States since 2014 [2–5].

A few small studies suggest HIV contributes to the ocular manifestations of syphilis [1, 3, 6–16]. Estimates of HIV co-infection among OS patients range from approximately 30% internationally [1, 6] to 50% in the United States [3]. Patients living with HIV have been diagnosed with OS in both early and late stages of syphilis [1, 7–9]. The median rapid plasma reagin (RPR) and Venereal Disease Research Laboratory (VDRL) titers are often higher in OS patients living with HIV [1]. Nearly half of patients concurrently diagnosed with OS and HIV were tested for HIV because they presented to a provider with OS symptoms [10]. Although most reported OS patients living with HIV are diagnosed with posterior uveitis and panuvietis, [8, 11–16] there is some variation in OS-defining diagnosis among OS patients living with HIV [7, 10] that may be related to CD4 counts [10]. Generally, patients living with HIV experience substantial resolution of OS symptoms when treated appropriately as per CDC guidelines [1, 7, 10, 11].

Among syphilis patients reported to the North Carolina (NC) Division of Public Health between 2014 and 2015, OS prevalence was higher in patients living with HIV compared to patients without documented HIV [4]. It is unclear why some patients living with HIV develop OS while others do not. Improved reporting and documentation of OS coupled with data that can be easily linked between HIV and STD surveillance systems make NC uniquely well-suited to address this question. Using population-based surveillance information, we compared demographic and clinical markers of disease to identify factors associated with the development of OS in syphilis patients by HIV diagnosis status.

Methods

We conducted a secondary analysis of surveillance data previously used to describe the epidemiology of OS in NC (with one additional year of follow-up) [4]. Briefly, we reviewed all newly reported syphilis cases (early and late) entered in the North Carolina Electronic Disease Surveillance System (NC EDSS) during 2014-2016. We defined OS as a patient diagnosed with syphilis and having clinical symptoms consistent with ocular disease that could not be explained by other causes [17]. For all syphilis cases, we abstracted

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

demographic characteristics, syphilis stage, RPR titer (a serologic screening test for syphilis antibodies), [18] cerebrospinal fluid (CSF) VDRL test results, symptoms, and risk factors from NC EDSS. For OS cases diagnosed during 2014-2015, we reviewed medical records to ascertain the OS-defining diagnosis, OS symptoms, and treatment, and attempted to interview these OS patients to assess OS symptom resolution [4].

Syphilis patients were matched to NC's enhanced HIV/AIDS Reporting System (eHARS) to identify patients living with HIV (no additional HIV infections were identified among OS patients from the medical record review). HIV-negative status was determined by a documented negative HIV test at the time of the syphilis diagnosis in NC EDSS or as ascertained from the medical record review. We classified all other patients as HIV-unknown-status. For patients living with HIV, we abstracted HIV diagnosis date from eHARS and CD4 counts and viral loads (VL) reported closest to and within six months before the syphilis diagnosis date from the NC Engagement in Care and HIV Outreach database. In sensitivity analyses, we varied the window period used to capture the most proximate VL and CD4 count before the syphilis diagnosis date to 12 months. Next, we repeated these analyses with the closest VL or CD4 in time to the syphilis diagnosis date (whether before or after) and within the 6- or 12-month window period. We defined viral suppression as a VL ≤200 copies/mL. Syphilis cases with HIV co-infection were classified as previously diagnosed (HIV diagnosis date >30 days before syphilis diagnosis date) or concurrently diagnosed (HIV diagnosis date ≤30 days from syphilis diagnosis date).

We estimated prevalence ratios (PR) and 95% confidence intervals (CI) to compare OS prevalence 1) by HIV status within demographic and clinical subgroups of syphilis patients and 2) by the timing of HIV diagnosis relative to the syphilis diagnosis date, viral suppression, and CD4 count ≤200 cells/mL among syphilis patients living with HIV using complete case analysis. In sensitivity analyses, we assessed the impact of different classifications of missing HIV lab values on the association between OS and both viral suppression and CD4 count ≤200 cells/mL. The proportion of OS patients who sought care from an ophthalmologist was compared by HIV status (HIV-positive versus HIV-negative/unknown status) using Fisher's exact test. We compared syphilis stage, RPR titer, VL, and CD4 count by OS status in syphilis patients living with HIV using the Wilcoxon rank sum test (continuous variables) and chi-square test (categorical variables). All analyses were conducted in SAS version 9.4 (Cary, NC). This analysis was part of a public health investigation and exempted from institutional review board (IRB) review.

Results

All syphilis patients

During 2014-2016, there were 7,123 confirmed syphilis cases reported in NC; 109 (1.5%) were classified as having OS (1 verified by darkfield microscopy to have *T. pallidum* in vitreous fluid; 78 had an ophthalmologic exam with findings consistent with OS; 30 only reported symptoms consistent with OS that had no other known cause). In total, 2,846 (40.0%) syphilis patients were living with HIV, of whom 59 (2.1%) had OS. Of the remaining 4,277 syphilis patients, 3,197 (74.7%) tested HIV-negative of whom 38 (1.2%) had OS, and 1,080 (25.3%) had an unknown HIV status of whom 12 (1.1%) had OS. OS was

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

more prevalent in syphilis patients living with HIV compared to those who were HIV-negative/unknown-status (PR: 1.8; 95% CI: 1.2, 2.6). Most OS patients were men (91.7%) and all OS patients living with HIV were men. White, non-Hispanic syphilis patients were 2.6 times more likely to have OS than Black, non-Hispanic patients (95% CI: 1.7, 3.8). Nonetheless, OS was more prevalent in patients living with HIV across all syphilis stages, ages, races, and risks. The median age and RPR titer were higher in OS patients compared to non-OS patients, regardless of the patient's HIV status **(**TABLE 1**)**.

OS patients

Among OS patients, those living with HIV were younger and had a higher median RPR than OS patients who were HIV-negative or unknown-status (TABLE 1). Overall, 47 of 109 (43%) OS patients had a CSF VDRL test performed. Most of the 32 patients with a reactive CSF VDRL test result were living with HIV (N=21; 65.6%). We reviewed the medical records for the 63 OS patients diagnosed between 2014 and 2015. In total, 35 (55.5%) patients were HIV-positive; both of the two OS patients reporting complete vision loss were living with HIV. Among these 63 OS patients, we did not observe a difference in the proportion of OS patients examined by an ophthalmologist by HIV status (74.3% (26/35) HIV-positive versus 82.1% (23/28) HIV-negative/unknown-status; p=0.4). Per the medical record review, uveitis was the most common OS diagnosis in patients living with HIV (N=11 panuveitis; N=4 posterior uveitis; N=5 anterior uveitis). Furthermore, eleven patients had a severe OS diagnosis (chorioretinitis, optic neuritis, or retinal detachment); nine (81.8%) were living with HIV. We interviewed 39 OS patients to assess OS symptom resolution. Overall, 14 of 20 (70.0%) patients living with HIV and 13 of 19 (68.4%) HIV-negative/unknown-status patients reported that once treated for OS, visual functioning returned to levels experienced before OS symptoms manifested. The remaining 12 patients had residual deficits.

Syphilis patients living with HIV

Among 2,846 patients living with HIV, 2,504 (88.0%) had a CD4 count (57 with OS) and 2,554 (89.7%) had a VL within 6 months before their syphilis diagnosis. Compared to non-OS patients, slightly higher proportions of OS patients living with HIV had an available CD4 count (N=55; 93.2%) or VL (N=57; 96.6%) during this timeframe. The median VL among all syphilis patients living with HIV was 40 copies/mL (IQR 20-19,243); 1,016 (39.8%) patients were virally unsuppressed. Virally unsuppressed patients were more likely to be diagnosed with OS than suppressed patients (PR: 1.7; 95% CI: 1.0, 2.8). When patients living with HIV who did not have a reported VL were considered unsuppressed, results were similar, although mitigated (PR: 1.5; 95% CI: 0.9, 2.5).

The median CD4 count among syphilis patients living with HIV was 505 cells/mL (IQR 324-712); and 310 (12.4%) patients had a CD4 count ≤200 cells/mL. Median CD4 counts were lower in OS patients than non-OS patients at every syphilis stage (TABLE 2). The prevalence of OS was higher in patients with a CD4 count ≤200 cells/mL than in patients with higher CD4 counts (PR: 2.3; 95% CI 1.3, 4.2). This association persisted after controlling for patient age (PR: 2.2; 95% CI 1.2, 4.0).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

The prevalence of OS was higher among syphilis patients diagnosed with HIV and syphilis concurrently compared to syphilis patients previously diagnosed with HIV infection (PR: 1.5; 95% CI: 0.8, 2.8). CD4 counts were lowest and VLs were highest in concurrently diagnosed OS patients. More OS patients had late latent or unknown duration syphilis compared to non-OS patients among concurrently diagnosed (69.2% versus 33.1% p=0.01) and previously diagnosed patients (41.3% versus 22.0%, p=0.002). OS patients were more likely than non-OS patients to have a CD4 count ≤200 cells/ml in previously diagnosed patients (25.0% versus 10.4%; p=0.005), but not among concurrently diagnosed patients (23.1% versus 22.2%; p=0.9).

Results from sensitivity analyses that varied the date range to capture HIV lab values and included missing data in VL and CD4 categories were similar to reported findings (Supplemental Tables 1A and 1B).

Discussion

Ocular syphilis was identified in a small proportion of syphilis patients, regardless of HIV status. However, OS was more prevalent in patients living with HIV. Most patients with severe OS and both patients who reported complete vision loss were living with HIV. OS patients living with HIV were younger than HIV-negative and unknown-status OS patients, but still older than non-OS patients living with HIV. OS was diagnosed more frequently in patients living with HIV who had late or unknown duration syphilis, an unsuppressed VL, or a CD4 count ≤200 cells/mL. Many of these patients were diagnosed with HIV and syphilis concurrently, suggesting this population was not receiving routine screening for syphilis or HIV at earlier stages of infection. Concerns about ocular symptoms may have prompted these patients to seek healthcare. With treatment, OS symptoms in patients living with HIV appeared to resolve at similar rates as HIV-negative or unknown-status patients.

The combination of older age and low CD4 counts in OS patients living with HIV suggest declining immune status may contribute to ocular manifestations of syphilis. Syphilis can result in a temporary drop in the CD4 count in patients coinfected with HIV that typically resolves after treatment [19–23]. Similar to previous studies, [10, 11] we observed OS patients to have lower CD4 counts than non-OS patients, regardless of when the patient was diagnosed with HIV relative to their syphilis diagnosis or the patient's age. OS was also more prevalent in patients with an unsuppressed VL, providing support for previous findings that inflammation associated with uncontrolled HIV replication could be an important prognostic factor for OS [24]. To date, there is no evidence that the recent nationwide increase in reported OS infection was due to a specific neurotropic strain of *T. pallidum* [25]. Although our study was not designed to do so, continued characterization of OS strains by HIV status may elicit an understanding of who is most at risk of developing ocular manifestations of syphilis.

Ocular syphilis may be associated with delayed syphilis diagnosis, particularly in people who also have undiagnosed, and thus uncontrolled, HIV. Almost 70% of OS patients with concurrently diagnosed HIV had late or unknown duration syphilis. These patients had the highest median VL and lowest median CD4 count of all syphilis patients living with HIV.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

However, since the median RPR was high (1:128) in this group, syphilis stage may have been misclassified and some of these patients actually may have had recently acquired syphilis. Regardless, OS screening as part of routine examination should be considered for any person, whether HIV positive or not, presenting to healthcare with ocular symptoms in areas with high syphilis rates.

People aware of their HIV infection may be receiving regular health care to control their disease, oftentimes from providers familiar with manifestations of syphilis. Therefore, these patients may be screened for OS more often due to higher clinical suspicion by their HIV care provider. Consequently, elevated rates of OS in patients living with HIV could be due to detection bias. OS prevalence was also much lower in women than in men; no women with OS was living with HIV. It is unclear whether this gender difference in OS prevalence is due to the relatively small number of women diagnosed with both syphilis and HIV, a failure on the part of providers to ask about ocular symptoms, or an unidentified biological factor. However, historical evidence suggests women have fewer complications related to untreated syphilis than men [26]. Future analyses with larger OS patient populations may have increased power to detect differences in OS recognition by various demographic and clinical characteristics, including HIV status, and thereby quantify potential bias.

Our assessment of both OS and HIV status was incomplete. An OS classification required a patient to be diagnosed with syphilis, report OS symptoms to a provider, and have these symptoms documented in NC EDSS. In all but one case, we were unable to verify the OS diagnosis in a biological specimen. Although there is potential for misclassification in the remaining cases, no other cause for the ocular symptoms were reported and it is reasonable to assume they have OS per CDC case definition [17]. At the time of their syphilis diagnosis, HIV status was not documented in surveillance data for 15% of patients. These patients were either not tested at the time of their syphilis diagnosis, or if tested, did not have their test results automatically captured in NC EDSS. VL and CD4 measurements near the time of the syphilis diagnosis were also missing for approximately 10% of known syphilis patients living with HIV. Because we observed no differences in the pattern of missing VL and CD4 data by OS or any other measured covariate, we assumed potential bias due to missing lab data to be negligible.

In this population-based assessment of syphilis patients, OS was rare, regardless of HIV status. We identified a higher prevalence of OS in patients living with HIV, particularly those who were unaware of their HIV infection. Complaints of ocular symptoms may help detect previously undiagnosed HIV, emphasizing the importance of screening for HIV and syphilis in tandem. Elevated rates of OS in older patients and those with low CD4 counts suggest immunodeficiency may play a role in the association between OS manifestations and HIV. Other related information not captured by surveillance could provide additional insight about factors that increase the risk of OS in syphilis patients living with HIV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Acknowledgements

The authors thank the Ocular Syphilis DIS Workgroup: Jason Hall, Victor Hough, Andre Ivey, Stephanie Hawks Sherard, Samantha Greene, Dishonda Taylor, Mike Mercurio, and Miraida Gipson. We also thank Evelyn Foust, Gui Liu, Charnetta Williams, Lauri Markowitz and the North Carolina Public Health Epidemiologists.

Funding: This work was supported jointly by the CDC and the North Carolina Division of Public Health.

References

1. Mathew RG, Goh BT, and Westcott MC, British Ocular Syphilis Study (BOSS): 2-year national surveillance study of intraocular inflammation secondary to ocular syphilis. Invest Ophthalmol Vis Sci, 2014 55(8): p. 5394–400. [PubMed: 24925878]
2. Woolston S, et al., A Cluster of Ocular Syphilis Cases - Seattle, Washington, and San Francisco, California, 2014–2015. MMWR Morb Mortal Wkly Rep, 2015 64(40): p. 1150–1. [PubMed: 26469141]
3. Oliver SE, et al., Ocular Syphilis - Eight Jurisdictions, United States, 2014-2015. MMWR Morb Mortal Wkly Rep, 2016 65(43): p. 1185–1188. [PubMed: 27811837]
4. Oliver SE, et al., Increases in Ocular Syphilis-North Carolina, 2014–2015. Clin Infect Dis, 2017 65(10): p. 1676–1682. [PubMed: 29020152]
5. Centers for Disease Control and Prevention Sexually transmitted disease surveillance 2016. Atlanta, GA: US Department of Health and Human Services, 2017.
6. Bollemeijer JG, et al., Clinical Manifestations and Outcome of Syphilitic Uveitis. Invest Ophthalmol Vis Sci, 2016 57(2): p. 404–11. [PubMed: 26848879]
7. Li JZ, et al., Ocular syphilis among HIV-infected individuals. Clin Infect Dis, 2010 51(4): p. 468–71. [PubMed: 20604717]
8. McLeish WM, et al., The ocular manifestations of syphilis in the human immunodeficiency virus type 1-infected host. Ophthalmology, 1990 97(2): p. 196–203. [PubMed: 2326008]
9. Parc CE, et al., Manifestations and treatment of ocular syphilis during an epidemic in France. Sex Transm Dis, 2007 34(8): p. 553–6. [PubMed: 17667532]
10. Tucker JD, et al., Ocular syphilis among HIV-infected patients: a systematic analysis of the literature. Sex Transm Infect, 2011 87(1): p. 4–8. [PubMed: 20798396]
11. Lee SY, et al., Clinical and laboratory characteristics of ocular syphilis: a new face in the era of HIV co-infection. J Ophthalmic Inflamm Infect, 2015 5(1): p. 56. [PubMed: 26297110]
12. Shalaby IA, et al., Syphilitic uveitis in human immunodeficiency virus-infected patients. Arch Ophthalmol, 1997 115(4): p. 469–73. [PubMed: 9109754]
13. Browning DJ, Posterior segment manifestations of active ocular syphilis, their response to a neurosyphilis regimen of penicillin therapy, and the influence of human immunodeficiency virus status on response. Ophthalmology, 2000 107(11): p. 2015–23. [PubMed: 11054325]
14. Kuo IC, Kapusta MA, and Rao NA, Vitritis as the primary manifestation of ocular syphilis in patients with HIV infection. Am J Ophthalmol, 1998 125(3): p. 306–11. [PubMed: 9512147]
15. Villanueva AV, et al., Posterior uveitis in patients with positive serology for syphilis. Clin Infect Dis, 2000 30(3): p. 479–85. [PubMed: 10722431]
16. Balba GP, et al., Ocular syphilis in HIV-positive patients receiving highly active antiretroviral therapy. Am J Med, 2006 119(5): p. 448 e21–5.
17. Centers for Disease Control and Prevention. STD surveillance case definitions. 2018; Available at: https://wwwn.cdc.gov/nndss/conditions/syphilis/case-definition/2018/. Accessed August 16, 2018.
18. Holmes King K., et al., Sexually Tranmitted Diseases. 4th ed. 2007, New York: The McGraw-Hill Companies.
19. Zetola NM and Klausner JD, Syphilis and HIV infection: an update. Clin Infect Dis, 2007 44(9): p. 1222–8. [PubMed: 17407043]
20. Sadiq ST, et al., The effects of early syphilis on CD4 counts and HIV-1 RNA viral loads in blood and semen. Sex Transm Infect, 2005 81(5): p. 380–5. [PubMed: 16199736]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

21. Kofoed K, et al., Syphilis and human immunodeficiency virus (HIV)-1 coinfection: influence on CD4 T-cell count, HIV-1 viral load, and treatment response. Sex Transm Dis, 2006 33(3): p. 143–8. [PubMed: 16505739]
22. Dyer JR, et al., Association of CD4 cell depletion and elevated blood and seminal plasma human immunodeficiency virus type 1 (HIV-1) RNA concentrations with genital ulcer disease in HIV-1-infected men in Malawi. J Infect Dis, 1998 177(1): p. 224–7. [PubMed: 9419194]
23. Buchacz K, et al., Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. AIDS, 2004 18(15): p. 2075–9. [PubMed: 15577629]
24. Biotti D, et al., Ocular syphilis and HIV infection. Sex Transm Dis, 2010 37(1): p. 41–3. [PubMed: 20118676]
25. Oliver S, et al., Molecular Typing of Treponema pallidum in Ocular Syphilis. Sex Transm Dis, 2016 43(8): p. 524–7. [PubMed: 27419819]
26. Gjestland T, The Oslo study of untreated syphilis; an epidemiologic investigation of the natural course of the syphilitic infection based upon a re-study of the Boeck-Bruusgaard material. Acta Derm Venereol Suppl (Stockh), 1955 35(Suppl 34): p. 3–368; [PubMed: 13301322]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1.

Ocular Syphilis (OS) prevalence by HIV status within demographic and clinical characteristic groups among syphilis patients reported in North Carolina, 2014-2016.

	TOTAL	HIV-Positive		HIV-Negative		HIV Unknown Status		OS Prevalence in HIV-Positive versus HIV-Negative/Unknown Status	
	N	N	Prevalence of OS[a] (%)	N	Prevalence of OS[a] (%)	N	Prevalence of OS[a] (%)	Prevalence Ratio	95% Confidence Interval
TOTAL	**7123**	**2846**	**2.1**	**3197**	**1.2**	**1080**	**1.1**	**1.8**	**1.2, 2.6**
Gender									
Male	**5913**	2790	2.1	2313	1.5	810	0.9	1.6	1.1, 2.4
Female	**1177**	43	0.0	870	0.5	264	1.9	NA	NA
Transgender	**33**	13	0.0	14	0.0	6	0.0	NA	NA
Race									
Black	**4499**	1909	1.4	1986	0.8	604	1.0	1.6	0.9, 2.8
White	**1852**	704	4.1	825	2.1	323	1.6	2.2	1.3, 3.7
Other	**759**	230	1.7	385	1.0	144	0.7	1.8	0.5, 6.8
Missing	**13**	3	0.0	1	100.0	9	0.0		
Age									
<40 years	**4886**	1910	1.3	2302	0.4	674	0.0	3.9	1.9, 8.1
≥40 years	**2237**	936	3.6	895	3.1	406	3.0	1.2	0.8, 1.9
MSM Risk[b]									
MSM	**4018**	2286	2.1	1377	1.0	355	0.3	2.4	1.4, 4.3
Non-MSM	**1895**	504	2.2	936	2.1	455	1.3	1.2	0.6, 2.4
Syphilis Stage									
Primary & Secondary	**2932**	1196	2.0	1318	1.1	418	0.2	2.3	1.2, 4.4
Non-Primary/Non-Secondary Early	**1959**	962	0.7	820	0.7	177	0.6	1.0	0.4, 2.9
Late or Unknown Duration	**2232**	688	4.1	1059	1.7	485	2.1	2.2	1.3, 3.8
Previous Syphilis Diagnosis									
No	**5891**	2009	2.5	2898	1.1	984	0.9	2.4	1.6, 3.6

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

	TOTAL	HIV-Positive		HIV-Negative		HIV Unknown Status		OS Prevalence in HIV-Positive versus HIV-Negative/Unknown Status	
	N	**N**	**Prevalence of OS[a] (%)**	**N**	**Prevalence of OS[a] (%)**	**N**	**Prevalence of OS[a] (%)**	**Prevalence Ratio**	**95% Confidence Interval**
Yes	**1232**	837	1.0	299	2.0	96	3.1	0.4	0.2, 1.1
Year Diagnosed									
2014	**1788**	694	1.7	746	0.9	348	0.3	2.4	1.0, 5.8
2015	**2659**	1087	2.1	1189	1.4	383	0.8	1.7	0.9, 3.0
2016	**2676**	1065	2.3	1262	1.1	349	2.3	1.7	0.9, 2.9
	Total	**Non-OS**	**OS**	**Non-OS**	**OS**	**Non-OS**	**OS**		
Median Age (IQR[d])	**31 (25-43)**	32 (26-44)	44 (32-50)	29 (23-41)	48 (36-56)	33 (25-46)	54 (50-62)		
Median RPR[c] (IQR[d])	**1:32 (1:8-1:128)**	1:64 (1:16-1:128)	1:128 (1:64-1:512)	1:32 (1:8-1:64)	1:96 (1:48-1:256)	1:32 (1:4-1:64)	1:64 (1:8-1:128)		

[a] per 100

[b] Among men only

[c] RPR=Rapid plasma regain titer, a serologic test to screen for syphilis. The titer refers to the greatest dilution of serum at which the test is still positive. [18]

[d] IQR=Interquartile Range

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Median CD4 cell count, viral load, and RPR[a] titer at the time of syphilis diagnosis[b] by syphilis stage and ocular syphilis (OS) status in syphilis patients with a previous[c] and concurrent[d] HIV diagnosis reported in North Carolina, 2014-2016.

			Previous HIV Diagnosis[c]			Concurrent HIV Diagnosis[d]			Total HIV-Positive Syphilis Cases		
			Median	IQR[e]	p[f]	Median	IQR[e]	p[f]	Median	IQR[e]	p[f]
CD4 Count (cells/ml)	Primary/Secondary	Non-OS[g]	496	329-719		422	248-575		480	309-694	
		OS[g]	308	125-765	0.2	398	152-629	0.9	360	129-708	0.2
	Non-Primary/Non-Secondary Early	Non-OS	570	372-773		434	215-572		551	362-761	
		OS	510	108-586	0.2	280	280-280	0.5	479	108-586	0.1
	Late or Unknown Duration	Non-OS	526	350-720		327	140-498		490	310-680	
		OS	515	369-657	0.7	260	221-325	0.3	388	260-566	0.2
	TOTAL	**Non-OS**	**529**	**350-740**		**379**	**218-550**		**507**	**327-718**	
		OS	**485**	**218-703**	**0.1**	**280**	**221-398**	**0.1**	**388**	**221-629**	**0.009**
Viral Load (copies/ml)	Primary/Secondary	Non-OS	30	20-9400		60,111	19,195-134,000		60	20-31,400	
		OS	502	20-84283	0.09	62,890	24,670-143,000	0.9	1550	20-86,825	0.2
	Non-Primary/Non-Secondary Early	Non-OS	20	20-140		41,620	12,560-117,130		20	20-1,924	
		OS	20	20-40	0.8	48,494	48,494-48,494	0.8	20	20-48,494	0.9
	Late or Unknown Duration	Non-OS	21	20-2870		59,117	13,510-165,561		59	20-26,595	
		OS	20	20-248	0.6	64,613	52,100-81,195	0.5	444	20-64,613	0.3
	TOTAL	**Non-OS**	**20**	**20-1670**		**54,995**	**16,972-147,000**		**40**	**20-18,470**	
		OS	37	20-9106	0.3	63,710	48,494-81,195	0.4	482	20-25,780	0.03
RPR titer	Primary/Secondary	Non-OS	64	32-256		64	32-128		64	16-128	
		OS	128	32-512	0.2	64	64-128	0.9	64	32-128	0.2
	Non-Primary/Non-Secondary Early	Non-OS	32	8-128		32	16-128		32	8-64	
		OS	192	128-512	0.04	512	512-512	0.1	256	64-256	0.01
	Late or Unknown Duration	Non-OS	32	8-128		32	4-128		16	2-32	
		OS	256	64-512	0.0001	128	64-256	0.009	128	64-256	<0.0001
	TOTAL	**Non-OS**	**64**	**16-128**		**64**	**16-128**		**32**	**8-64**	
		OS	**128**	**64-512**	**<0.0001**	**128**	**64-256**	**0.02**	**64**	64-256	**<0.0001**

[a] RPR=Rapid plasma regain titer, a serologic test to screen for syphilis. The titer refers to the greatest dilution of serum at which the test is still positive.[18]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

[b] CD4 cell count and viral load reported closest to and within six months of the syphilis diagnosis date in the NC Engagement in Care and HIV Outreach database

[c] HIV diagnosis date >30 days prior to syphilis diagnosis date

[d] HIV diagnosis date ≤30 days from the syphilis diagnosis date

[e] IQR=Interquartile Range

[f] p-value based on Wilcoxon Rank Sum Test comparing Median OS value versus Non-OS value

[g] OS=Ocular Syphilis Patient; Non-OS=not an ocular syphilis patient