



# Subsequent HIV Disease Risk Following Syphilis Diagnosis in a Southern MSM Population

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## Background:

Pathela (Pathela, Braunstein, Blank, Shepard, & Schillinger, 2015) in New York City reported the risk of subsequent HIV infection diagnosis within 24 months among MSM was 1:20, or a 5% overall risk for MSM diagnosed with either primary or secondary syphilis (Clinical Infectious Diseases® 2015;61(2):281-7). We applied the methods described in the Pathela study to reported disease registries for Shelby County, Tennessee, to determine whether our experience was similar to, better than, or worse than the experience reported in New York City. Shelby County is an urban southern county that includes the City of Memphis, the largest metropolitan area in Tennessee. Shelby County has a population of 940,000+ residents, 52% of which are non-Hispanic Black residents.

## Methods:

The initial study population included 1,175 people diagnosed with either Primary or Secondary Syphilis from 2005-2012 inclusive. After eliminating duplicate reports, HIV Cases diagnosed within 60 days of Syphilis diagnosis, and age less than 12 years old or older than 65 years old Syphilis Cases, 992 unique Syphilis patients were matched against new HIV Cases (2005 - 2015) in the Enhanced HIV/AIDS Reporting System (eHARS). Data and statistical analysis was conducted in SAS 9.3, including descriptive epidemiology, Kaplan - Meier survival analysis was performed to identify differences in HIV Free survival between the risk factors, and multivariate Cox proportional hazards modeling was conducted to identify predictors of survival. To probe the relationship between risk factors and subsequent HIV infection multivariate logistic regression analyses were conducted. Data were represented graphically and in tabular form with estimate values and calculated 95% confidence intervals.

## Match Process:

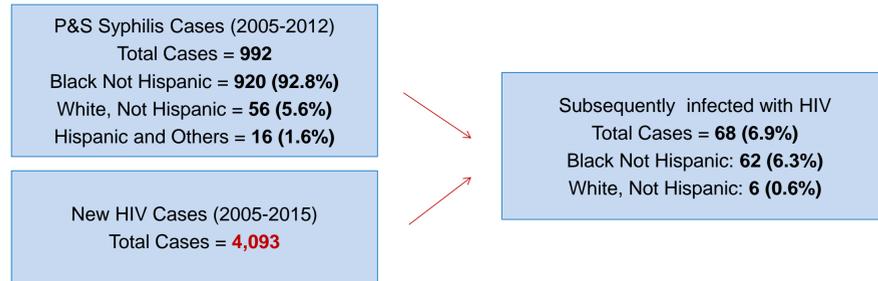


Table 1: HIV Incidence Rate (per 1,000 persons) by Demographic and Behavioral Characteristics

	P&S Syphilis Cases		Number of Newly Diagnosed HIV Cases		incidence proportion	Mean HIV Free Survival	person-years of follow-up	HIV Incidence Rate (per 1,000 person-years)		
	N	%	N	%				Months	N	N
<b>All</b>	<b>920</b>	<b>100%</b>	<b>62</b>	<b>6.7%</b>		<b>36.8</b>	<b>8,954</b>	<b>6.9</b>	<b>6.8</b>	<b>7.1</b>
<b>Sex</b>										
Female	334	36%	8	2.4%		40.8	3,305	2.4	2.3	2.5
Male	586	64%	54	9.2%		36.3	5,649	9.6	9.3	9.8
<b>Age at Syphilis Dx</b>										
<35 years old	578	63%	49	8.5%		38.0	5,713	8.6	8.4	8.8
35+ years old	342	37%	13	3.8%		32.2	3,242	4.0	3.9	4.2
<b>Risk/Exposure</b>										
HeteroSexual	652	71%	12	1.8%		46.0	6,474	1.9	1.8	1.9
MSM	268	29%	50	18.7%		34.6	2,480	<b>20.2</b>	19.4	21.0
<b>Stages of Syphilis</b>										
Primary Syphilis	145	16%	6	4.1%		43.7	1,434	4.2	4.0	4.4
Secondary Syphilis	775	84%	56	7.2%		36.0	7,520	7.4	7.3	7.6
<b>Other bacterial STDS</b>										
Chlamydia	208	23%	15	7.2%		31.7	2,029	7.4	7.1	7.7
Gonorrhea	131	14%	19	14.5%		39.0	1,238	<b>15.4</b>	14.5	16.2
Not Infected (Syphilis only)	581	63%	28	4.8%		38.1	5,688	4.9	4.8	5.1

Table 2: Cox Proportional Hazard Analysis of factors associated with time to mortality to follow up

Parameter	Analysis of Maximum Likelihood Estimates		
	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Male vs Female	0.325	0.08	1.327
MSM vs Hetero Sexual	<b>4.13</b>	<b>1.15</b>	<b>14.84</b>
35+ years old vs <35 years old	<b>2.555</b>	<b>1.154</b>	<b>5.659</b>
Chlamydia vs Not Infected	0.985	0.496	1.957
Gonorrhea vs Not Infected	1.013	0.56	1.831

Figure 1: Kaplan - Meier Survival Estimate

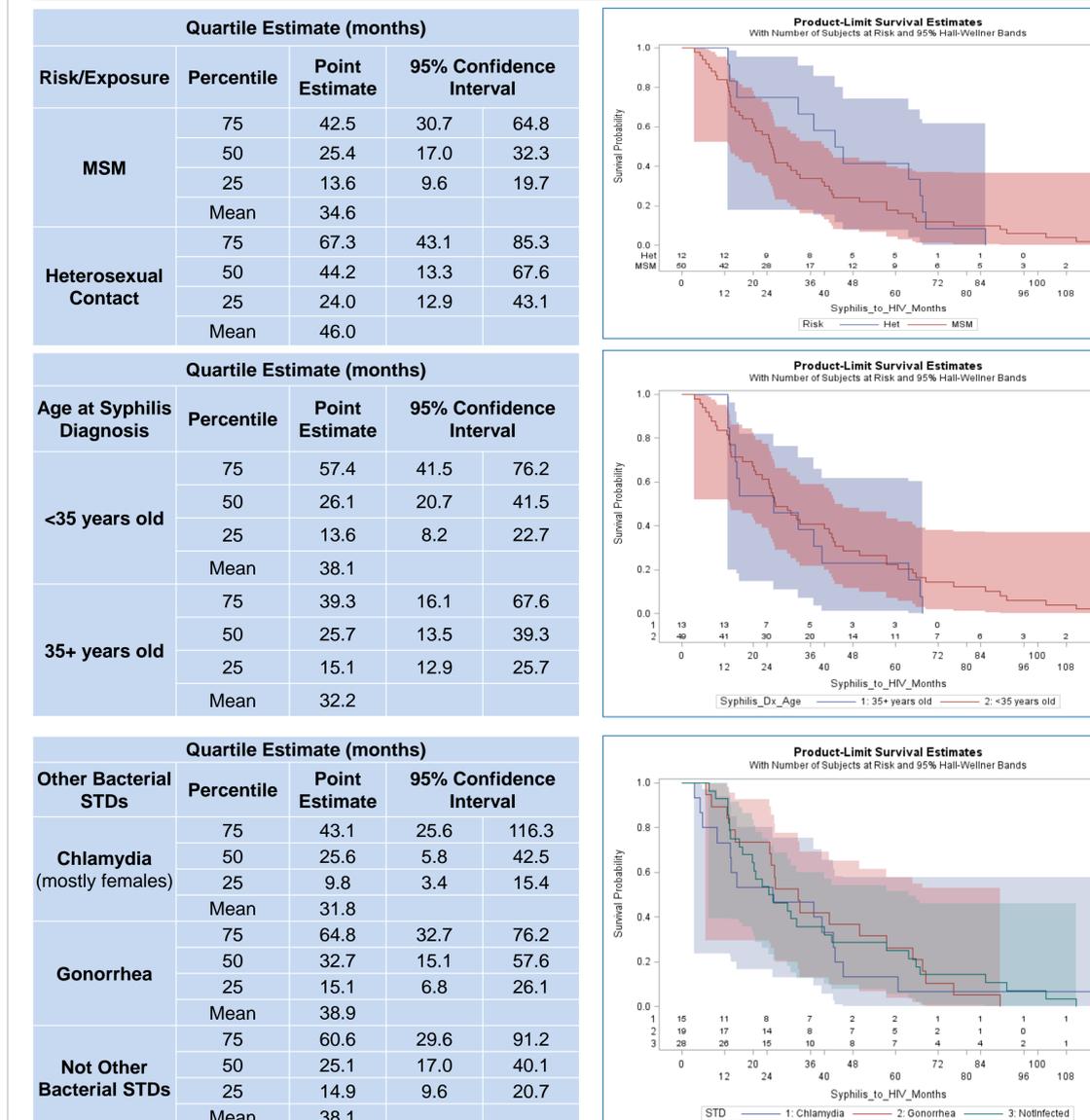


Figure 2: Subsequent HIV Incidence Rate (Per 1,000 persons) of P&S Syphilis, 2005 - 2015

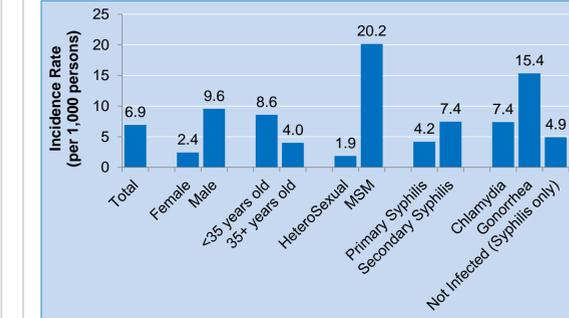


Figure 3: Adjusted Odds Ratio and 95% CL

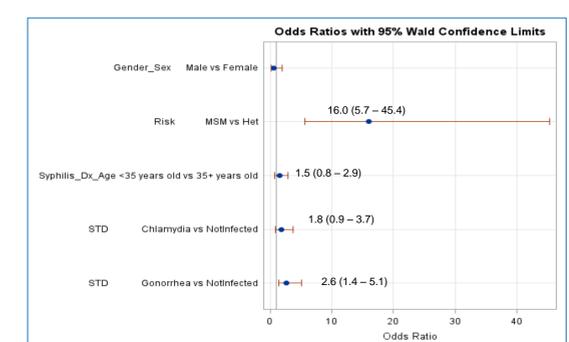


Table 3: Number of Subsequently infected HIV cases within 24 and 36 months of P&S Syphilis

	P&S Syphilis Cases	Number of Subsequent HIV Cases	24 Months		36 Months	
			# of Syphilis Cases Fail to Survive	# of HIV infections One in	# of Syphilis Cases Fail to Survive	# of HIV infections One in
<b>Total</b>	<b>920</b>	<b>62</b>	<b>25</b>	<b>37</b>	<b>37</b>	<b>25</b>
<b>Sex</b>						
Female	334	8	3	111	3	111
Male	586	54	22	27	34	17
<b>Age at Syphilis Diagnosis</b>						
<35 years old	578	49	19	30	29	20
35+ years old	342	13	6	57	8	43
<b>Risk/Exposure</b>						
HeteroSexual	652	12	3	217	4	163
MSM	268	50	22	12	33	8
<b>Other bacterial STDS</b>						
Chlamydia	208	15	7	30	8	26
Gonorrhea	131	19	5	26	11	12
Not Infected (Syphilis only)	581	28	13	45	18	32

## Results:

Between January 1 2005 and December 31 2012, 920 Black P&S Syphilis patients who did not have evidence of prior HIV infection were included for the analytical study. Overall, 62 of 920 were subsequently diagnosed HIV+ in the study cohort. The mean age was 32.4 years (range, 14.4 - 64.7). Annual incidence rate was 6.9 per 1,000 P&S Syphilis patients. For specific subpopulations, however, annual incidence rate was greater. For MSM the annual IR was 20.2 and was 15.4 for patients with Gonorrhea infection (Figure 2). Kaplan - Meier Survival Estimate (Figure 1) shows that 50% HIV Free survival times were less for MSM P&S patients (25 months compared with 44 months HIV Free for Heterosexual contacts). One in 12 and one in 8 MSM P&S Syphilis patients were subsequently infected with HIV within 24 months and 36 months respectively. One in 26 and one in 12 P&S Syphilis patients with Gonorrhea infection were subsequently infected with HIV within 24 months and 36 months respectively (Table 3).

Adjusted Hazard ratio in Cox's Proportional Hazard Model (Table 2) shows that after controlling for sex, P&S Syphilis Diagnosed Age, Infection with other bacterial STDs, being MSM with P&S Syphilis are **4.1 times** (95% CL: 1.15 - 14.8) more likely; and being older (35+ years old) are **2.6 times** (95% CL: 1.15 - 5.66) more likely to be infected with HIV at **any time point** compared to those heterosexual with P&S Syphilis patients.

Adjusted odds ratio for the main effect in logistic regression model (Figure 3) shows that after controlling for sex, P&S Syphilis Diagnosed Age, Stages of Syphilis, and Infection with other STDs, MSMs with P&S Syphilis had **cumulatively 16 times** (95% CL: 5.7 - 45.4) the odds of being more likely to be infected with HIV compared to those Heterosexual P&S Syphilis patients; Being infected with Gonorrhea also increased the risk of HIV infection for 2.6 fold (95% CL: 1.4 - 5.1) compared to those not infected with other bacterial STDs.

## Conclusions:

HIV negative MSM patients diagnosed with P&S Syphilis are at extremely high risk to subsequently be diagnosed with HIV Disease. Particularly for young (<35 years old) Black MSM, the risk may exceed **10% that they will become infected within 24 months**. HIV-, Syphilis + MSM must be offered pre-exposure prophylaxis and other interventions to lower their risk of HIV.

## References:

- Pathela, P., Braunstein, S. L., Blank, S., Shepard, C. & Schillinger, J. A. The high risk of an HIV diagnosis following a diagnosis of syphilis: a population-level analysis of New York City men. *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.* **61**, 281-287 (2015).
- Baeten, J. M. et al. Antiretroviral Prophylaxis for HIV-1 Prevention among Heterosexual Men and Women. *N. Engl. J. Med.* **367**, 399-410 (2012).