

Delayed but adequate serologic response to syphilis treatment in HIV-positive adults



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BACKGROUND

Increasing rates of co-infection between HIV and syphilis, nefarious synergy
Issues with syphilis management

- Imperfect diagnostic test: difficult to differentiate false positive, treatment failure, serofast, reinfection
- Inconsistent guidelines for HIV-positive adults
- Prior studies conducted before widespread use of ART

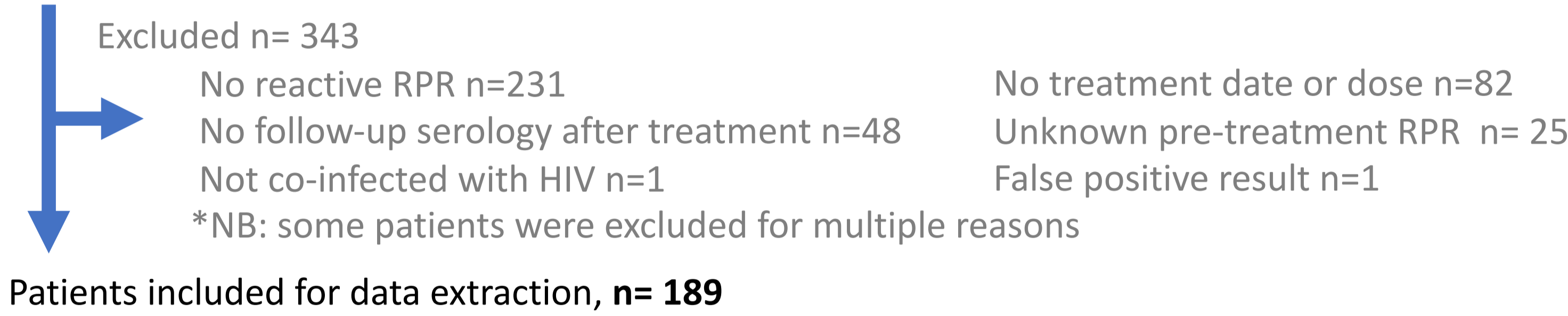
Primary Outcome: To investigate the serological response to syphilis treatment in patients who are co-infected with HIV

Secondary Outcome: To explore any clinical correlates that will predict serologic response to treatment

METHODS

Patient Population

All patients in the Toronto General Hospital HIV Clinic with an abnormal syphilis serology from January 1, 2000 – January 1, 2017, **n= 532**



Data Extraction

- Retrospective chart review of medical records
- First chronologically available syphilis episode fulfilling all inclusion criteria was used; previous and subsequent episodes of syphilis were ignored
- Correlation with demographic data maintained in a database by clinic staff

Statistics

- Kaplan Meier estimates: time to four-fold response and seroreversion from baseline RPR
- Univariable and multivariable proportional hazards models: associations between clinical covariates and time to a four-fold response and seroreversion from baseline RPR

RESULTS

Patient Demographics

Age, median (IQR)	42 (35.0, 48.0)
Caucasian, n (%)	105 (57.1)
Male, n (%)	189 (100)
MSM, n (%)	158 (87.3)
CD4 count, median (IQR)	443 (272, 609)
Log10 VL, median (IQR)	1.69 (1.59, 4.14)
VL <= 50, n (%)	90 (55.9)
On ART, n (%)	141 (74.6)
Previous AIDS, n (%)	52 (27.5)
Syphilis Episode, n (%)	
1	134 (70.9)
2	47 (24.9)
3	7 (3.7)
4	1 (0.5)
Stage, n (%)	
Primary	22 (11.6)
Secondary	53 (28.0)
Early Latent	23 (12.2)
Late Latent	53 (28.0)
Neurosyphilis	36 (19.0)
Missing	1 (1.1)
Treatment, n (%)	
Benzathine IM x1	51 (27.0)
Benzathine IM x2-3	85 (45.0)
Benzathine IV	40 (21.2)
Doxycycline	9 (4.8)
Titers done per year, mean (IQR)	3.26 (2.06, 4.89)
Follow-up in years, median (IQR)	2.55 (1.53, 6.14)

Table 1. Demographics of the included 189 patients.

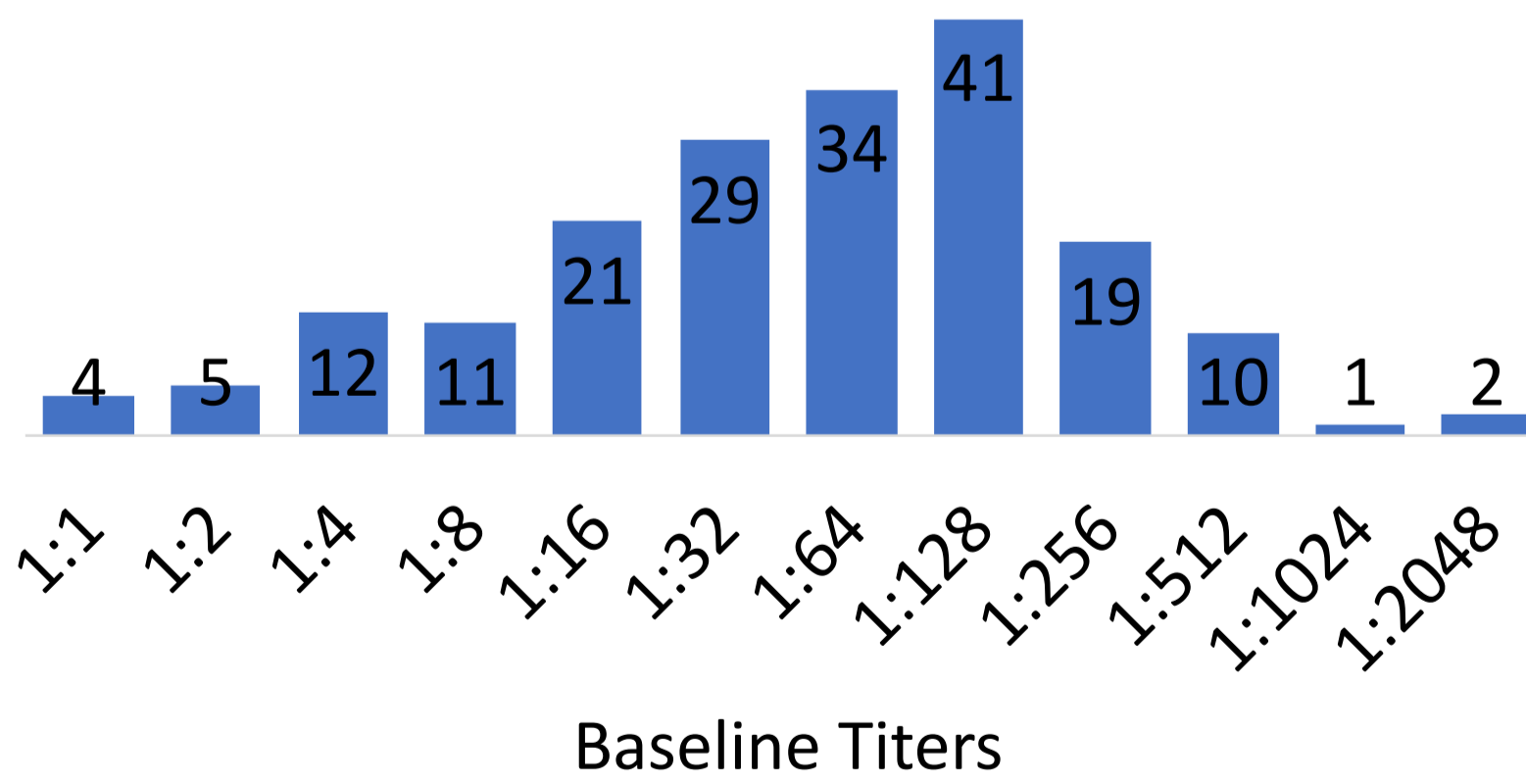


Figure 1. Distribution of baseline syphilis titers at time of diagnosis.

Time to Adequate Serologic Response and Seroreversion

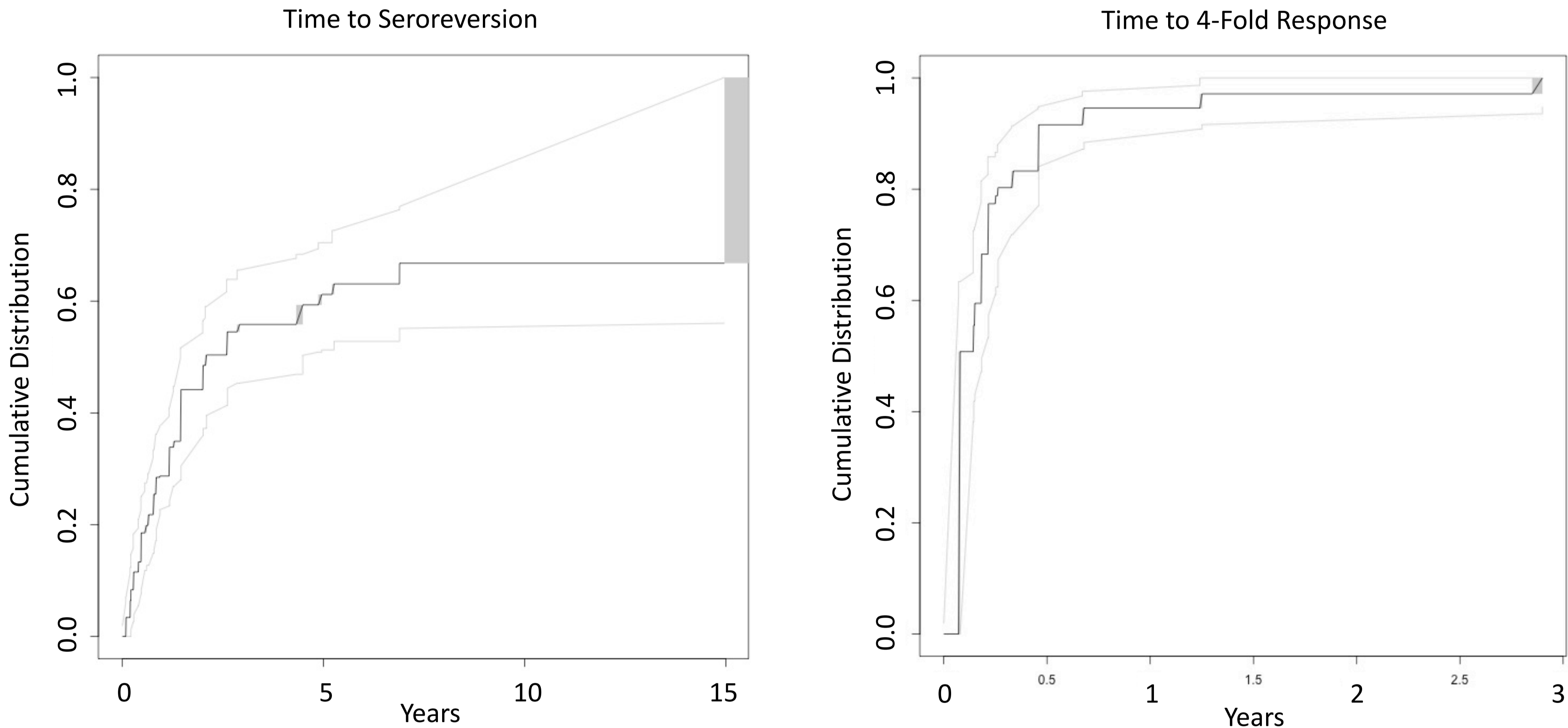


Figure 2. Kaplan Meier estimates generalized for interval censored data for time to reach a 4-fold response and seroreversion from baseline RPR. The probability of achieving a four-fold decrease or a non-reactive RPR by year 1 was 0.95 (0.87, 0.98) and 0.29 (0.22, 0.38), respectively.

Clinical Correlates to Time to Adequate Serologic Response and Seroreversion

	Time to Seroreversion				Time to 4-Fold Response			
	Univariable		Multivariable		Univariable		Multivariable	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Age (per 10 years)	0.87 (0.69, 1.1)	0.24	0.89 (0.66, 1.17)	0.39	0.97 (0.82, 1.14)	0.67	0.94 (0.75, 1.16)	0.55
CD4 (per 100 cells/mm3)	0.95 (0.85, 1.05)	0.28	0.91 (0.83, 1.02)	0.09	0.96 (0.88, 1.05)	0.38	0.96 (0.87, 1.07)	0.48
Stage								
Primary/ Secondary	Reference		Reference		Reference		Reference	
Early Latent	0.37 (0.16, 0.82)	0.0149	0.52 (0.23, 1.18)	0.12	0.66 (0.22, 1.98)	0.45	0.84 (0.12, 5.71)	0.86
Late Latent	0.38 (0.21, 0.65)	0.0006	0.49 (0.25, 0.95)	0.0358	0.42 (0.26, 0.66)	0.0002	0.37 (0.17, 0.83)	0.0152
Neurosyphilis	0.25 (0.13, 0.46)	0.0000	0.26 (0.12, 0.6)	0.0015	0.60 (0.34, 1.04)	0.07	0.62 (0.28, 1.38)	0.24
VL <=50	1.13 (0.75, 1.69)	0.56	0.94 (0.56, 1.4)	0.81	1.1 (0.77, 1.57)	0.62	1.01 (0.56, 1.82)	0.96
>1 Treatment	0.44 (0.25, 0.77)	0.0043	0.47 (0.18, 1.19)	0.11	1.03 (0.77, 1.37)	0.85	1.84 (0.76, 4.47)	0.18
Previous Syphilis	0.5 (0.29, 0.88)	0.0154	0.39 (0.2, 0.74)	0.0044	0.95 (0.66, 1.37)	0.79	0.84 (0.49, 1.44)	0.52

Table 2. Univariable and multivariable proportional hazards models show that late latent syphilis is associated with a decreased likelihood of achieving a 4-fold response and seroreversion. HIV factors such as CD4 and VL suppression did not have any effect.

ACKNOWLEDGEMENTS

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CONCLUSIONS

- Serologic response to syphilis treatment in HIV infected MSM was high
- By one year, the probability of achieving a 4-fold response was very high (0.95) but the probability of achieving seroreversion was low (0.29)
- Patients with late latent syphilis are less likely than patients with primary or secondary syphilis to reach a 4-fold response or seroreversion
- Serologic response and seroreversion was not impacted by CD4 count or VL suppression

LIMITATIONS

- Retrospective study
- Predominately MSM with their first episode of syphilis treated in an out-patient setting