

Risk factors for first and subsequent syphilis diagnoses among HIV-positive gay and other men who have sex with men in Ontario

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HIV and STIs

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CHANGING THE COURSE OF THE
HIV PREVENTION, ENGAGEMENT AND
TREATMENT CASCADE



OHTN 2013
RESEARCH
CONFERENCE

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OCS
OHTN COHORT STUDY

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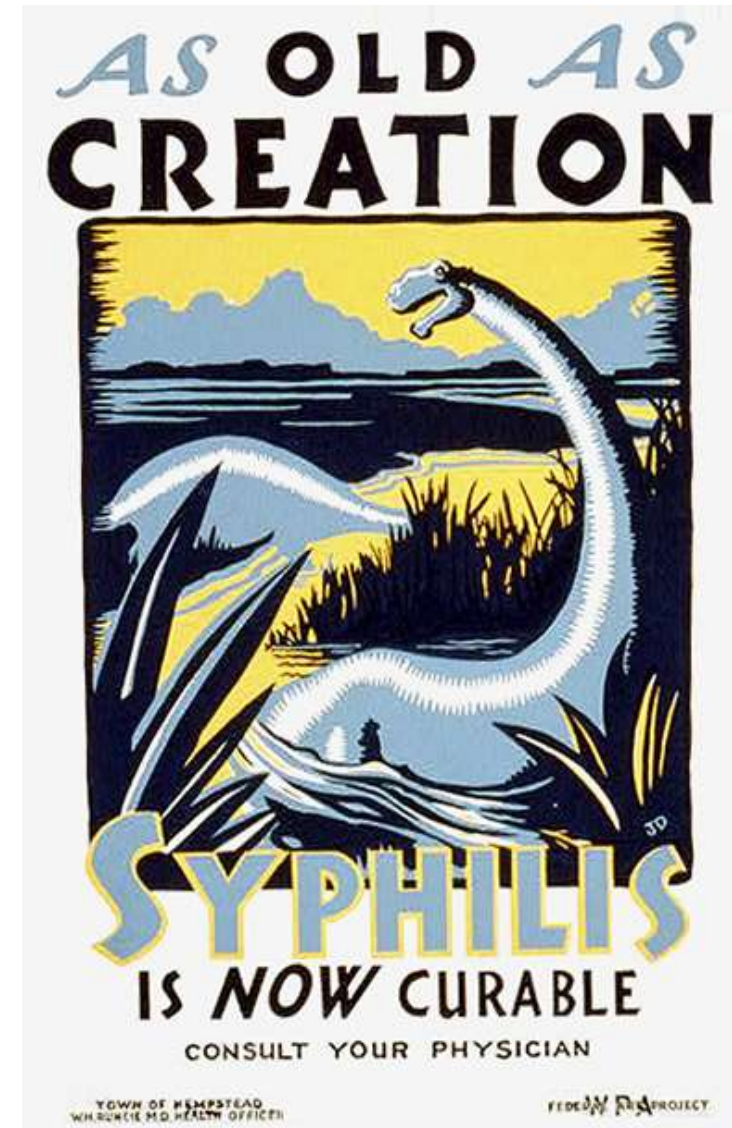


1) Ontario HIV Treatment Network; 2) University of Toronto; 3) Public Health Ontario;
4) St. Michael's Hospital, Toronto; 5) Ontario Ministry of Health and Long Term Care;
6) University Health Network, Toronto.

Re-emergence of syphilis

- Syphilis has re-emerged as a significant infection among gay and other men who have sex with men (MSM) [1]
- In Ontario, most reported cases of infectious syphilis in Toronto and Ottawa
- Concurrent HIV infection present in 42-47% of cases → over-represented in syphilis transmission networks [2]
- For men co-infected with HIV [3-5]
 - response to syphilis treatment can be suboptimal
 - development of neurosyphilis may be accelerated
 - treatment decisions can be more complex
 - HIV infectiousness may be enhanced

1. Public Health Agency of Canada: *Canadian Guidelines on Sexually Transmitted Infections*. 2010
2. Public Health Ontario. *Monthly Infectious Diseases Surveillance Report*. 2013; 2(6)
3. Tan et al. *Can J Inf Dis Med Microbiol* 2011, 22(Suppl SB):19B.
4. Rompalo et al. *Sex Transm Dis* 2001, 28:158–65.
5. Rebbapragada et al. *Drug Discov Today* 2007, 4(4):237–46.



Objective

To identify risk factors for first and subsequent syphilis diagnoses among HIV-positive MSM in Ontario



OHTN Cohort Study (OCS) Design

- Ongoing observational, open dynamic cohort of HIV-positive persons in care in Ontario
 - HIV Ontario Observational Database (1994-1999)
 - HIV Infrastructure Information Program (2000-2006)
 - Renamed OCS in 2007
- Over 6,100 participants recruited from specialized HIV clinics & primary care practices throughout Ontario
- Data from medical charts (manual abstraction or clinical management systems) & face-to-face interviews
- Record linkage with **Public Health Ontario Laboratories** → conduct all syphilis serologic testing in province



Analysis

5,933 participants enrolled as of December 2011

3,987 followed-up in 2006-10

2,775 MSM

2,271 with 1+ syphilis test in 2006-10

- Analysis restricted to MSM under follow-up from 2006 to 2010 who had at least one syphilis test during that period
- Incidence first syphilis diagnosis
 - Negative syphilis serology → reactive syphilis serology
- Incidence syphilis re-diagnosis
 - Previously reactive serology → 4-fold rise in RPR titre
- Excluded years up to and including HIV diagnosis
- Poisson regression to calculate incidence densities and rate ratios with 95% confidence intervals with GEE framework to account for recurrent events



Characteristics of MSM included in analyses of first diagnosis and re-diagnosis of syphilis

	In analysis of first diagnosis (n=1799)	In analysis of re-diagnosis (n=586)	In combined analysis (n=2271)
Sum person-years of follow-up	5798	1808	7275
Mean age at baseline* (SD)	45 (9)	47 (11)	46 (10)
Toronto	68%	81%	70%
Ottawa	11%	8%	11%
Other region of Ontario	21%	11%	19%
White race/ethnicity	73%	72%	73%
Median year HIV diagnosis (IQR)	1997 (91-03)	1997 (91-03)	1996 (91-03)
Initiated ART <2006	71%	66%	71%
Initiated ART in 2006-10	23%	25%	23%
ART-naïve as of last follow-up	6%	9%	6%
Mean CD4 at baseline* (SD)	497 (262)	491 (252)	497 (262)
Undetectable HIV viral load at baseline*	65%	62%	65%

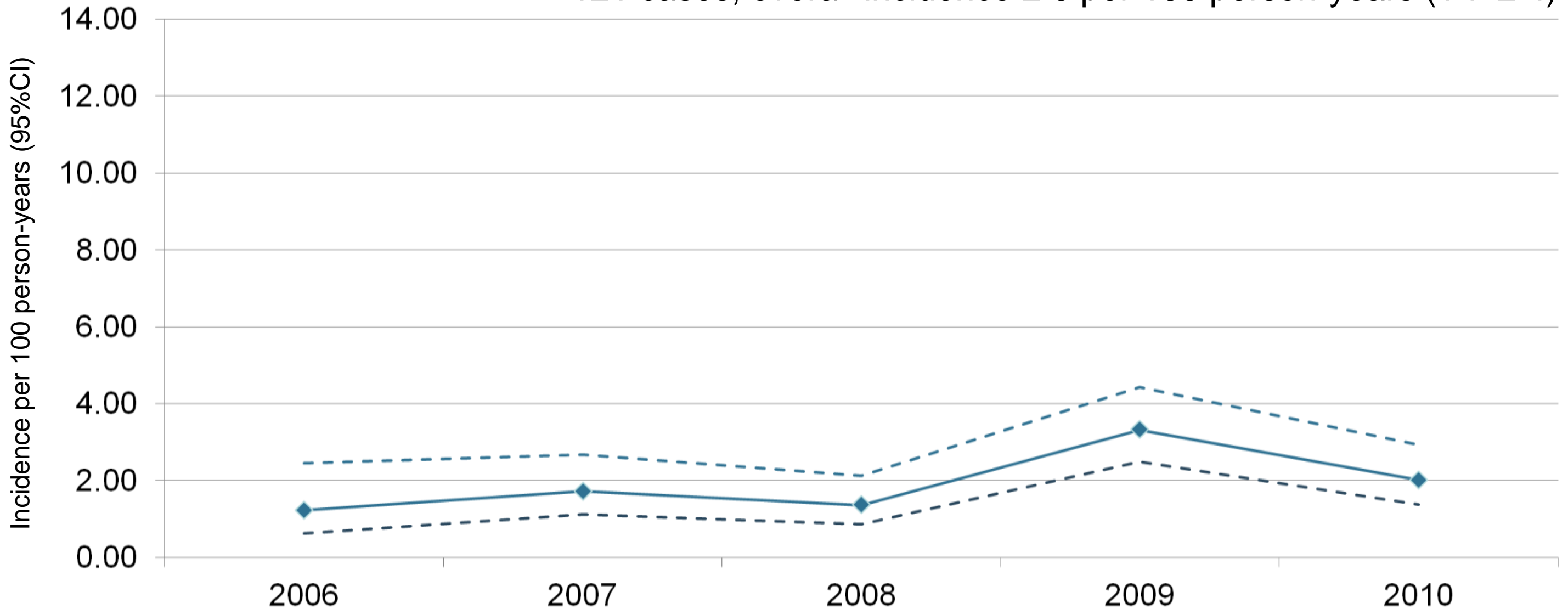
* Baseline = later of cohort enrolment date, year after HIV diagnosis, or January 1, 2006

ART, HIV antiretroviral treatment



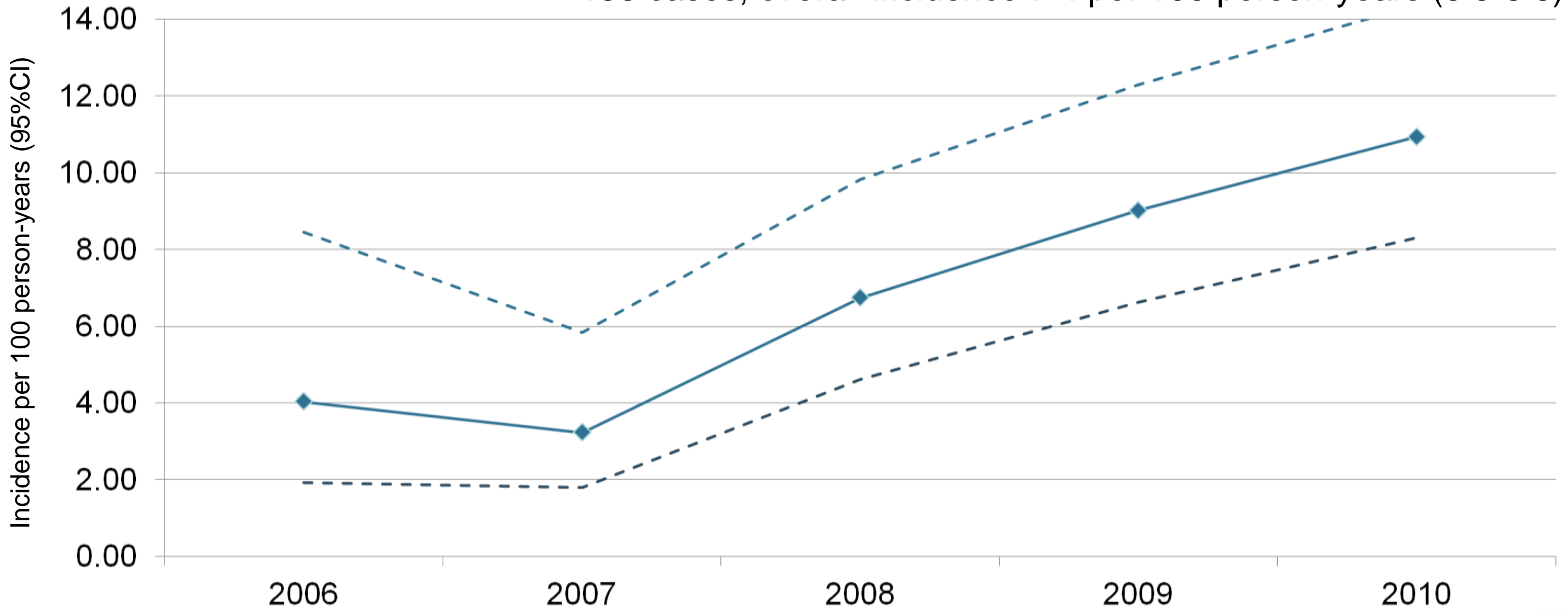
Incidence of **first syphilis diagnosis** among HIV+ MSM with previous negative serology

121 cases, overall incidence 2.0 per 100 person-years (1.7-2.4)



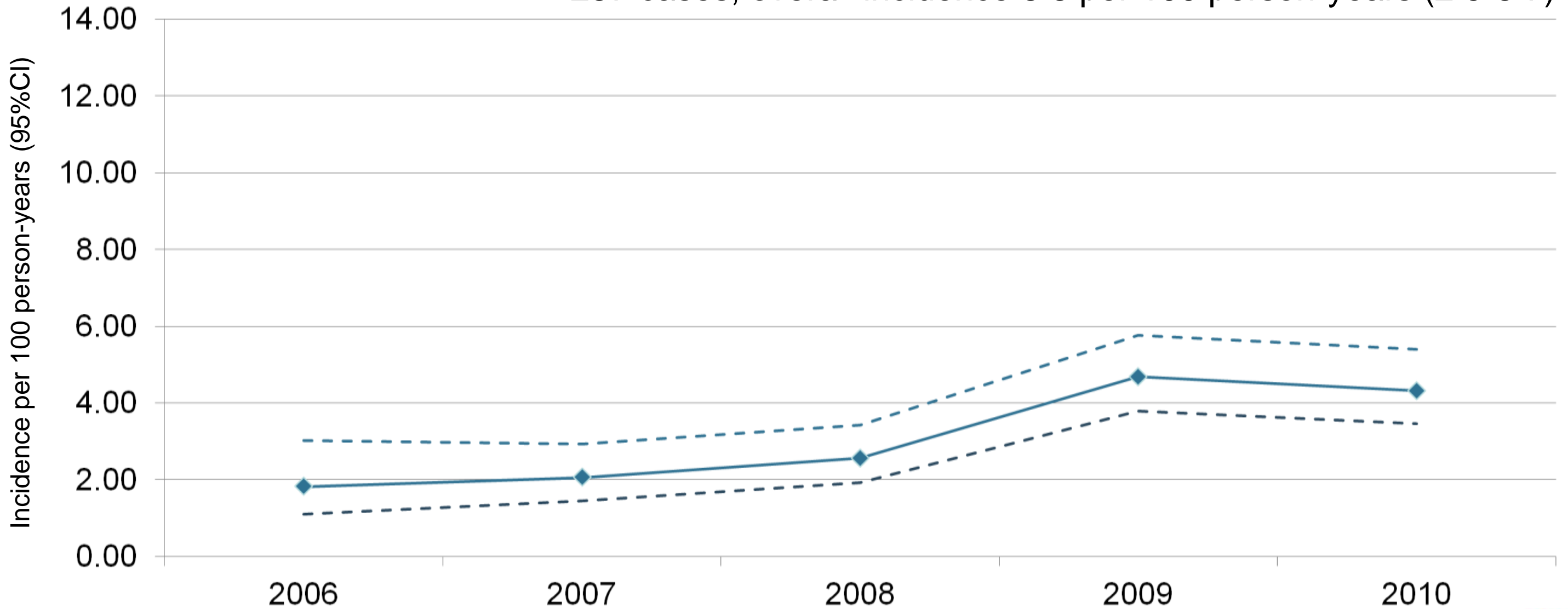
Incidence of **syphilis re-diagnosis** among HIV+ MSM with previous reactive serology

136 cases, overall incidence 7.4 per 100 person-years (6.3-8.8)



Total incidence of syphilis diagnoses among HIV+ MSM, **combined first and re-diagnoses**

257 cases, overall incidence 3.3 per 100 person-years (2.9-3.7)



Independent risk factors for syphilis diagnosis

Risk factor	Adjusted Rate Ratio (95%CI)
Calendar year (1-unit increase)	1.2 (1.1, 1.4)
Aged <30 versus 50+ years	3.4 (2.0, 5.8)
Aged 30-49 versus 50+ years	1.6 (1.2, 2.3)
Toronto versus other Ontario	5.7 (2.6, 13)
Ottawa versus other Ontario	3.1 (1.1, 8.4)
Past syphilis diagnosis (time-updated)	4.9 (3.6, 6.8)
Detectable viral load (time-updated)	1.4 (1.1, 1.8)

No evidence that risk factors differ for first versus subsequent syphilis diagnoses

Poisson regression with generalized estimating equations to account for repeated syphilis diagnoses events

Adjusted for all variables shown

No evidence of independent effects of race/ethnicity, CD4 cell count, ART, or hepatitis B or C co-infection

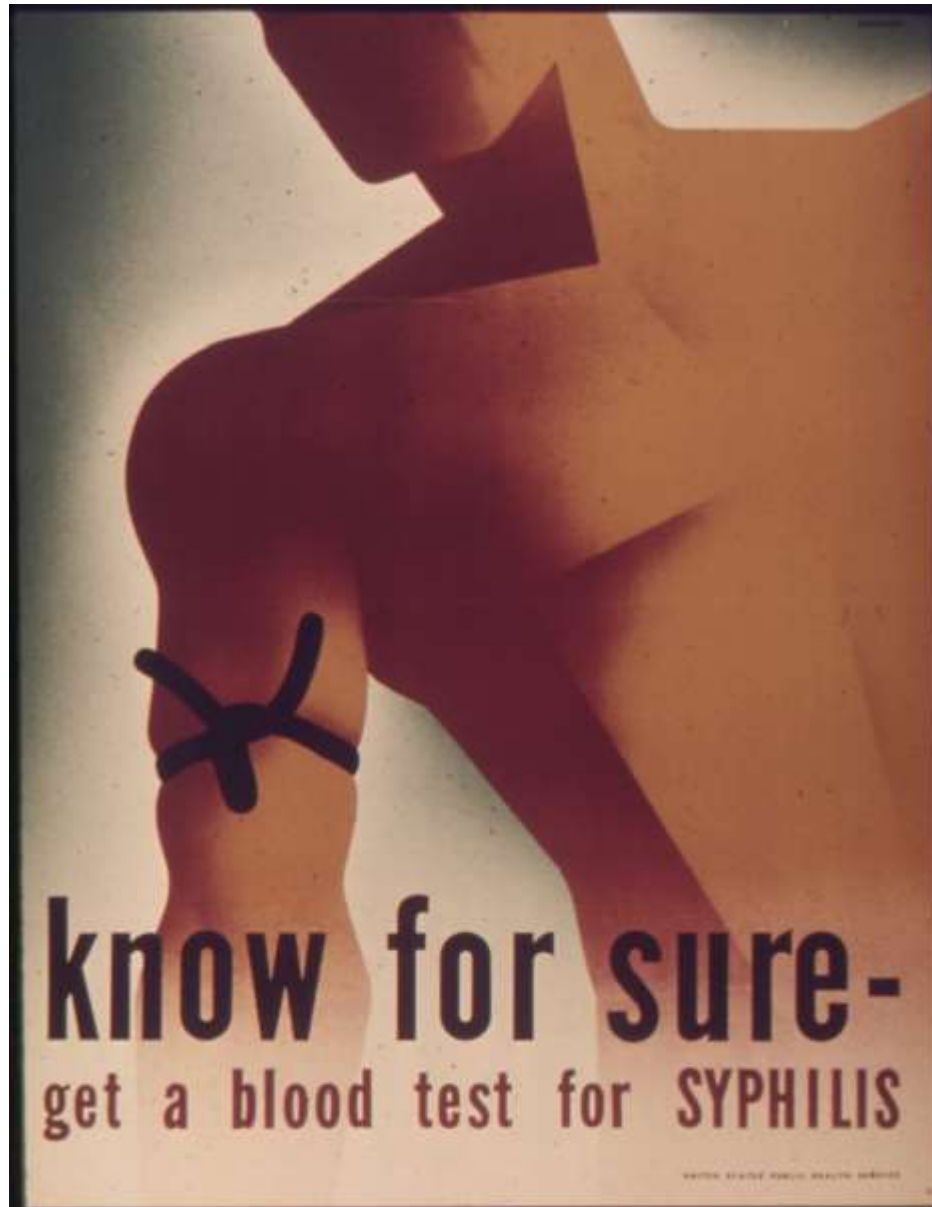


Extremely high rates of syphilis co-infection

- Incidence 350 times greater than in general male population in Ontario [1]
 - 2010 general male population: 0.011 per 100PY
 - 2010 HIV+ MSM: 3.3 per 100PY
- Rates highest among younger men and in Toronto and Ottawa
- Men with previous syphilis diagnosis nearly 5 times more likely to have subsequent new syphilis diagnosis
 - Cannot rule out possibility of treatment failure but our definition of re-diagnosis (4-fold rise in RPR titre) would be consistent with re-infection
 - Suggests repeated & ongoing syphilis transmission within core group of high-risk men



Implications for Policy and Practice



- Novel syphilis control efforts needed
- Previously reported syphilis testing rates among HIV-positive MSM in our cohort considerably below international guidelines
 - Only 55% undergoing screening at least annually as of 2009 [1]
 - Little improvement as of 2012 (only 61% tested annually)
- Exploring potential strategies to improve timely detection & treatment of syphilis among MSM with HIV, including implementation of routine syphilis testing with HIV labs
- Future analysis will include examination of sexual behaviours & subsequent syphilis risk in 2011 onwards

1. Burchell AN, Allen VG, Moravan V et al. *BMC Inf Dis* 2013; 13:246.



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