ENHANCED SYPHILIS SCREENING AMONG HIV+ MEN

EPB065

Cluster-randomized trial of routine syphilis screening among men attending HIV outpatient clinics in Ontario, Canada

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Background

Syphilis testing and treatment of new infections, if detected early, is simple and inexpensive. We previously carried out the Enhanced Syphilis Screening Among HIV-positive Men (ESSAHM) Trial that paired opt-out syphilis tests with routine HIV bloodwork to improve early syphilis case detection (*Clin Infect Dis* 2022; 74(5):846-853). One of the trial objectives was **to determine if routinized syphilis testing reached men at higher risk of infection** (*Implementation Sci 2015;* 11, 8). However, this could not be tested using trial data alone as few patient covariates were collected given the pragmatic trial approach. Thus, we re-analysed ESSAHM Trial intervention effects using data from a concurrent cohort study that ascertained sociodemographic characteristics and sexual histories.

Methods

The **ESSAHM Trial** used a stepped wedge cluster-randomized trial (SW-CRT) design. Four outpatient HIV clinics introduced a practice change to pair syphilis testing with routine HIV viral loads in a step-wise fashion over 5 six-month periods. All clinics were in the control condition in step 1. Clinics were then randomized to one of four roll-out schedules such that, by step 5, all were in the intervention condition.

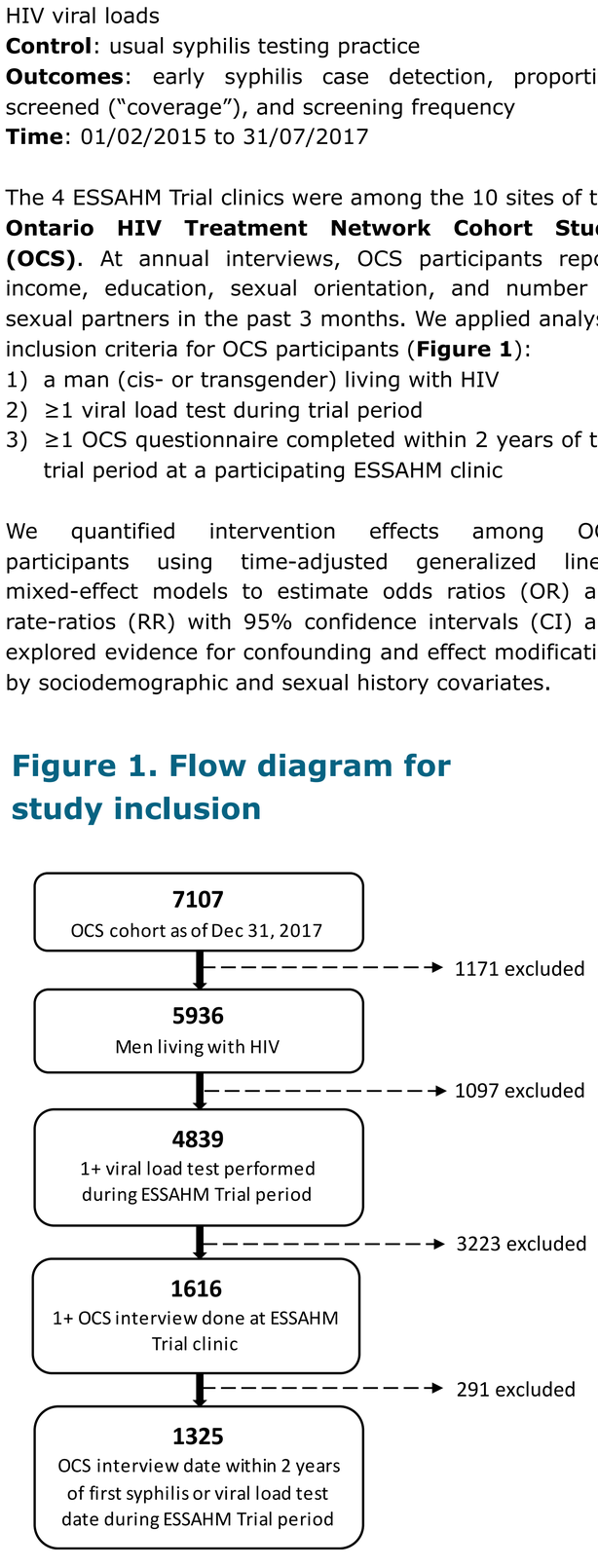
Population: HIV-positive men attending HIV outpatient clinics in Toronto and Ottawa, Canada
Intervention: standing orders for syphilis testing with HIV viral loads
Control: usual syphilis testing practice
Outcomes: early syphilis case detection, proportion screened ("coverage"), and screening frequency
Time: 01/02/2015 to 31/07/2017

The 4 ESSAHM Trial clinics were among the 10 sites of the **Ontario HIV Treatment Network Cohort Study (OCS)**. At annual interviews, OCS participants report income, education, sexual orientation, and number of sexual partners in the past 3 months. We applied analysis inclusion criteria for OCS participants (**Figure 1**):

1) a man (cis- or transgender) living with HIV
2) ≥1 viral load test during trial period
3) ≥1 OCS questionnaire completed within 2 years of the trial period at a participating ESSAHM clinic

We quantified intervention effects among OCS participants using time-adjusted generalized linear mixed-effect models to estimate odds ratios (OR) and rate-ratios (RR) with 95% confidence intervals (CI) and explored evidence for confounding and effect modification by sociodemographic and sexual history covariates.

Figure 1. Flow diagram for study inclusion



Results

Thirty-four percent (1325/3895) of ESSAHM trial participants were also OCS participants who met the analysis inclusion criteria. They had a mean age of 52.0 years and 86% were men who have sex with men (**Table 1**). At baseline, 25% (n=316) reported 2+, 30% (n=365) reported 1, and 45% (n=556) reported 0 sex partners.

There were 75 diagnoses of early syphilis (control: 26, intervention: 49). Comparing intervention to control periods, there were increases in case detection (OR 1.83, CI 0.85, 3.93), the proportion screened (OR 2.81, CI 2.20, 3.59), and number of tests per year (RR 1.73, CI 1.51, 1.97) (**Table 2**). There was no evidence of confounding by sociodemographic characteristics. However, intervention effects were modified by number of sex partners (**Table 3**).

Table 1. Characteristics of OCS participants who were also participants ESSAHM Trial at step 1 when all clinics were in control condition (a)

	n (%)
Number of viral loads per person in 6-month period	
Mean (SD)	1.41 (0.74)
Result of (first) HIV viral load	
Undetectable (<40 copies/mL)	868 (87.5%)
Known past history of syphilis at baseline (b)	148 (14.9%)
Age	
Mean (SD)	52.0 (11.5)
Less than 30 years	39 (3.9%)
30-39	115 (11.6%)
40-49	202 (20.4%)
50-59	397 (40.0%)
60 and older	239 (24.1%)
Personal Income (CAD)	
Less than $20,000	343 (34.6%)
$20,000 to $39,999	225 (22.7%)
$40,000 to $59,999	167 (16.8%)
$60,000 to $79,999	112 (11.3%)
$80,000 to $99,999	62 (6.3%)
$100,000 or more	59 (6.0%)
Education	
Less than high school	106 (10.7%)
High school	176 (17.7%)
Some post-secondary education	154 (15.5%)
Completed trade school/college	208 (21.0%)
Completed university	238 (24.0%)
Post-graduate	109 (11.0%)
Race	
Indigenous	21 (2.1%)
African/Caribbean/Black	130 (13.1%)
Asian	81 (8.2%)
Latin American	52 (5.2%)
White	658 (66.3%)
Other /Unknown	39 (3.9%)
Sexual Orientation	
Heterosexual/Straight	210 (21.2%)
Gay	692 (69.8%)
Bisexual	85 (8.6%)
Men who have sex with men (MSM)	848 (85.5%)
Number of sex partners, past 3 months	
None	422 (42.5%)
One	268 (27.0%)
2-4	157 (15.8%)
5+	84 (8.5%)
Unknown	61 (6.2%)
Number of male sex partners, past 3 months	
None	511 (51.5%)
One	203 (20.5%)
2-4	143 (14.4%)
5+	80 (8.1%)
Unknown	55 (5.5%)
Number of female sex partners, past 3 months	
None	836 (84.3%)
One	86 (8.7%)
2+	11 (1.1)
Unknown	59 (5.9%)
Multiple partners living with HIV, past 3 months	
None or one partner of any status	680 (68.5%)
2+ but not living with HIV	130 (13.1%)
2+ living with HIV	111 (11.2%)
Unknown	71 (7.2%)
Multiple HIV-negative/unknown status partners, past 3 months	
None or one partner of any status	680 (68.5%)
2+ but not HIV-negative/unknown status	104 (10.5%)
2+ HIV-negative/unknown status	136 (13.7%)
Unknown	72 (7.3%)

Frequency (percent) unless specified otherwise. CAD = Canadian currency. All proportions may not add to 100% due to missing data (not greater than 2.4%).

(a) Baseline characteristics are shown for male patients under study during the first six-month step of the SW-CRT, when all clinics were in the "control" setting. The 333 men who entered the study in subsequent steps are not shown.

(b) Past history of syphilis as determined by reactive syphilis serology in the year preceding the trial start.

Table 2. Intervention effects on early syphilis case detection, screening coverage, and screening frequency

	Unadjusted Ratio (95%CI)	Time-adjusted Ratio (95%CI)
Early syphilis detection (a)	2.44 (1.45, 4.11)	1.83 (0.85, 3.93)
Screening coverage (a)	6.47 (5.50, 7.60)	2.81 (2.20, 3.59)
Screening frequency (c)	2.25 (2.08, 2.43)	1.73 (1.51, 1.97)

CI, confidence interval. Referent = control periods.
(a) Either (1) seroconversion with prior negative syphilis serology within the previous 12 months; or (2) in men previously diagnosed with syphilis, a 4-fold or greater rise in RPR titre from the last titre within the prior 12 months, indicative of re-infection Odds ratio estimated by general linear mixed model using a logit link.
(b) Proportion of men with at least one syphilis test during a six-month step. Rate ratio estimated by general linear mixed model using a log link.
(c) Count of syphilis serology test episodes per six-month step. Rate ratio estimated by general linear mixed model using a log link.

Table 3. Multiplicative interactions between sexual behaviours and intervention effects on early syphilis case detection, screening coverage, and screening frequency

Sexual partnership history	Early syphilis detection: Time-adjusted (95%CI)	Screening coverage: Time-adjusted (95%CI)	Screening frequency: Time-adjusted (95%CI)
Number of male and female sex partners			
≤1	1.46 (0.53, 4.00)	3.58 (2.71, 4.72)	2.05 (1.76, 2.39)
2+	3.05 (1.14, 8.12)	2.01 (1.39, 2.92)	1.30 (1.09, 1.56)
P-value for interaction	0.1629	0.0018	<0.0001
Multiple partners living with HIV			
≤1 of any HIV status	1.42 (0.52, 3.91)	3.59 (2.72, 4.76)	2.04 (1.75, 2.38)
2+ but not living with HIV	1.57 (0.44, 5.57)	2.35 (1.46, 3.78)	1.13 (1.05, 1.67)
2+ living with HIV	5.38 (1.51, 19.12)	1.91 (1.09, 3.35)	1.14 (0.97, 1.61)
P-value for interaction (a)	0.0495	0.0264	<0.0001
Multiple HIV-negative / unknown status partners			
≤1 of any HIV status	1.51 (0.54, 4.20)	3.61 (2.73, 4.77)	2.06 (1.77, 2.40)
2+ but not HIV-negative/unknown status	5.13 (1.44, 18.33)	2.33 (1.34, 4.05)	1.35 (1.05, 1.73)
2+ HIV-negative/unknown status	2.77 (0.77, 0.96)	1.97 (1.22, 3.19)	1.27 (1.00, 1.61)
P-value for interaction (a)	0.3686	0.0117	<0.0001

CI, confidence interval. Reference = control periods.
(a) P-value contrast is between 2+ living with HIV (or HIV-negative/unknown status) versus ≤1.

Conclusions

Among all men under follow-up, routine syphilis screening produced an 83% increase in early case detection that was non-statistically significant. But among men with two or more sex partners (who would have been more likely to have had sexual exposure to syphilis), early case detection tripled. Although the magnitude of increases in screening coverage and frequency were less among men with multiple partners compared to men without, there was still improvement compared to usual care. Altogether, these findings support the implementation of routine syphilis screening for men living with HIV.

Acknowledgements

We gratefully acknowledge the participation of the clinicians and support staff at the participating HIV clinics, Public Health Ontario, and the Ontario HIV Treatment Network (OHTN). We also thank the people living with HIV who organized to create the OCS, contribute to its data, support the governance of data, and guide the research process; and members of the Governance and Scientific Steering Committees.

The ESSAHM Trial was supported by the Canadian Institutes of Health Research (CIHR, operating grant MOP 130440 and Foundation Award to ANB) and by the CIHR Canadian HIV Trials Network (CTN-275). The OCS is supported by the Ontario Ministry of Health. During the trial, ANB received support from a CIHR New Investigator Salary Award, OHTN Endgame Leader award, and a Non-Clinician Scientist award from the Department of Family and Community Medicine, Faculty of Medicine, University of Toronto. DHST and SM were supported by OHTN and CIHR New Investigator Awards. ANB, DHST and SM are Canada Research Chairs (Tier 2). PM, SW, and JR were supported by OHTN Chair Awards. PM was supported by a University of Ottawa Department of Medicine Research Award.