Enhancing diagnostic data for HIV surveillance: The Laboratory Enhancement Study

Robert S Remis, Carol Swantee, Maraki Fikre Merid, Robert WH Palmer, Margaret Fearon, Mark Fisher, Elaine Whittingham and Carol Major
Department of Public Health Sciences, University of Toronto. HIV Laboratory, Laboratories Branch, Ontario Ministry of Health and Long-Term Care

Introduction

- Serodiagnostic data useful for HIV surveillance
- Less sensitive ("detuned" or STAHRS) assay of HIV-positive specimens identifies persons who were recently infected (e.g.< 4 months)
- Can also calculate HIV incidence density, a critical indicator usually difficult to measure

Study objectives

- To estimate HIV incidence density among persons undergoing HIV testing according to exposure category and region of test
- To monitor trends in HIV incidence density among specific populations particularly affected by the HIV epidemic

Data collection and management

- Questionnaire sent with all new HIV diagnoses and 1:200 sample of HIV-negative results
- Data collected on risk factors for HIV infection and HIV test history
- Questionnaire returned by mail, fax or telephone interview
- Data entered in Microsoft Access

Laboratory methods

- EIA assay modified as follows:
  - serum diluted to 1: 20,000
  - incubation period reduced to 30 minutes
  - cut-off value increased
- Abbott 3A11 EIA kit from until October 2000
- From October 2000, used Vironostika assay (Bio-Merieux) allowing for different "window period" at different cut-off (70-336 days)

Data analysis, basic

- Calculated questionnaire completion rate using Kaplan-Meier survival analysis
- Modeled exposure category distribution assuming proportions of cases without data same those without data on lab requisition but with data from questionnaire
- Calculated incidence density initially using formula from original publication on STARHS (Janssen et al, JAMA 1998)

Data analysis, adjustment

- Developed analytic approach to adjust crude estimates using formula which incorporates positive testing bias (Remis et al, 14th ICA 2002)
- Calculated incidence at five values of "window period" and fit to modeled incidence density using formula incorporating P_{sce} (proportion testing "prematurely") and I_{true} (true incidence density).
- Developed software with goodness-of-fit to identify values of P_{sce} and I_{true} which minimised sum of the squares of "residuals" observed versus expected

Study questionnaires mailed and returned, Oct 1999-Dec 2003

	Questionnaires			Kaplan-Meier returned by	
	Mailed	Returned	Proportion	4 mon.	8 mon.
HIV-positive	4,465	2,982	67%	73%	78%
HIV-negative	4,315	3,079	71%	73%	78%
Total	8,780	6,061	69%		

Exposure category classification according to HIV test requisition, returned questionnaires and modelled distribution, HIV-positives

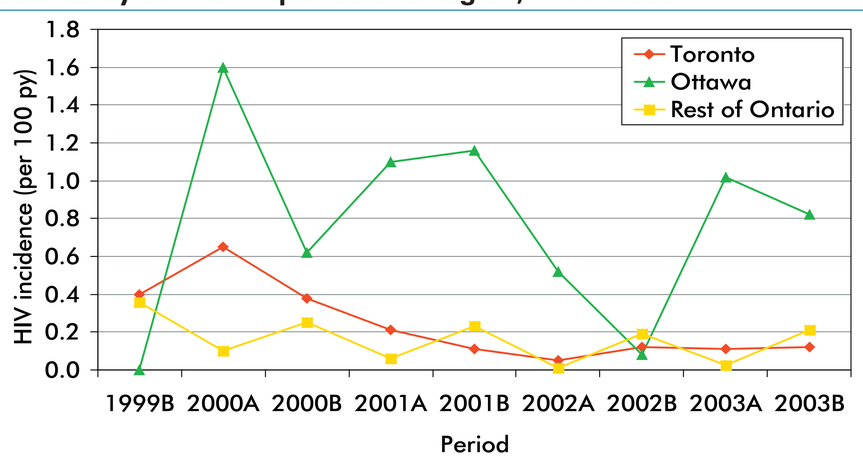
	HIV test requisition		Returned questionnaires among NIR		Projected final distribution	
MSM	**1,097**	**54%**	**545**	**38%**	**2,027**	**45%**
MSM-IDU	32	2%	45	3%	109	2%
IDU	188	9%	97	7%	353	2%
Endemic	**170**	**8%**	**379**	**27%**	**816**	**8%**
HR Hetero	122	6%	67	5%	236	18%
LR Hetero	398	19%	230	16%	790	5%
Other	38	1%	34	2%	76	18%
NIR	2,049					2%
Total	4,471			100%	4,471	100%
% NIR		54%				

HIV incidence (per 100 person-years) for selected exposure categories by health region

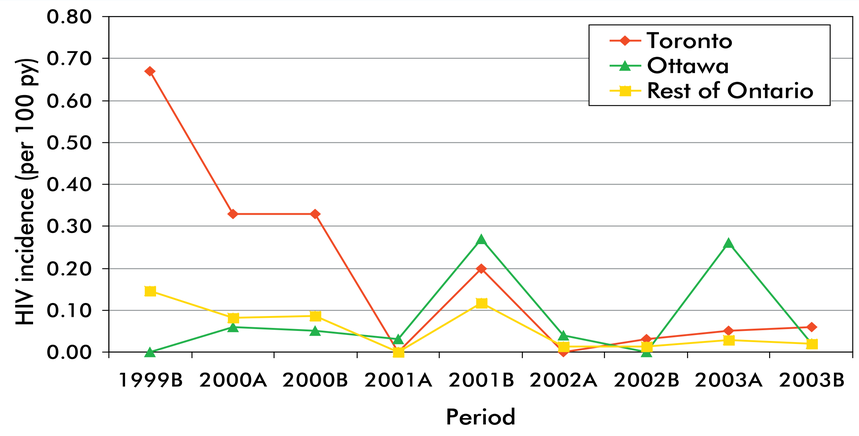
	Toronto		Ottawa		Rest of Ontario		Overall	
	Tested	Incidence	Tested	Incidence	Tested	Incidence	Tested	Incidence
MSM	30,838	2.8	7,005	1.9	16,147	0.89	53,990	2.1
MSM-IDU	526	6.2	106	15.7	1,740	0.27	2,371	2.3
IDU	19,118	0.23	5,165	0.82	38,046	0.14	62,329	0.22
HR Hetero	19,971	0.14	5,096	0.087	29,742	0.049	54,809	0.087
LR Hetero	363,871	0.021	95,649	0.018	435,224	0.010	894,744	0.016

MSM: HIV incidence by six-month period and region, 1999-2003

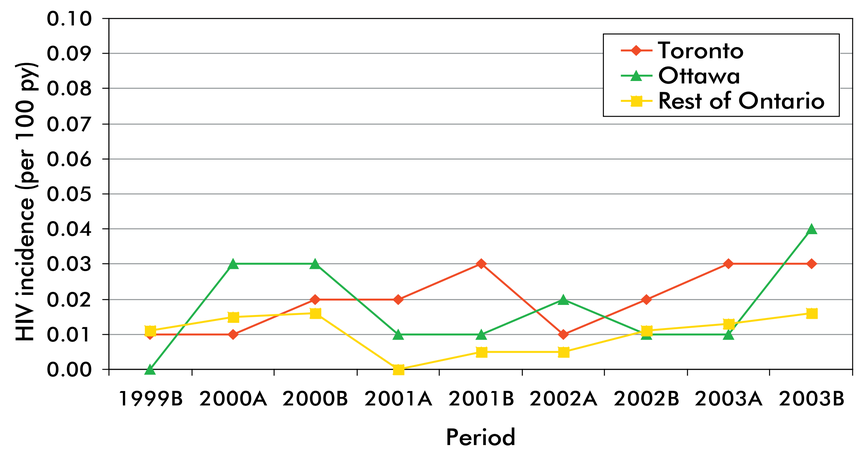
IDU: HIV incidence by six-month period and region, 1999-2003



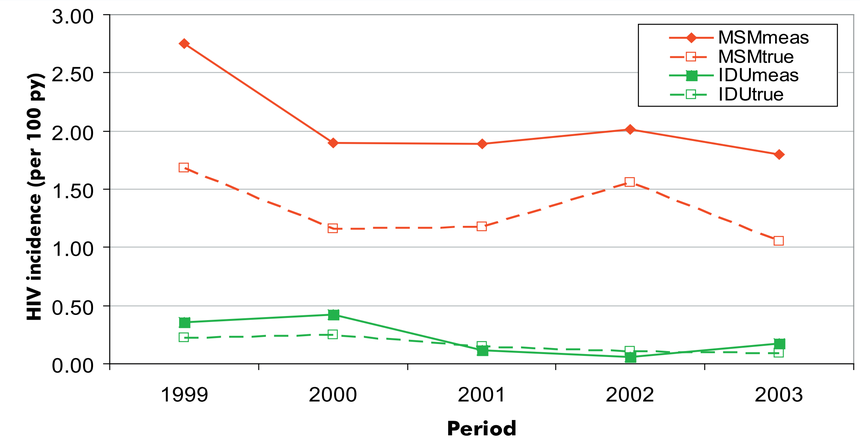
High risk heterosexual: HIV incidence by six-month period and region, 1999-2003



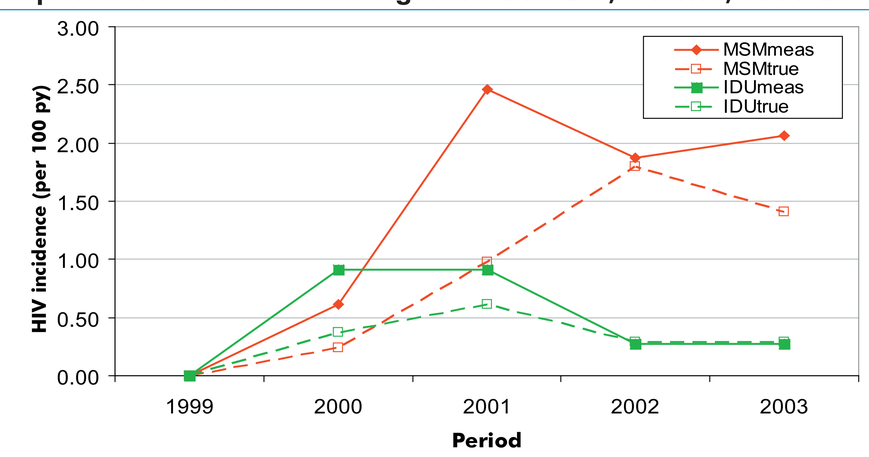
Low risk heterosexual: HIV incidence by six-month period and region, 1999-2003



Crude and adjusted HIV incidence among MSM and IDU, Toronto, 1999-2003



Crude and adjusted HIV incidence among MSM and IDU, Ottawa, 1999-2003



Study limitations

- Discordant samples and HIV tests by exposure category modeled
- Persons who test may not be representative of entire population at risk
- Persons who become infected may test sooner; thus, calculated HIV incidence likely higher (2-3 fold) than true incidence
- However, these estimates were adjusted as described above

Summary of findings – Trends in HIV incidence

MSM

- Toronto: no evidence of increasing HIV incidence despite syphilis outbreak
- Ottawa: increased incidence
- Elsewhere: stable at lower level

IDU

- Ottawa: incidence highest in Ontario
- Elsewhere: sustained low rate is reassuring

Conclusions

- HIV serodiagnostic program extremely useful for HIV surveillance
- Due to important problems in missing and unrepresentative data on risk factors and HIV test history, standard laboratory data must be enhanced on an ongoing basis
- Despite limitations, detuned assay provides critical information on HIV incidence
- Calculated incidence density can be adjusted to eliminate testing bias
- Adjustment yields values as low as 50% of crude values
- Bias appears to vary across exposure category, region and over time
- Adjusted values more useful for evaluation and modeling

Acknowledgements

At the HIV Laboratory:

- Lisa Santangelo and Cindi Farina, data collection
- Lynda Healey, detuned assay
- Elaine McFarlane, data entry screens
- Len Neglia, mailing of questionnaires

• Neil Hershfield,developed custom software to adjust incidence densities
• Regional public health laboratories, mailing of negative questionnaires
• Physicians who prescribe HIV testing and provided supplementary data for LES

Project funding

• Ontario HIV Treatment Network and the
• Centre for Infectious Disease Prevention and Control, Health Canada