CATIE

Canada's source for HIV and hepatitis C information

La source canadienne de renseignements sur le VIH et l'hépatite C

Reaching the Undiagnosed Webinar Series

New testing technologies and approaches for syphilis – learning from other countries

Please make sure you access the audio portion:
Toll-free access number: 1-866-500-7712
Access code: 4949626

The webinar will commence shortly.

All participants will be muted until the question period.

Webinar Series 2017-2018

Reaching the Undiagnosed

Innovative approaches for HIV, HCV and other Sexually Transmitted Infection (STIs) Testing

Presented by:

CATIE Canada's source for HIV and hepatitis C information

National Collaborating Centre for Infectious Diseases

Centre de collaboration nationale des maladies infectieuses

REACH 2.0

HIV, HVC and STIs: why is this a global issue?

- **357.4 million new STIs** (CT, NG, Syphilis, TV) in 2012.
  - Pelvic inflammatory diseases, ectopic pregnancy, infertility, chronic pelvic pain, seronegative arthropathy, neurological and cardiovascular diseases, neonatal death.
- **71 million with chronic hepatitis C infection** in 2015
  - 1.7 millions new infections
  - 2.3 million HIV/HCV co-infected
  - 704,000 deaths attributed to HCV in 2013
- **1.8 million new HIV** in 2016
  - 36.7 million people living with HIV in 2016.
  - 53% accessing antiretroviral therapy in 2016.
  - 1 million died from AIDS-related illnesses in 2016.
- Adverse health consequences on individuals and substantial strain on health systems and budgets – important to intervene at early stages

UNAIDS, WHO, Lancet Infectious Diseases Commission

HIV, HCV and STIs: why is this a national issue?

- **118,280 new STIs** (87% CT, NG, Syphilis) in 2012
  - On the rise (2005-2014)↑ **49%** CT; ↑ **61%** NG, ↑ **95%** infectious syphilis
  - 25 to 50% co-infection with HIV
- **Up to 245,987 with chronic hepatitis C infection** in 2011
- **2,570 new HIV infections** in 2014
  - 65,040 Canadians were living with HIV in 2014 .
- **Important inequality** in health and economic burden, for women, for First Nations and Inuit, for the chronically poor

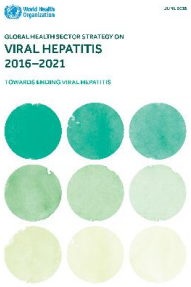
Public Health Agency of Canada, CATIE, CCDR January 2017

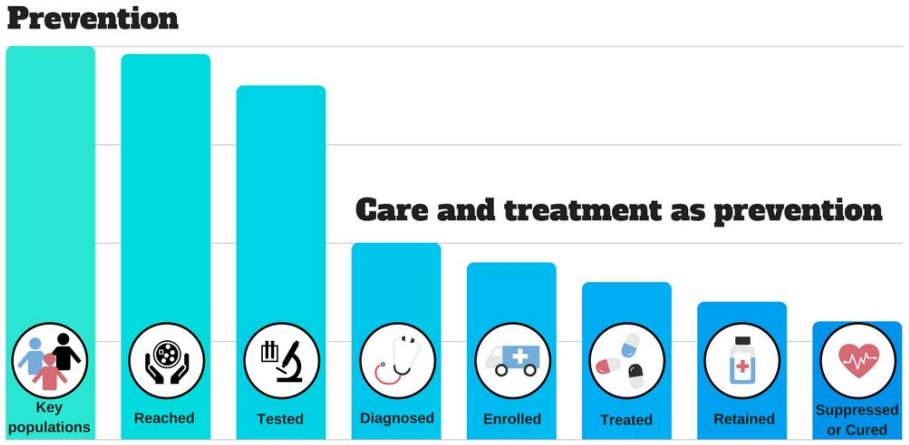
HIV, HCV and STIs: Towards elimination by 2030

Global vision

Country strategies

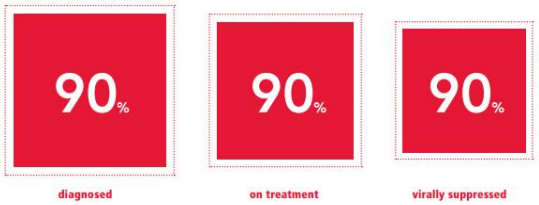
Local actions





Global Targets : How are we doing in Canada?

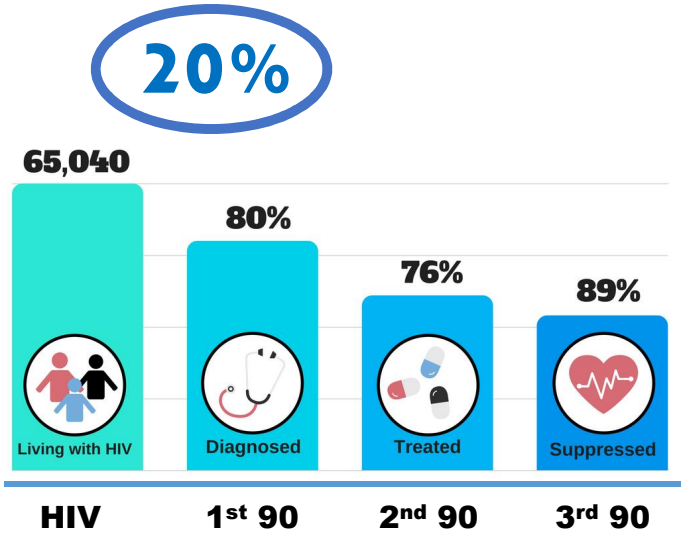
By 2020

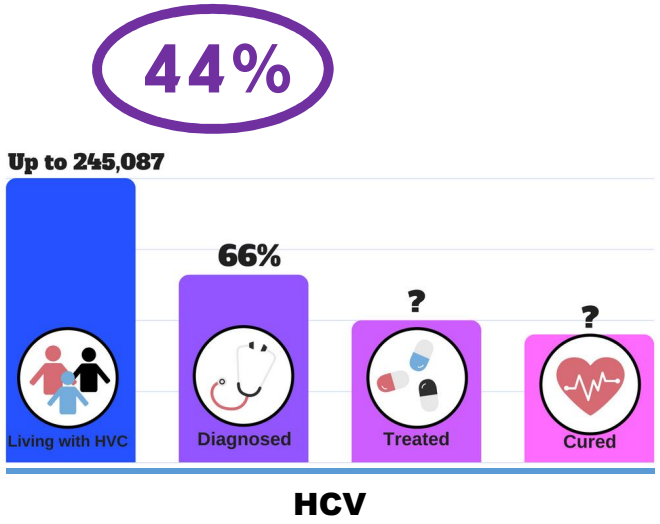


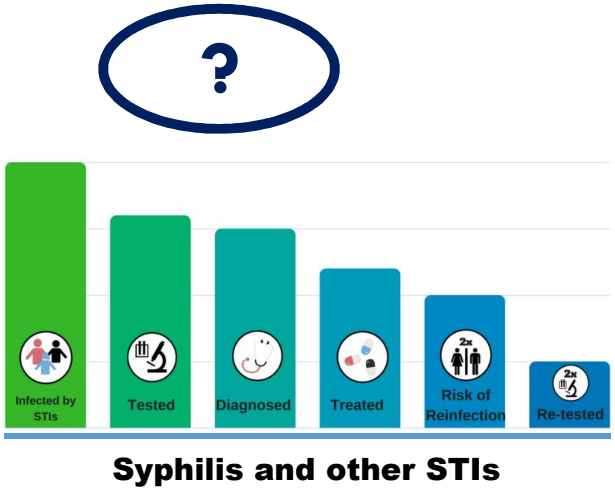
Reducing by 30% new chronic HCV infections

Reducing HCV mortality by 10%

T. Pallidum with the elimination of congenital syphilis, which implies that **strong systems** are in place to ensure **screening and treatment** of all pregnant women and control of syphilis in **specific populations**.







Public Health Agency of Canada

No one-size-fits-all model for testing

Reaching the right people, at the right time, at the right place, with the most effective programs

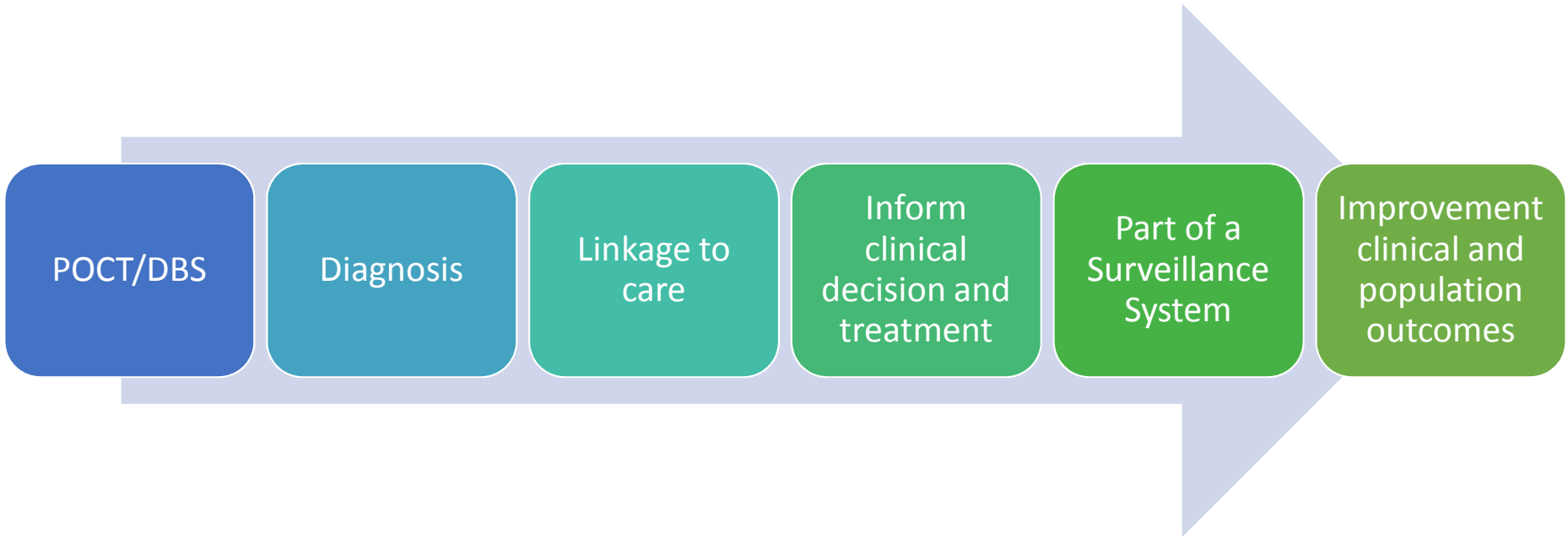
POCT with lay testers integrated in community program

DBS in remote communities

POCT Duo Test in Gay men's Clinic

Self-testing at home

Policy decisions matter more than individual behaviours….



About this series….

- To explore new ways to reach the undiagnosed.
  - Focus on what has been done in Canada, and could be scaled-up for the benefits of all Canadians.
  - Create a space to understand and discuss barriers and opportunities for the scale-up of these new approaches, recognizing specificities and difference in contexts that exist in this country.

- Webinar #1
  - POCT in non-traditional settings in Canada
- Webinar #2
  - POC HIV/syphilis multiplex – what can we learn from other countries?
  - Reflect on the acceleration of these technologies into Canada standard practice and public health strategy

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How to Diversify HIV and Syphilis Testing in Canada to Better Reach the Undiagnosed

Rick Galli

Content:

- Background on HIV and Syphilis testing landscape
- Opportunities for expanding POCT through use of RDT's
- How practitioners and decision makers can help accelerate integration of POCT into standard practice
- Regulatory barriers in introducing new technologies
- New tools in the box:
  - HIV/syphilis Multiplex POC
  - HIV self testing
- "Non-traditional" testing pilots

Some Quick Facts…

- After more than 30 years of widespread laboratory testing, 1 in 5 Canadians living with HIV are still unaware of their infection
- Canada is falling behind the rest of the world in reaching UNAIDS 90-90-90 objectives for elimination of HIV, particularly in the first 90 (testing)
- After a steady decrease for more than a decade, syphilis is on the rise:
  - Large cities with well-established MSM populations have been the most affected by this rise*
  - Given that there are well-established epidemics of HIV infection among MSM from large metropolitan areas, an increasing number of cases of concurrent syphilis and HIV infection were being reported.*

  *(Dr. Jeffrey D. Klausner, UCLA and STD Prevention and Control Services, San Francisco Dept. of Public Health, 1360 Mission St., Ste. 401, San Francisco, CA 94103)
  - Currently no POC syphilis or HIV/syphilis multiplex tests licensed in Canada
  - Oraquick HCV POC test licensed in Canada in January 2017: 44% of HCV-infected remain undiagnosed.

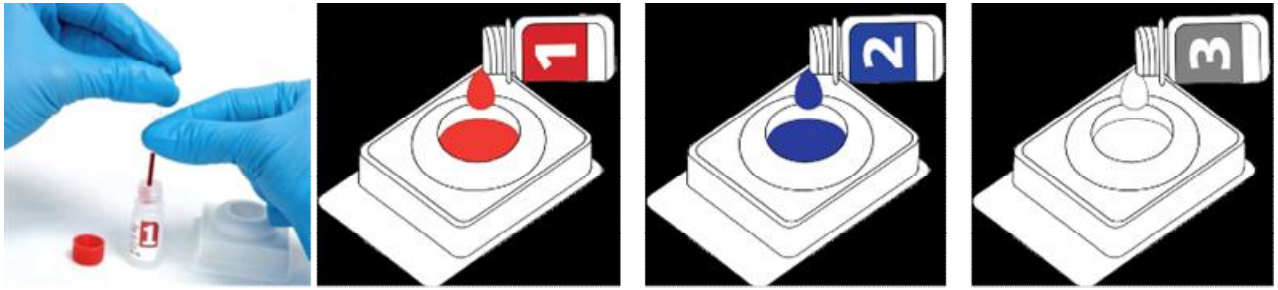
HIV POC Testing has been available in Canada since 2006

- Facts

- Only one product currently approved for POC testing: INSTI, with results available in 60 seconds
- Health Canada approved since 2006 (with additional approvals by US FDA, CE, and WHO prequalification)
- In use across Canada **except** for Atlantic Canada.

Simple Procedure – facilitates the testing experience

Sample, Pour, Interpret immediately



*All sample collection materials provided (lancet, pipet and alcohol swab.)

HIV POC Testing in Canada – the "Pilot Period"

- **BC Pilot Launched April 2011**: Even though only 5% of HIV tests in the province were POC tests, over 30% of new HIV diagnoses were first detected using POC HIV testing in BC during the evaluation period. (*S. Fielden BCCDC: Evaluation Findings from the Pilot Phase of BC's Provincial Point of Care HIV testing Program: The First 18 Months*)

- **Ontario 2007-2011:** The POC program attracts more high risk clients than the routine testing program (32% vs 16%) and the positivity rates are 3 times higher (0.64% vs 0.22%). Test performance has been excellent to date. (*F. McGee, CDC Conference on HIV Diagnostic Testing, Atlanta GA, December, 2012*)

- **Alberta: 2007 – 2009**: 1708 individuals were tested: 875 (50.3%) tests in pregnant women, 730 (42%) in source individuals in blood and body fluid exposures and 119 (5.8%) in acutely ill persons. Twenty-five (1.4%) samples were reactive by rapid HIV testing, of which 13 were reactive previously. Sensitivity of the rapid HIV test compared to standard HIV testing was 100%, specificity was 99.9%.(*B.E. Lee et al. / Rapid HIV tests in acute care settings in an area of low HIV prevalence in Canada. Journal of Virological Methods 172 (2011) 66–71)*

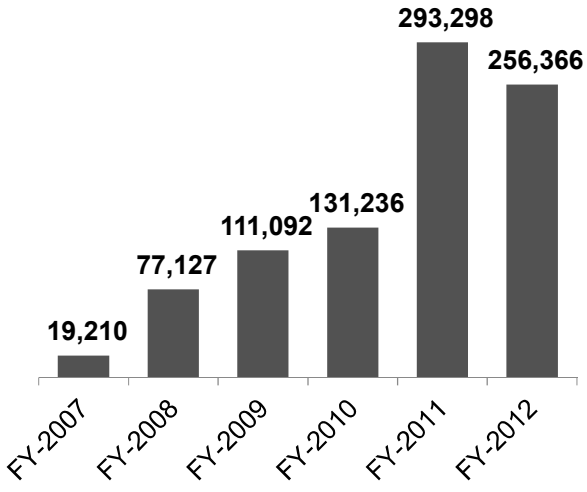
BC: Number of new HIV diagnoses by POC as compared to standard lab testing by Health Authority / Region, Apr 2011-Sept 2012

	Point of Care Testing			**Standard Laboratory Testing**			
	New Diagnosis	# Tests Done	Diagnosis Rate	New Diagnosis	# Tests Ordered	Diagnosis Rate	% New Diagnosis by POC
VCHA	118	15,982	**0.7%**	163	137,471	0.1%	**41.6**
NHA	6	358	**1.7%**	26	17,682	0.1%	**18.8**
FHA	2	324	0.6%	58	81,592	0.1%	3.3
VIHA	0	226	0.0%	26	31,675	0.1%	0.0
IHA	0	139	0.0%	18	34,288	0.1%	0.0
Total	126	**17,029**	**0.7%**	291	302,708	0.1%	**30.2**

INSTI™HIV Test Adoption History in Europe and Canada

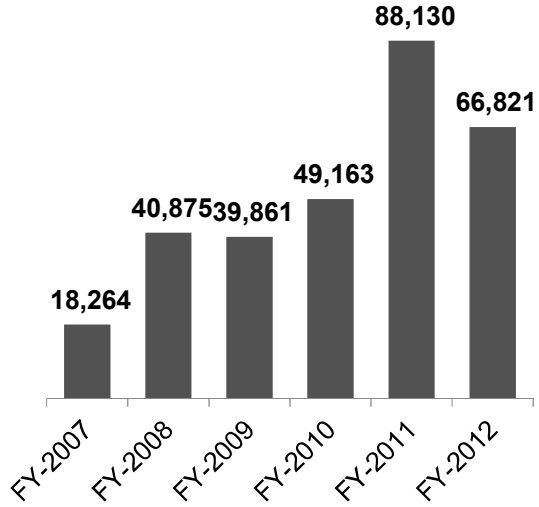
INSTI™ Units

1



2013: 356,901
2014: 451,879

1



2013: 78,815
2014: 80,401

US and Canadian POCT Trends

- Sample Data from US National HIV Prevention Inventory, 2012 Testing Survey Report (NASTAD):
  - In 2011, a total of 1,940,484 POC tests were conducted across 38 health departments
  - This accounts for **58 %** of all HIV tests conducted in health department supported programs

- In Canada:
  - In 2011, a total of 88,130 INSTI rapid test were distributed, and approximately 1,500,000 total HIV tests were conducted
  - This accounts for **5.9%** of all HIV tests conducted across Canada.
  - POCT in use in all provinces and territories except Atlantic Canada

So why is uptake in HIV POC testing in Canada so limited?

- **Potential Benefits – little argument??**
  - Ease of use
  - Faster results
  - More people receive results
  - Wider access to HIV testing
  - Immediate linkage to care
  - **Cost effectiveness** – single visit; "all in" costs are less than lab test model.
  - Widespread client and provider acceptance

- **Potential Harms – are they still??**
  - Risk of undermining consent
  - Pre-test counselling compression
  - Post test counselling – possible delivery of false positive results
  - **Cost effectiveness** – no reimbursement; third party funding? Limited global budgets.
  - Few POC method choices
  - Quality assurances
  - Loss of surveillance data

Source: Rapid HIV Testing in Canada, Canadian AIDS Society, 2007, 2011.

What can we do?

- CATIE, 2016: **NATIONAL DELIBERATIVE DIALOGUE ON REACHING THE HIV UNDIAGNOSED:**
  - SCALING UP EFFECTIVE PROGRAMMING APPROACHES TO HIV TESTING AND LINKAGE TO PREVENTION AND CARE www.catie.org
- **HIV Point-of-Care Testing (POCT) in Canada: Action Plan 2015-2020**
  - For more information please contact Dr. Jacqueline Gahagan, Professor of Health Promotion, Dalhousie University, 6230 South Street, Halifax, NS B3H 3J5 C ANADA. Tel: 902.494.1155 Email: jgahagan@dal.ca

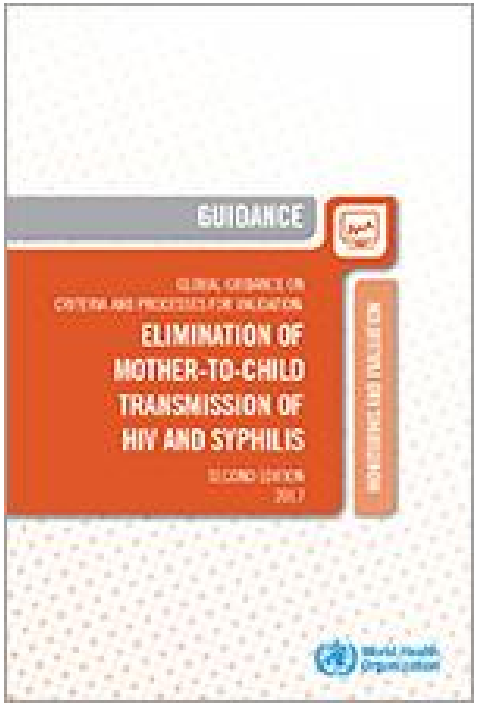
New tools, New Thinking….

- Multiplex
- HIV Self Testing
- Pharmacy Testing: APPROACH, Walgreens initiatives
- DBS: PHAC program (Dr. John Kim, John.Kim@phac-aspc.gc.ca)
- Health Canada guidelines on HIV POC and Self tests: opens the door for more HIV RDT devices to be licensed

INSTI HIV Self Test is based on the INSTI 60-Second HIV Platform

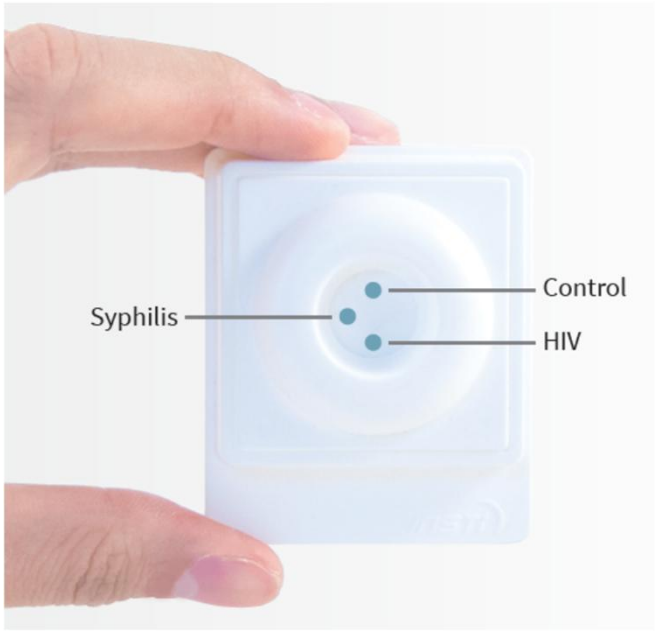
- Studies in sub-Saharan Africa with intended users show highly accurate results can be obtained by self testers from broad demographics: N=849
- Sensitivity: 239/242=98.76% (95%CI= 96.4-99.6)
- Specificity: 605/607=99.67% (95%CI= 98.8-99.9)
- 2017 WTP study in Kenya showed that 67% of participants preferred blood-based INSTI to oral-fluid self test.
- Canadian self test study protocol for multi-centre observed self test study approved by U. of T REB

Global STI Prevalence



As of October 2017, countries/territories validated for elimination of MTCT of HIV and syphilis, in order of validation are: Cuba, Thailand, Belarus, Armenia (HIV only), Republic of Moldova (syphilis only), Anguilla, Montserrat, Cayman Islands, Bermuda, Antigua and Barbuda, St Christopher and Nevis. (WHO)

INSTI Multiplex HIV-1 HIV-2 Syphilis Ab Test



CE Marked, sold in Europe: France, UK, Norway, Spain, Germany, Belgium, Estonia, Greece.

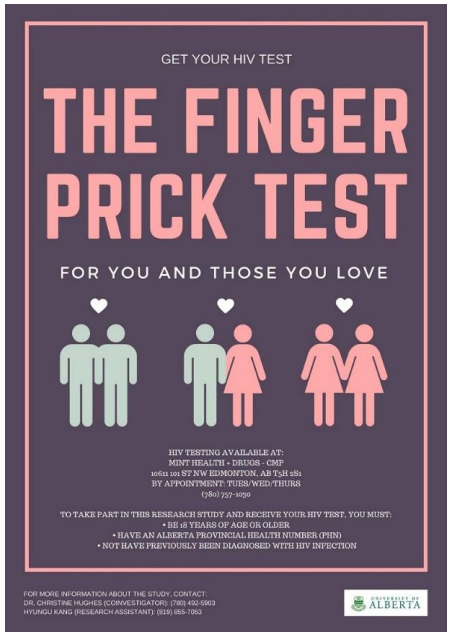
Sensitivity of Serological Tests in Untreated Syphilis

Test	Primary	Secondary	Latent	Tertiary
VDRL	78	100	95	71
RPR	86	100	98	73
FTA-Abs	84	100	100	96
TP-PA	76	100	97	94
EIA	93	100	100	ND
INSTI	**82.5**	**100**	**95.5**	**ND**

Syphilis antibody test sensitivities vary according to clinical stage of infection. Sensitivity in early primary cases can be <50%. The best sensitivity is expected in secondary syphilis, approaching 100%, with latent syphilis it is usually 90-100%.

HIV POC Testing in pharmacies

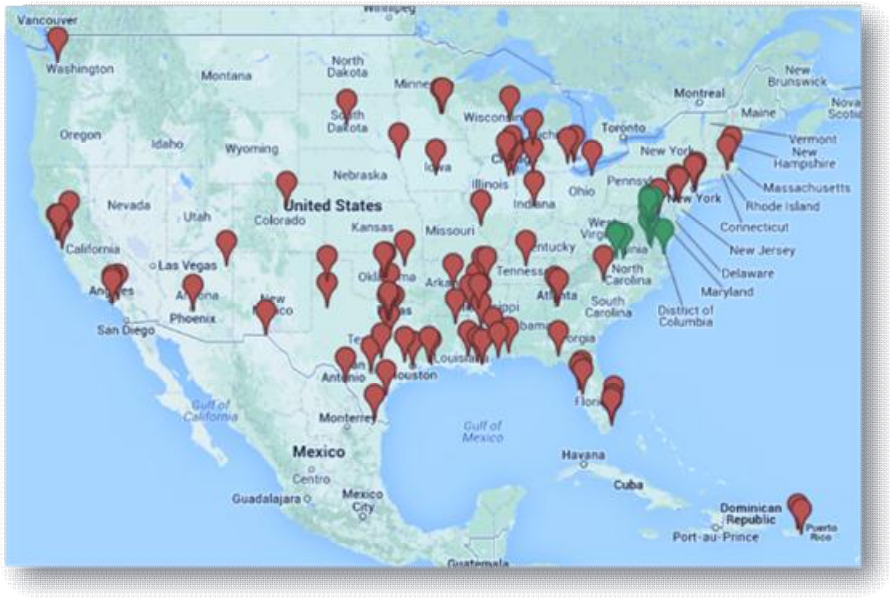
- APPROACH*



- ***Adaptation of POCT for Pharmacies to Reduce risk and Optimize Access to Care in HIV***
- Phase 1 completed 2017: typeII hybrid Implementation-Effectiveness design to create and assess the pharmacy-based HIV testing model.
- Phase 2 implementation science grant submitted.
- Dr. Debbie Kelly, Memorial University of Newfoundland, dvkelly@mun.ca

Walgreens Pharmacy Testing in US

"A Stigma- Free setting"



- Free INSTI POC Pilot in 13 pharmacies in Virginia, in partnership with State public health 2015
- Highly successful in attracting first-time testers, finding the previously undiagnosed
- Success resulted in expansion into 33 pharmacies
- Dec 2017, added oral fluid HIV self testing

POC Testing in Dental Clinics?

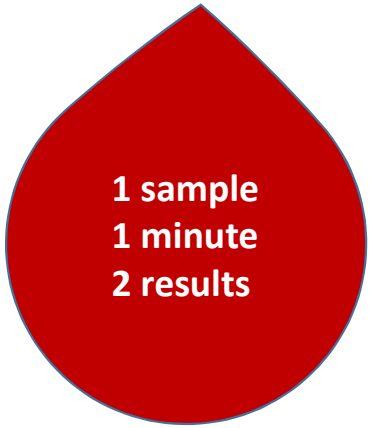
Mar 08 – Dec 09: 3565 HIV POC tests at Harlem Hospital's onsite outpatient dental clinic:

Of the 19 confirmed positive:
- 15 linked to care
- 9 had either ER, GP or Dental Clinic in the past year but no HIV test was offered.
- 6 met criteria for AIDS

1. Pollack HA et al. Dental. Examinations as an Untapped Opportunity to Provide HIV Testing for High Risk Individuals. Am J of Public Health Jan2010.
2. Greenberg et al. Dentists' Attitudes Towards Chairside Screening of Medical Conditions. JADA Jan 2010.
3. Blackstock et al. Evaluation of a Rapid HIV Testing Initiative in an Urban, Hospital-Based Dental Clinic. AIDS Patient Care and STDs 2010.

Advantages of Testing for HIV & Syphilis concurrently

- 1 minute results possible
- More patients treated
- Reliable results
- Increased workflow efficiency
- Early intervention
- Improved patient satisfaction
- Improved syphilis PMTCT in LMIC



- Fewer missed diagnoses
- Reduced anxiety
- Less delay
- Less misdiagnosis
- Use less staff, resources
- Saves time
- No loss to follow up

In Conclusion…

- Despite widespread HIV and syphilis testing programs throughout Canada, syphilis incidence continues to rise in key populations, and up to 20% of HIV-infected individuals remain undiagnosed.
- Opportunities exist to expand HIV POC testing in both traditional and non-traditional settings.
- HIV self testing a reality in global settings; coming to Canada?
- HIV/syphilis multiplex RDT a reality in global settings: coming to Canada?
- Regulatory processes now established for license of HIV self tests and POC tests in Canada
- No “one size fits all” model: new tools, new thinking, new implementation

Dual HIV-Syphilis Rapid Diagnostics Tests

Rosanna W Peeling
Professor and Chair, Diagnostic Research
Director, International Diagnostics Centre
London School of Hygiene & Tropical Medicine

The International Diagnostics Centre

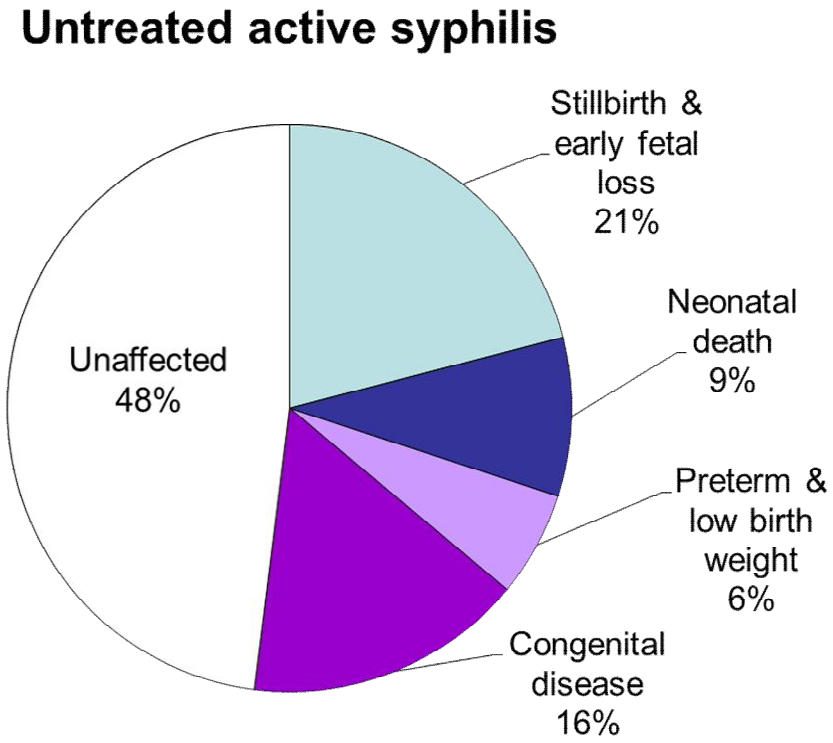
www.idx-dx.org

Outline of Presentation

- Need for dual HIV and syphilis rapid tests
- Dual HIV-Syphilis rapid test Landscape and trade-offs between access and accuracy
- WHO information note on the use of dual tests
- Experience of implementation in developing countries
- Summary

Burden of Mother-to-Child Transmission of Syphilis

- Globally nearly 1 million pregnant women are infected with syphilis each year
- 52% of pregnant women infected with syphilis will have an adverse outcome if untreated



Source: Gomez G et al, 2013. WHO, 2014.

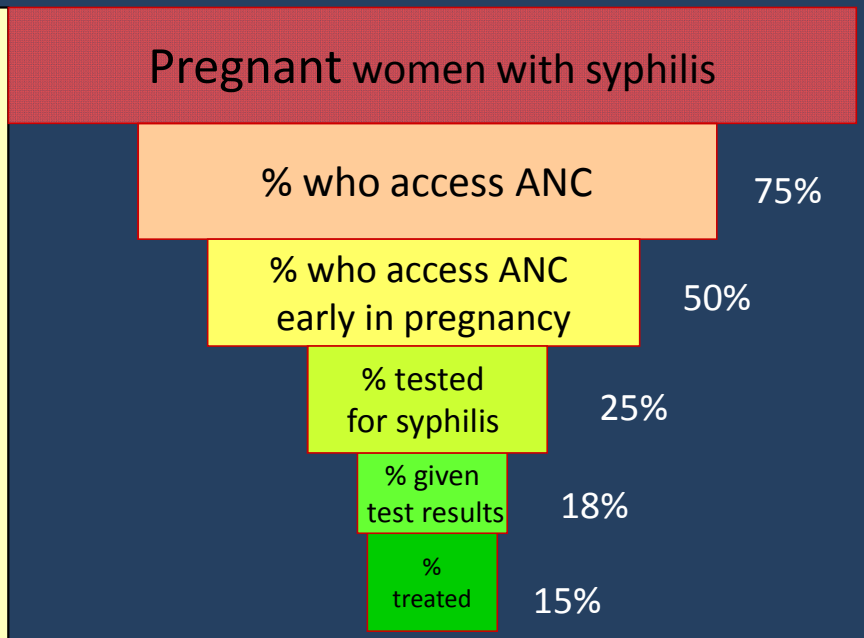
Inequity of Access to Diagnostics

The 2004 Health Development Report cited the lack of access and unaffordability as two major reasons why services fail

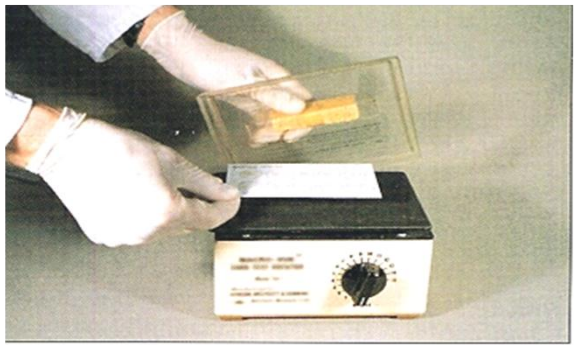
Distance to Nearest Medical Facility for the Poorest 5th of the population:

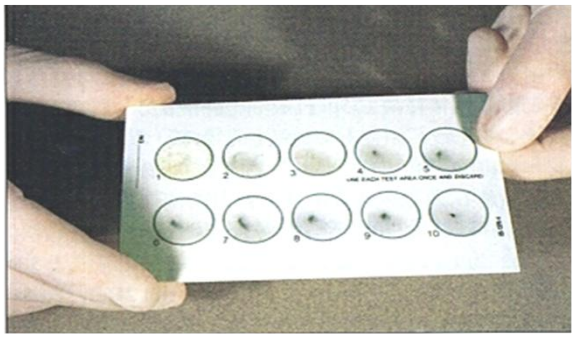
Country	Distance (km)
Benin	7.5
Bolivia	11.8
Chad	22.9
Haiti	8.0
Madagascar	15.5
Niger	26.9
Tanzania	4.7
Uganda	4.7
Zimbabwe	8.6

Selected from the 2004 World Health Report, p.22



Rapid vs Point-of-care (POC): Rapid Plasma Reagin (RPR) Test



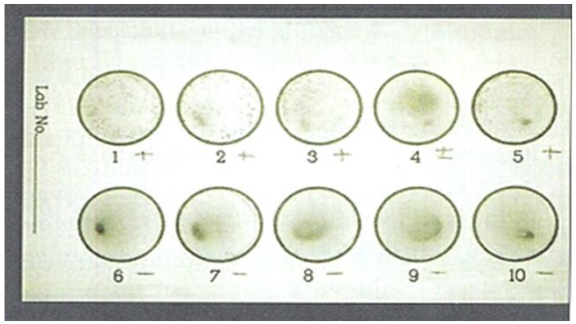


Sensitivity: 85-95%

Specificity: 95-98%

Time to result: 8-10 min

Cost/test = $ 0.2



- Needs electricity for:
  - centrifuge
  - shaker
  - fridge for reagent storage
- Requires training
- Humid atmosphere
- Batching

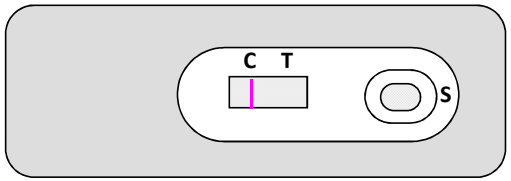
Detects cardiolipin – not specific for syphilis, prone to biological false positive results

- False negative results due to prozone effect

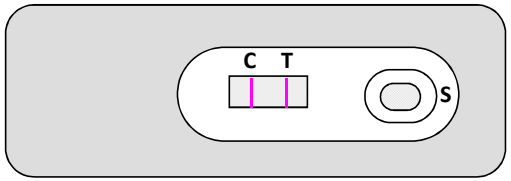
Rapid Tests for HIV or Syphilis

Procedure:

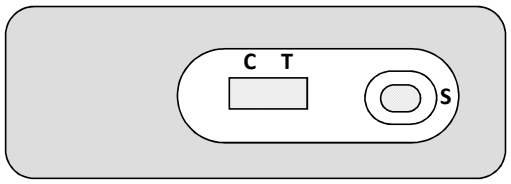
1. Use dropper provided, dispense 1 drop of serum/whole blood to sample well S
2. Add 2 drops of diluent buffer to sample well S
3. Read results after 15 minutes



Negative



Positive



Invalid

Rapid tests for syphilis

- detect treponemal antibodies
- More specific than non-treponemal tests
- Treponemal antibodies persist for years
- Not useful for monitoring response to treatment

Systematic Reviews of Rapid Syphilis Tests

All POCTs for the serodiagnosis of syphilis are immunochromatographic strips to detect antibodies to treponemal antigen(s). 6 were included in these reviews

Tucker et al 2011:

- No. of studies included: 15
- No. of study participants = 22,000
- Reference standards: TPPA, ELISA, TPHA, FTA-ABS
- Median sensitivity: 86% (interquartile range 0·75–0·94)
- Median specificity: 99% (interquartile range 0.98–0.99)

Yafari et al 2013:

- No. of studies included: 25
- Reference standards: TPPA, ELISA, TPHA, FTA-ABS
- Pooled Sensitivity = 84% for serum; 80% for whole blood
- Pooled Specificity = 96% for serum; 98% for whole blood

Performance of Rapid Syphilis Tests

In laboratories, using serum samples, sensitivity: 74-90%; specificity: 94-99%
In clinics, using finger-prick whole blood samples: sensitivity: 74-86%; specificity: 96-99%

POCT	Sample	Parameters	Assuming imperfect reference standards (95% CrI)*
Alere Determine	Serum	Sensitivity	90.04% (80.45, 95.21)
		Specificity	94.15% (89.26, 97.66)
	Whole blood	Sensitivity	86.32% (77.26, 91.70)
		Specificity	95.85% (92.42, 97.74)
SD Syphilis 3.0	Serum	Sensitivity	87.06% (75.67, 94.50)
		Specificity	95.85% (89.89, 99.53)
	Whole blood	Sensitivity	84.50% (78.81, 92.61)
		Specificity	97.95% (92.54, 99.33)
Syphicheck-WB	Serum	Sensitivity	74.48% (56.85, 88.44)
		Specificity	99.14% (96.37, 100.0)
	Whole blood	Sensitivity	74.47% (63.94, 82.13)
		Specificity	99.58% (98.91, 99.96)
Visitect Syphilis	Serum	Sensitivity	85.13% (72.83, 92.57)
		Specificity	96.45% (91.92, 99.29)
	Whole blood	Sensitivity	74.26% (53.62, 83.68)
		Specificity	99.43%, (98.22, 99.98)

Adapted from Jafari *et al*.[17]
*Adjustments were made for imperfect reference standards using the Bayesian hierarchical summary receiver operating characteristic curve method. The results are point estimates of sensitivity and specificity for each test, using serum and whole blood, around a 95% credible interval (as opposed to a CI).
CrI, credible interval; NA, not available; POCT, point-of-care testing; TP, treponemal.

Toskin I, *et al*. *Sex Transm Infect* 2017;**93**:S69–S80. doi:10.1136/sextrans-2016-053071

Rationale for the dual Elimination of Mother-to-Child Transmission (eMTCT) of HIV and Syphilis

Avoiding HIV and dying of syphilis

A mother in Haiti seeks prenatal care at a local health clinic, accepts HIV voluntary counselling and testing, and, after testing HIV-positive, takes short-course antiretroviral therapy for prevention of mother-to-child transmission (PMTCT). Postpartum, she gives her baby antiretroviral therapy and provides artificial milk to protect against HIV transmission through breastfeeding. Is this a success story for PMTCT? No, the baby died at 3 weeks from congenital syphilis. Is this an isolated case? No, we have seen several babies in Haiti who have died of congenital syphilis after completion of PMTCT. The Haitian Government, in collaboration with non-governmental organisations, is leading the way in providing comprehensive care in

www.thelancet.com Vol 364 October 30, 2004

Peeling et al. Lancet 364: 1561-2 2004

	Syphilis	HIV
Community awareness	±	✔
Requires ANC attendance	✔	✔
Early ANC better than later ANC	✔	✔
Maternal testing recommended by MOH	✔	✔
POC tests available	✔	✔
POC tests in use nationally	✔	✔
Requires test supply chain and lab QA/QC	✔	✔
One-time treatment	✔	Not available
Low cost treatment	✔	Not available
Partner notification and engagement useful	✔	✔
Standard infant diagnostic test available	Not available	✔

Source: Disease Control Priorities

Why dual HIV-Syphilis vs single tests?

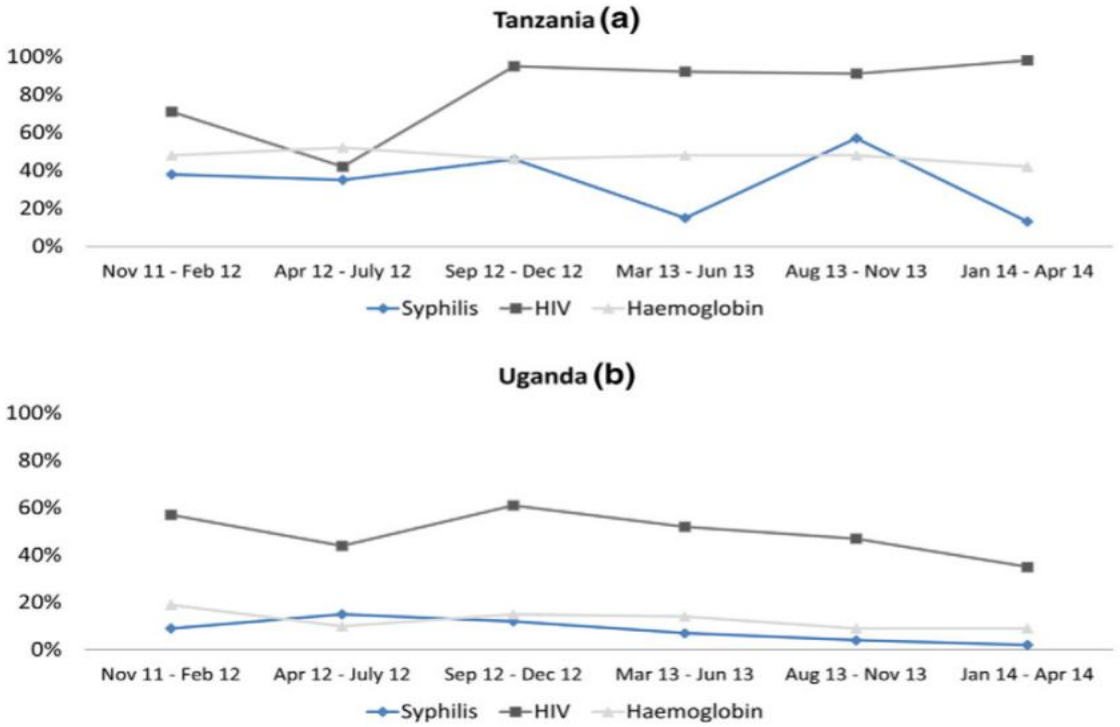
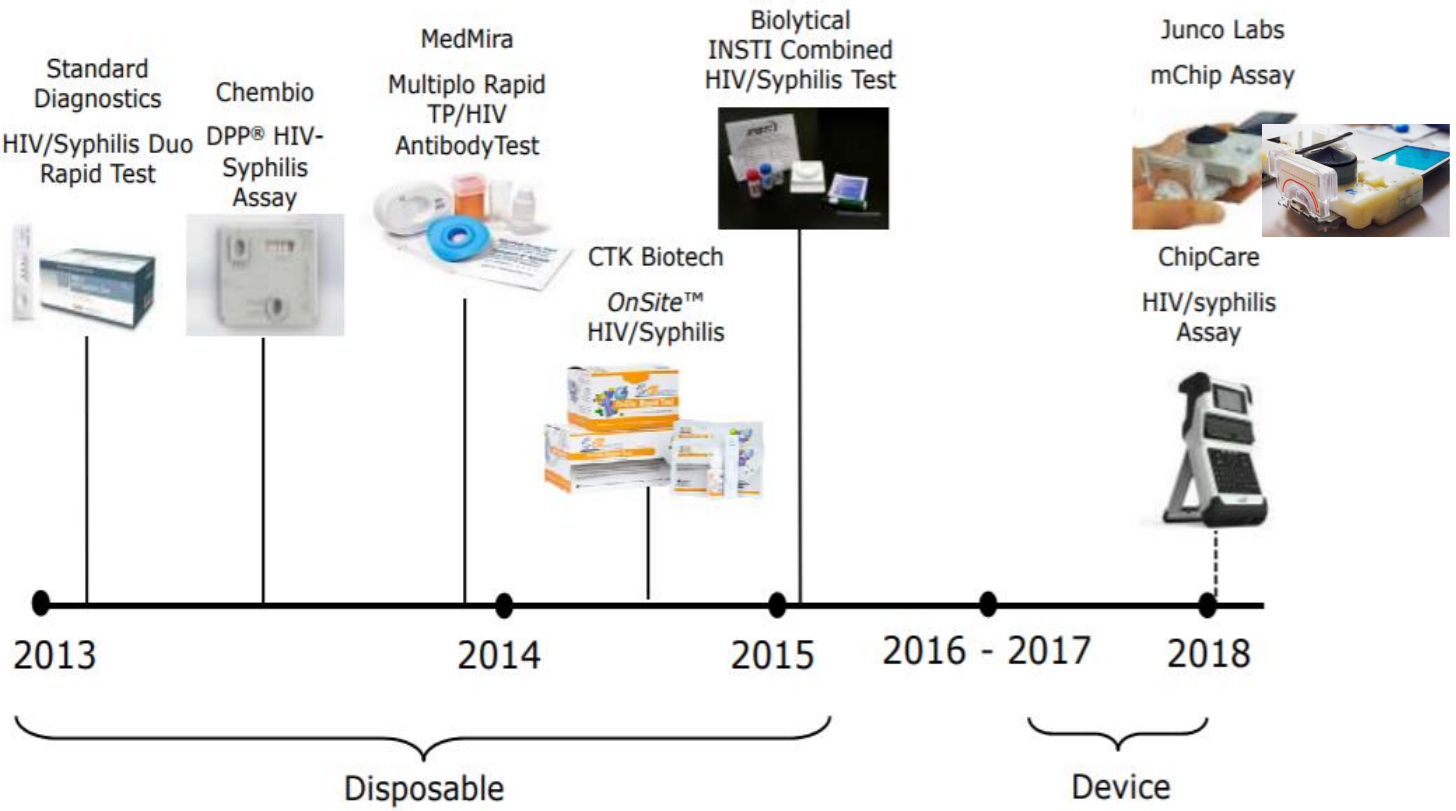


Fig. 2. Proportion of health facilities with availability of screening tests at different time points in Tanzania (a) and Uganda (b).

Baker et al Int J Gyn Ob 130: S43–S50, 2015

POC HIV/Syphilis Tests – Available and Pipeline*



*Estimated as of March 2017 - timeline and sequence may change

---- No market launch date set by company.

http://www.who.int/reproductivehealth/topics/rtis/Diagnostic_Landscape_2017.pdf

Target Product Profile: Dual HIV-Syphilis Test

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Intended Use	To detect HIV infection and to detect active syphilis infection in pregnant women			
Goal of Test	Qualitative detection of HIV antibodies/antigens and qualitative detection of antibodies against *Treponema pallidum* for the serodiagnosis of syphilis			
Target Patient	Expectant women at risk of infection for HIV and syphilis			
Target Use Setting	Health centers, health posts, PMCTCs, VCTs and community outreach			
Results	Clear positive, negative or invalid result with minimal/no instructions for interpretation			
Equipment	Disposable Test Only; Reader Preferred			
PERFORMANCE	**HIV Infection**		**Syphilis**	
Reference Test/Gold Standard	ELISA/EIA		TPPA	
	Minimal	**Optimal**	**Minimal**	**Optimal**
Clinical Sensitivity	>98%	>99%	>85%	>98%
Clinical Specificity	>98%	>99%	>95%	>98%
Quantitation	None: Qualitative Test			
MINIMAL AND OPTIMAL OPERATIONAL CHARACTERISTICS FOR COMBINED HIV/SYPHILIS ASSAY				
	Minimal		**Optimal**	
Sample Specimen	Fingerstick capillary blood (maximum 50µL)		Fingerstick capillary blood (maximum 20µL)	
Sample Preparation	Minimal sample processing; no more than 1 operator step		Integrated	
Steps performed by healthcare worker between sample preparation and result	No more than 3 operator steps (only one of which is timed), excluding waste disposal		1 operator step (none of which is timed), excluding waste disposal	
Additional 3rd party consumables	None, except for sample collection			
Cold Chain	None required at any point in supply chain or storage			
Kit	All materials required for assay and reagents, including buffers or other consumables to diagnose one patient, included in individually packaged, self-contained kit			
Kit Stability and storage conditions	Stable for 12 months at 2°C to 30°C (2°C to 40°C preferred), 70% humidity, including transport stress (48h with fluctuations up to 50°C and down to 0°C)		Stable for 24 months at 0°C to 40°C, 90% humidity, including transport stress (48h with fluctuations up to 50°C and down to 0°C)	

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ASSURED Tests for improving Access to STI testing

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

A = Affordable

S = Sensitive

S = Specific

U = User-friendly

R = Rapid and robust

E = Equipment-free

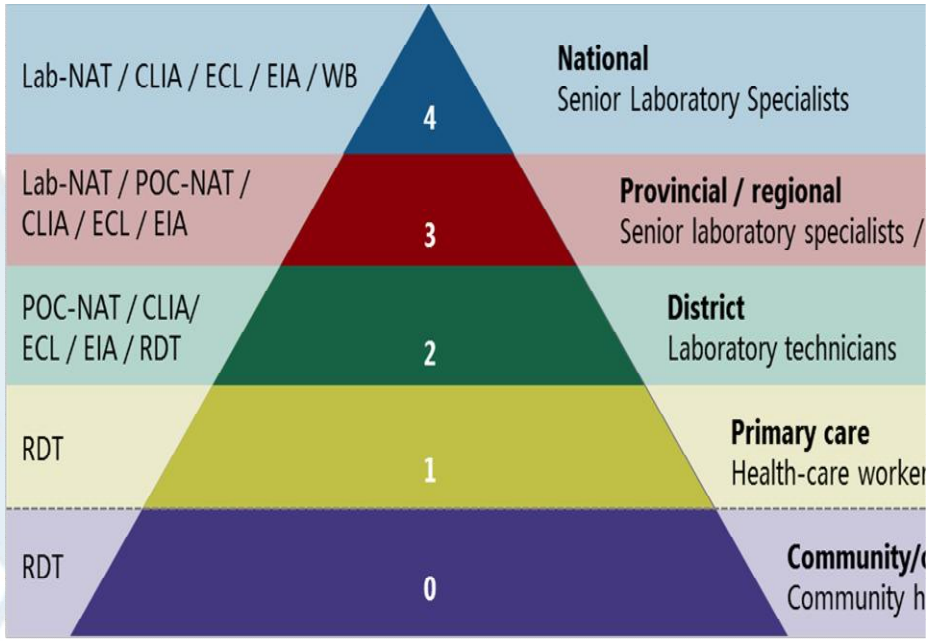
D = Deliverable

✓ **Affordable**

✓ **Accurate**

✓ **Accessible**

Trade-off between Access vs Sensitivity



Access	Sensitivity			
	100	**90**	**80**	**70**
100	100	90	80	70
90	90	81	72	63
80	80	72	64	56
70	70	63	56	49
60	60	54	48	42
50	50	45	40	35
40	40	36	32	28
30	30	27	24	21
20	20	18	16	14
10	10	9	8	7

NAT: Nucleic acid tests: Lab-NAT: laboratory-based; POC-NAT: at point-of-care;
CLIA: chemiluminescence immunoassay; ECL: electrochemiluminescence immunoassay;
EIA: enzyme immunoassay; RDT: rapid diagnostic test

FDA Approval:
Oral HIV Test Requirements

OraQuick Test	Professional Use		Over-the-Counter	
	Minimum Recommended Performance for the lower bound of 2-sided 95% CI	Actual Performance	Minimum Recommended Performance for the lower bound of 2-sided 95% CI	Actual Performance
Sensitivity	**98%**		**95%**	
Specificity	**98%**		**95%**	

*95%CI = 95% Confidence Interval

FDA Approval: OraSure HIV Test

Accuracy	Professional Use		Over-the-Counter	
	Minimum Recommended Performance: lower bound of 2-sided 95% CI	Actual Performance	Minimum Recommended Performance for the lower bound of 2-sided 95% CI	Actual Performance
Sensitivity	**98%**	99.3% (98.4-99.7%)	**95%**	92.98% (86.6-96.9%)
Specificity	**98%**	99.8% (99.6-99.9%)	**95%**	99.98% (99.9-100%)

A risk-benefit model showed that in the first year of use:

~ 4,500 new HIV infections identified among those not aware of their HIV status
~ 2,700,000 who would test negative

~4,000 transmissions would be averted, outweighing the individual risk of ~1,100 false negative results
The product would need to have clear messages on the implications of test results

World Health Organization

WHO Information Note on the Use of Dual HIV/Syphilis Rapid Diagnostic Tests (RDT)

Figure 1: WHO recommended HIV testing strategy for high prevalence settings (above 5%)

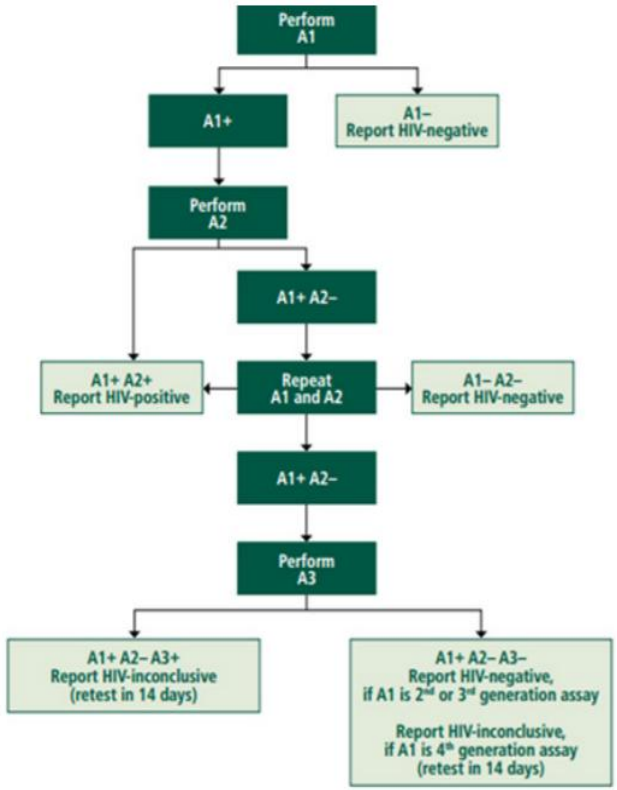
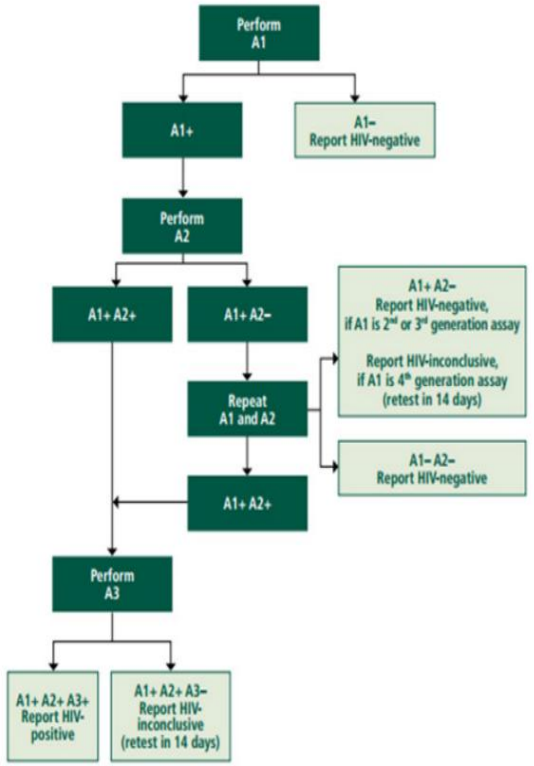


Figure 2: WHO recommended HIV testing strategy for low prevalence settings (below 5%)

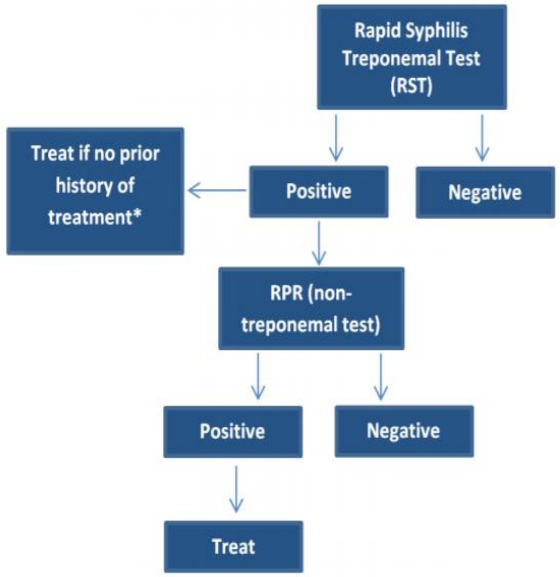


http://apps.who.int/iris/bitstream/10665/252849/1/WHO-RHR-17.01-eng.pdf

WHO Information Note on the Use of Dual HIV/Syphilis Rapid Diagnostic Tests (RDT)

http://apps.who.int/iris/bitstream/10665/252849/1/WHO-RHR-17.01-eng.pdf

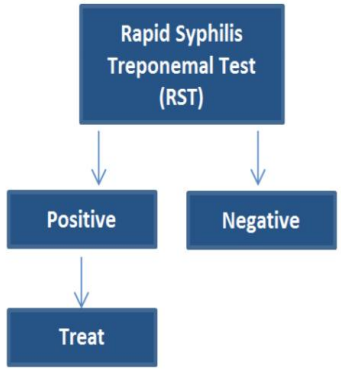
Figure 4: WHO interim recommended syphilis testing and treatment strategy for high syphilis prevalence settings (above 5%)



** Pregnant women who have tested positive and received treatment during a previous pregnancy should be considered for re-treatment upon receiving a positive syphilis test result in subsequent pregnancies.*

- Some patients may be serofast, i.e. maintain a persistent non-trep response despite rounds of treatment;
- Re-infection is difficult to detect in some patients

Figure 3: WHO interim recommended syphilis testing and treatment strategy for low syphilis prevalence settings (below 5%)



- Given the serious consequences of syphilis in pregnancy, The risk of over-treatment is small compared to the risk of missing the opportunity to treat a truly infected case

Singh AE, Romanowski B. Clin Microbiol Rev 1999;12:187–209
Peeling RW et al. Nat Rev Dis Primers. 2017 Oct 12;3:17073

Performance of dual HIV/syphilis tests in laboratory evaluation in China and Nigeria

	Comparison with HIV ELISA		Comparison with TPPA/TPHA	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
SD Bioline	**99.0** (98.0-99.5)	**99.0** (98.0-99.5)	**96.6** (95.0-97.7)	**99.1** (98.2-99.6)
Chembio	**99.6** (98.8-99.9)	**97.9** (96.7-98.7)	**97.0** (95.5-98.0)	**99.6** (98.9-99.9)
MedMira	**99.5** (99.4-99.8)	**98.3** (97.2-99.0)	**94.2** (92.3-95.7)	**97.2** (95.8-98.1)

International Journal of Gynecology and Obstetrics

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

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LABORATORY EVALUATION

Laboratory evaluation of three dual rapid diagnostic tests for HIV and syphilis in China and Nigeria

Yue-Ping Yin [a], Evelyn Ngige [b], Chukwuma Anyaike [b], Gbenga Ijaodola [b], Taiwo A. Oyelade [c], Rui Gama Vaz [c], Lori M. Newman [d], Xiang-Sheng Chen [a,*]

N=1,514 specimens

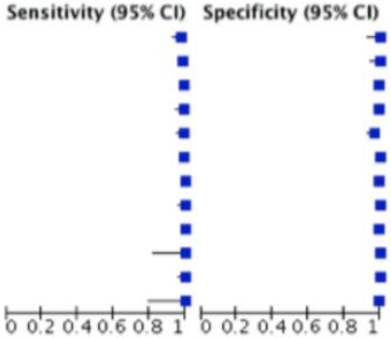
Performance of HIV Component of the Dual HIV syphilis tests

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

a) Diagnostic test accuracy for HIV, stratified by manufacturer

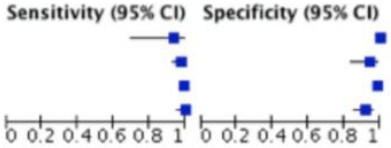
i) SD Bioline: HIV component

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
[33] Humphries (SD Bioline)	94	0	2	53	0.98 [0.93, 1.00]	1.00 [0.93, 1.00]
[45] Black	185	0	2	62	0.99 [0.96, 1.00]	1.00 [0.94, 1.00]
[38] Yin (SD Bioline)	721	8	7	778	0.99 [0.98, 1.00]	0.99 [0.98, 1.00]
[41] Bristow	104	2	1	308	0.99 [0.95, 1.00]	0.99 [0.98, 1.00]
[42] Bristow	128	5	1	164	0.99 [0.96, 1.00]	0.97 [0.93, 0.99]
[30] Ondondo	345	0	1	352	1.00 [0.98, 1.00]	1.00 [0.99, 1.00]
[35] Bristow	1123	4	1	1208	1.00 [1.00, 1.00]	1.00 [0.99, 1.00]
[36] Dagnra	107	0	0	203	1.00 [0.97, 1.00]	1.00 [0.98, 1.00]
[39] Shimelis	200	1	0	199	1.00 [0.98, 1.00]	0.99 [0.97, 1.00]
[44] Shakya	19	0	0	9981	1.00 [0.82, 1.00]	1.00 [1.00, 1.00]
[31] Chiappe	91	0	0	571	1.00 [0.96, 1.00]	1.00 [0.99, 1.00]
[34] Omoding	16	1	0	203	1.00 [0.79, 1.00]	1.00 [0.97, 1.00]



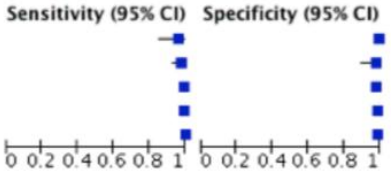
ii) MedMira: HIV component

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
[43] Bristow	15	0	1	159	0.94 [0.70, 1.00]	1.00 [0.98, 1.00]
[33] Humphries (MedMira)	94	3	2	49	0.98 [0.93, 1.00]	0.94 [0.84, 0.99]
[38] Yin (Medmira)	724	13	4	773	0.99 [0.99, 1.00]	0.98 [0.97, 0.99]
[37] Bristow	74	10	0	114	1.00 [0.95, 1.00]	0.92 [0.86, 0.96]



iii) Chembio: HIV component

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
[32] Hess	44	2	2	606	0.96 [0.85, 0.99]	1.00 [0.99, 1.00]
[33] Humphries (Chembio)	94	1	2	52	0.98 [0.93, 1.00]	0.98 [0.90, 1.00]
[38] Yin (Chembio)	725	17	3	769	1.00 [0.99, 1.00]	0.98 [0.97, 0.99]
[47] Kalou	426	9	1	554	1.00 [0.99, 1.00]	0.98 [0.97, 0.99]
[40] Leon	151	4	0	295	1.00 [0.98, 1.00]	0.99 [0.97, 1.00]



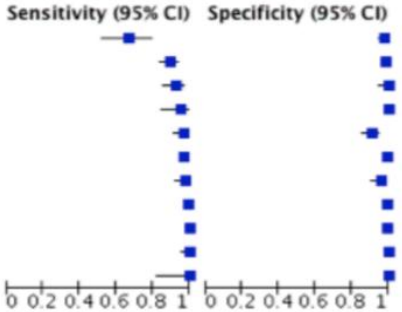
Gliddon HD, et al. Sex Transm Infect 2017;93:S3–S15.

Performance of Syphilis Component of the Dual HIV syphilis tests

b) Diagnostic test accuracy for syphilis, stratified by manufacturer

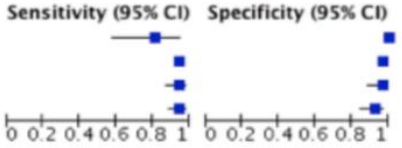
i) SD Bioline: Syphilis component

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
[45] Black	34	4	17	194	0.67 [0.52, 0.79]	0.98 [0.95, 0.99]
[41] Bristow	149	3	18	243	0.89 [0.84, 0.93]	0.99 [0.96, 1.00]
[33] Humphries (SD Bioline)	80	0	6	64	0.93 [0.85, 0.97]	1.00 [0.94, 1.00]
[44] Shakya	42	13	2	9943	0.95 [0.85, 0.99]	1.00 [1.00, 1.00]
[42] Bristow	109	17	4	168	0.96 [0.91, 0.99]	0.91 [0.86, 0.95]
[38] Yin (SD Bioline)	710	7	25	772	0.97 [0.95, 0.98]	0.99 [0.98, 1.00]
[39] Shimelis	83	4	2	96	0.98 [0.92, 1.00]	0.96 [0.90, 0.99]
[35] Bristow	609	4	2	1444	1.00 [0.99, 1.00]	1.00 [0.99, 1.00]
[31] Chiappe	198	2	0	465	1.00 [0.98, 1.00]	1.00 [0.98, 1.00]
[30] Ondondo	85	0	0	559	1.00 [0.96, 1.00]	1.00 [0.99, 1.00]
[34] Omoding	19	0	0	201	1.00 [0.82, 1.00]	1.00 [0.98, 1.00]



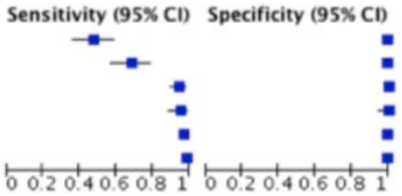
ii) MedMira: syphilis component

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
[43] Bristow	17	0	4	153	0.81 [0.58, 0.95]	1.00 [0.98, 1.00]
[38] Yin (Medmira)	692	22	43	757	0.94 [0.92, 0.96]	0.97 [0.96, 0.98]
[33] Humphries (MedMira)	81	2	5	62	0.94 [0.87, 0.98]	0.97 [0.89, 1.00]
[37] Bristow	104	6	6	77	0.95 [0.89, 0.98]	0.93 [0.85, 0.97]



iii) Chembio: syphilis component

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
[32] Hess	37	3	41	576	0.47 [0.36, 0.59]	0.99 [0.98, 1.00]
[46] Bowen	55	6	25	1702	0.69 [0.57, 0.79]	1.00 [0.99, 1.00]
[40] Leon	142	0	8	300	0.95 [0.90, 0.98]	1.00 [0.99, 1.00]
[33] Humphries (Chembio)	82	0	4	64	0.95 [0.89, 0.99]	1.00 [0.94, 1.00]
[38] Yin (Chembio)	713	3	22	776	0.97 [0.96, 0.98]	1.00 [0.99, 1.00]
[47] Kalou	639	2	8	341	0.99 [0.98, 0.99]	0.99 [0.98, 1.00]



Gliddon HD, et al. Sex Transm Infect 2017;93:S3–S15.

Performance of the ChemBio DPP Trep-Non Trep Combo Test

Table 3 Performance of DPP Syphilis Screen & Confirm Assay (Chembio Diagnostics Systems)

Study	Sample	Parameters % (95% CI)	DPP Treponemal line	DPP Non-treponemal line
Castro *et al*[20]	Banked serum samples	Sensitivity	96.5 (NA)	98.4 (NA)
		Specificity	95.5 (NA)	98.6 (NA)
Yin *et al*[21]	Whole blood (n=1323)	Sensitivity	96.7 (95.1–97.9)	87.2 (84.0–89.9)
		Specificity	99.3 (98.3–99.7)	94.4 (92.6–95.8)
	Finger prick blood (n=488)	Sensitivity	96.4 (93.5–98.0)	85.5 (82.4–89.4)
		Specificity	96.4 (93.5–98.0)	96.1 (92.9–97.9)
	Blood plasma (n=1323)	Sensitivity	94.6 (92.5–96.1)	88.4 (85.3–90.9)
		Specificity	99.6 (98.7–99.9)	95.0 (93.3–96.3)
Causer *et al*[22]	Serum (n=1005)	Sensitivity	89.8% (87.3–91.9)	94.2 (91.8–96.0)
		Specificity	99.3% (97.0–99.9)	62.2 (57.5–66.6)

NA, not applicable.

Toskin I, et al. Sex Transm Infect 2017;93:S69–S80.

Rapid Test Sensitivity*	Non-Trep titre ≤ 1:2	Non-Trep titre ≥ 1:4
STD Clinic	59-71%	96-100%
Outreach	71-81%	100%

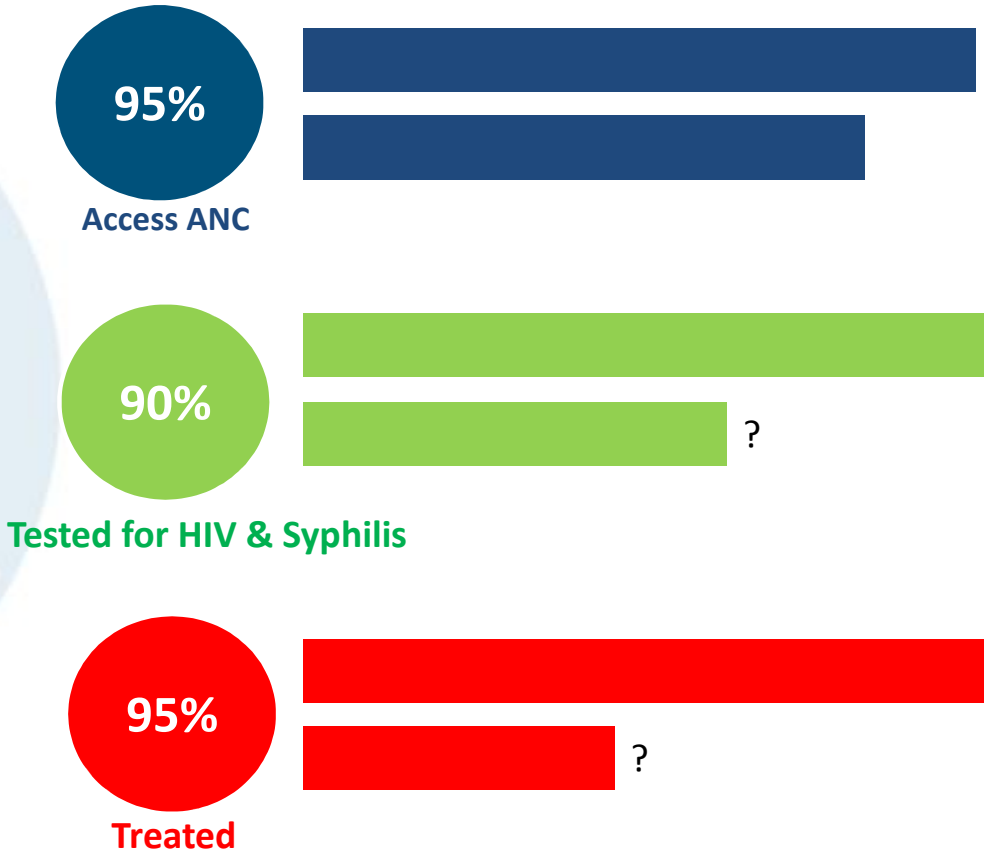
*using venous or finger prick whole blood

Yin et al. Clin Infect Dis 2013; 56: 659-665

For syphilis in pregnancy, a non-trep titre of ≥1:8 was found to be associated with adverse outcomes of pregnancy

Watson-Jones D et al. J Infect Dis 2002;186:940–7

Global Targets for eMTCT HIV/Syphilis



As of 2017:

5 countries have achieved elimination:

- Cuba (2015)
- Thailand (2016)
- Belarus (2016)
- Moldova (Syphilis only, 2016)
- Armenia (HIV only, 2016)

www.idc-dx.org

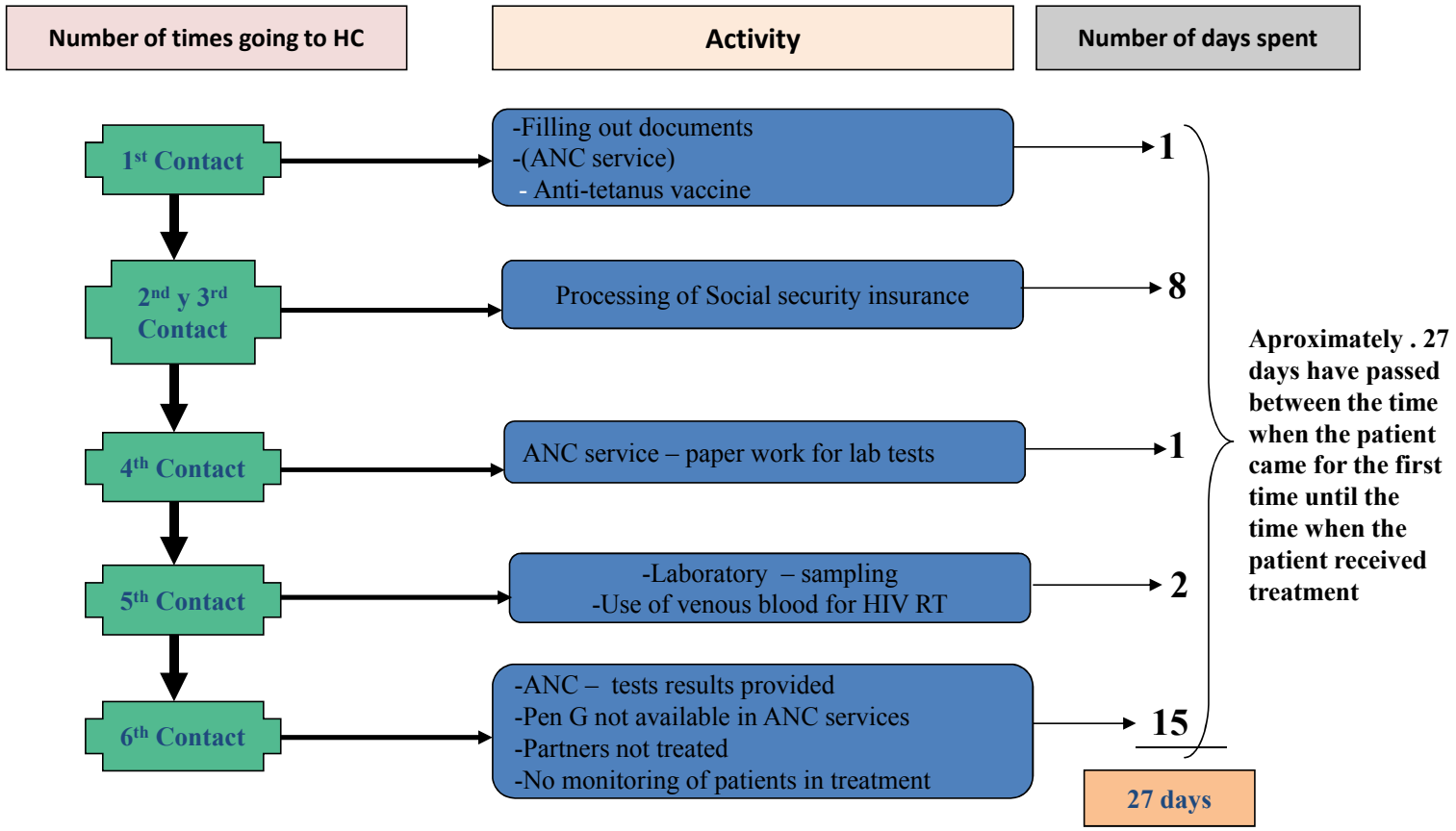
Implementation of HIV-Syphilis Tests

- Workshops on the performance of the dual tests and algorithms for their use have been carried out in Africa, latin America and Asia since 2014, mainly for prenatal screening
- The Alere (now Abbott) dual test has been approved by the WHO Pre-qualification programme and can be purchased for US $1.50 by developing countries
- Pilots and demonstration projects using the dual tests has been performed and the most effective means to reduce adverse outcomes of pregnancy was to use a dual HIV/syphilis RDT for prenatal screening, with an ICER of $12.11 per DALY

Challenges:

- Many countries have separate funding streams and venues for prenatal screening of HIV and syphilis
- There is a need for sustainable financing mechanisms for these tests similar to the Global Access to Vaccine Initiative (GAVI)
- There is a need to simplify the 4 dual testing algorithms
- The use of this test in key populations remains problematic (identification of re-infection and management of serofast status)

PERU Cisne Project: Rapid Syphilis Tests as Catalyst for Health System Strengthening



Garcia P et al. PLoS One Jun 26;8(6):e66905

Data Connectivity: Automated reporting from POC tests/readers

The need is actually not only for connectivity but also for intelligence to improve quality of testing, optimize supply chain management for better patient outcomes

1. Quality Assurance, especially in the case of POCT
2. Patient treatment
3. Public health monitoring
4. Outbreak response
5. LI(M)S interfacing
6. Stock management
7. Operator performance; Instrument performance

Assuring the Quality of POC Tests and Testing

- National or regional laboratories should monitor performance of tests used at primary and secondary care levels by sending out proficiency panels and monitor quality of tests and testing
  http://www.ajlmonline.org/index.php/ajlm/issue/view/9

- Proficiency panels for HIV-Syphilis tests can be made using the Dried Tube Specimen method developed by the US CDC:
  - 45 uL of positive and negative sera are air dried in a small tube with a small vol of Trypan Blue dye in biological safety cabinet overnight.
  - The tubes are capped and are stable for 1 year at room temperature

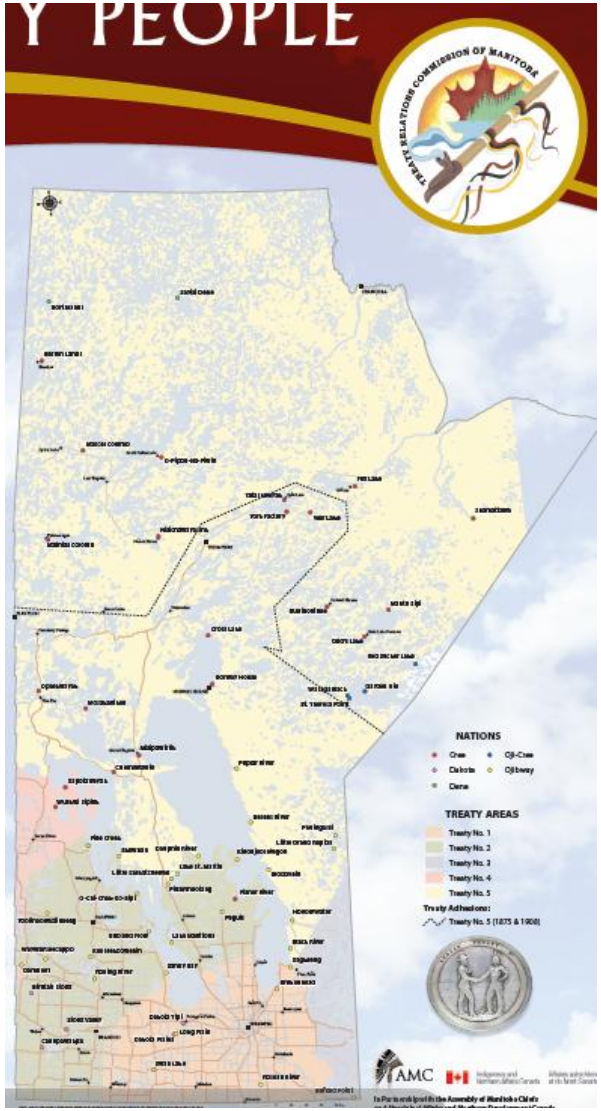
(Bharat SP. J Virol Methods 163:295-300, 2010)

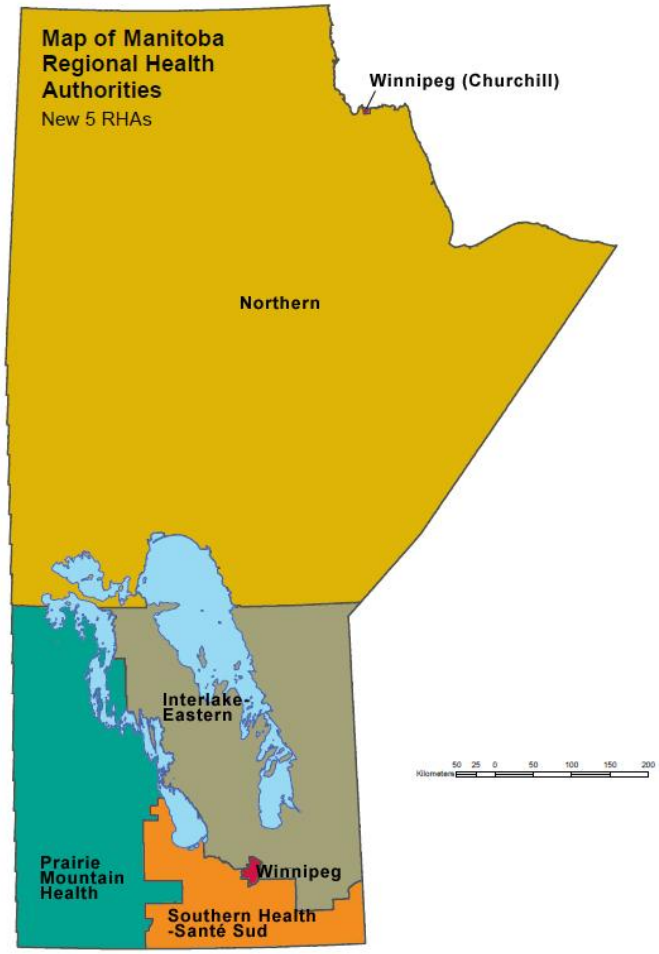
Summary

1. Several dual HIV-Syphilis rapid tests have been shown to have acceptable performance
2. Dual HIV-Syphilis rapid tests allow integration of prenatal screening programmes for HIV and Syphilis and are important tools to help countries reach targets for dual elimination of Mother-to-Child Transmission of HIV and Syphilis
3. Implementation of the dual test in the context of the Elimination of Mother to Child Transmission of HIV-Syphilis need to include quality assurance of tests and testing, connectivity to capture data in real time and linkage to care and treatment
4. Dual HIV-Syphilis tests are useful for screening in key populations but confirmatory tests should be made available at the point-of-care

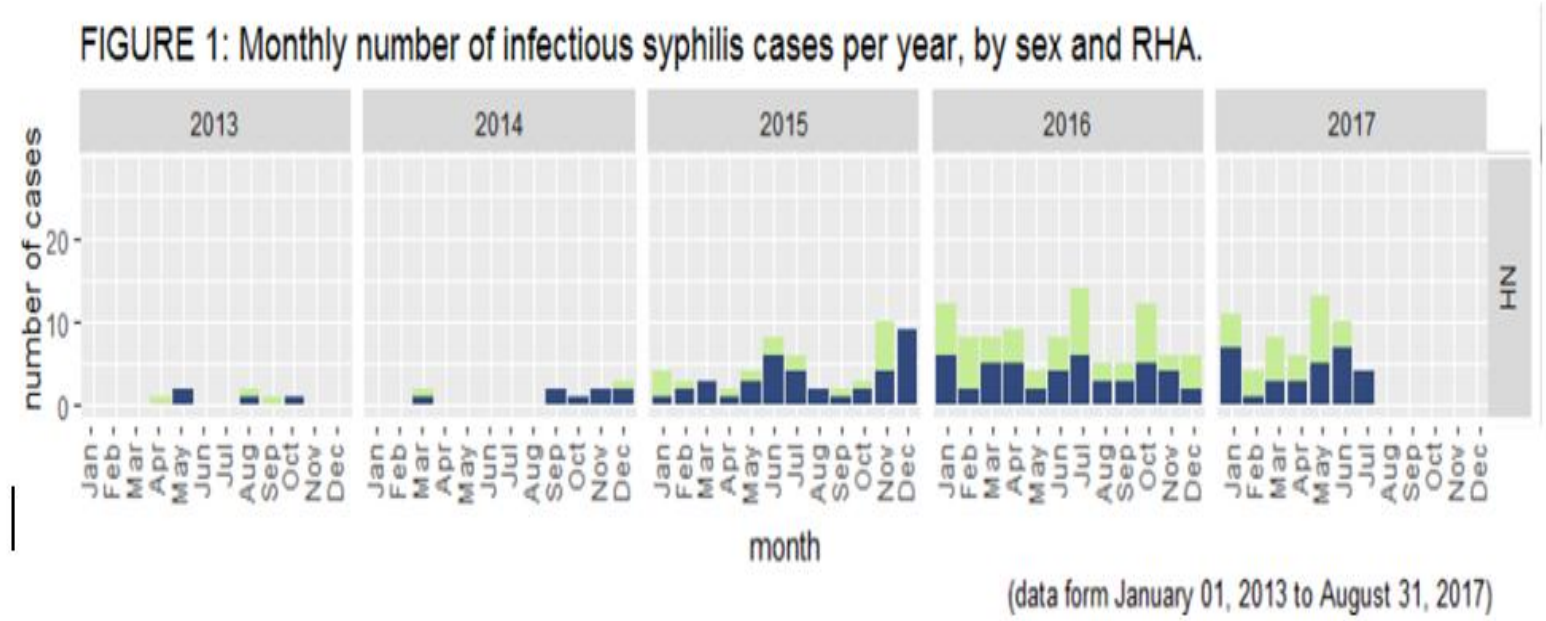
Syphilis in Northern Manitoba

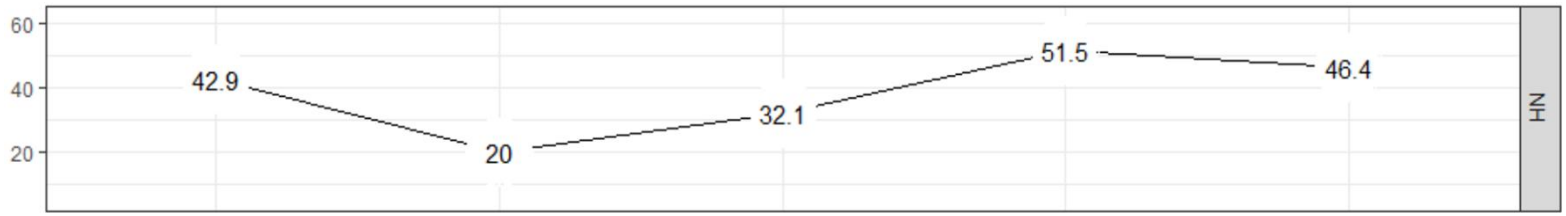
Dr. Michael Isaac
Medical Officer of Health
Northern Health Region


Y PEOPLE
TREATY RELATIONS COMMISSION OF MANITOBA
NATIONS
Cree
Dene
Dakota
Ojibway
Oji-Cree
TREATY AREAS
Treaty No. 1
Treaty No. 2
Treaty No. 3
Treaty No. 4
Treaty No. 5
Treaty Adhesions:
Treaty No. 5 (1875 & 1908)
AMC

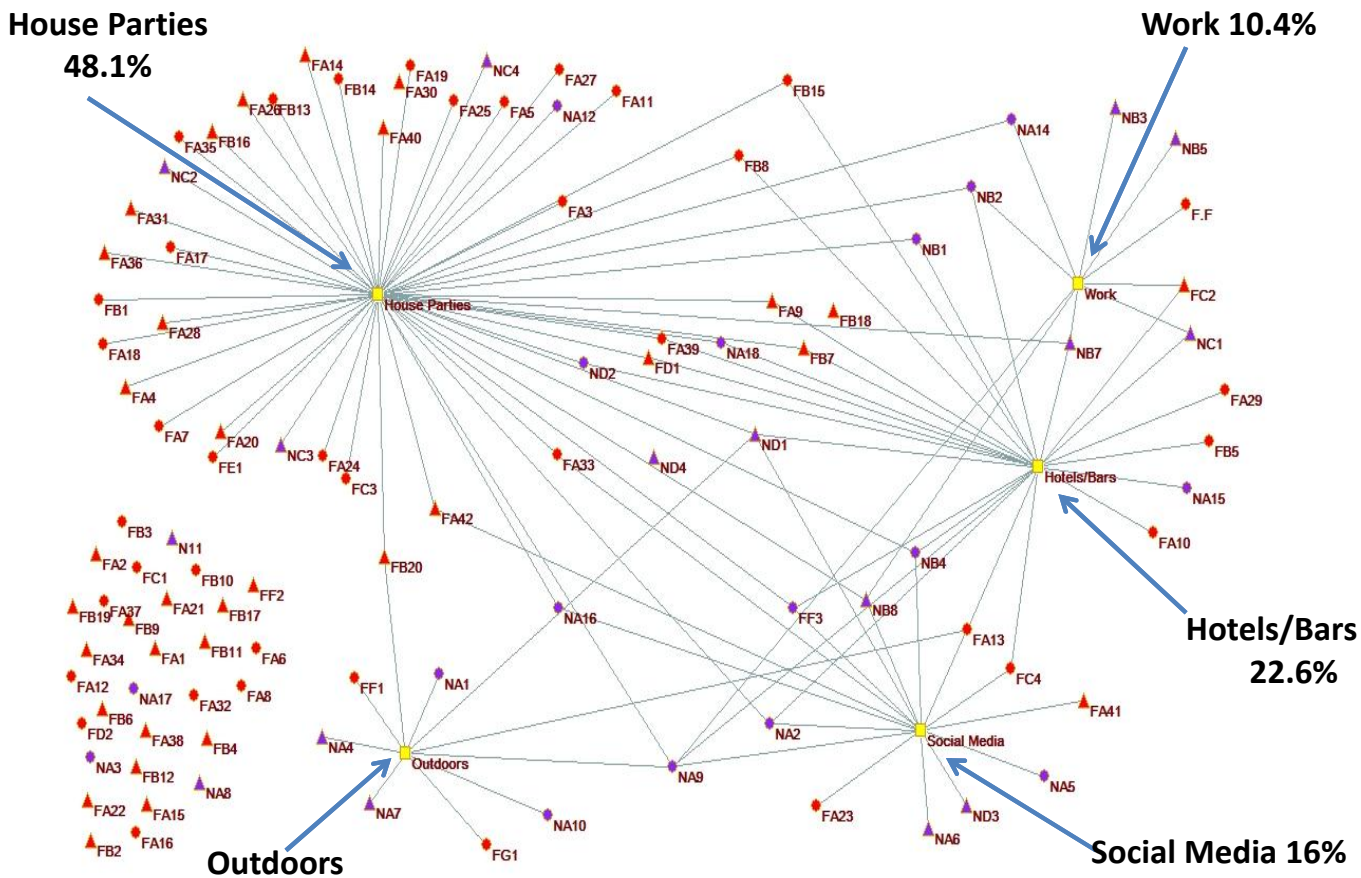

Map of Manitoba
Regional Health
Authorities
New 5 RHAs
Winnipeg (Churchill)
Northern
Interlake-
Eastern
Prairie
Mountain
Health
Winnipeg
Southern Health
-Santé Sud
50 25 0 50 100 150 200
Kilometers

Syphilis Outbreak



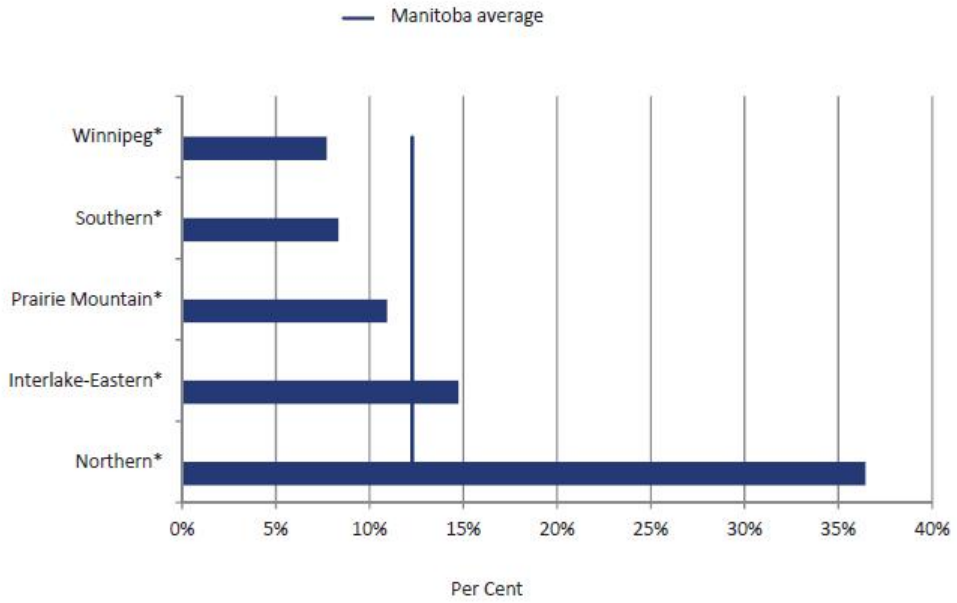


Social Networks: Syphilis cases and locations where they met new sexual partners over the last 12 months.



Inadequate prenatal care

Figure 4.46. Rates of Inadequate Prenatal Care by RHA, 2007/08 - 2008/09.



Source: Manitoba Centre for Health Policy, Perinatal Services and Outcomes in Manitoba, 2012.
NOTE: * Significantly different from Manitoba rate ($p<0.05$).

Factors Favoring Syphilis POCT

- Syphilis serology logistics – turnaround time ~7 d, precarious journey for samples
- Follow up challenges – travel, lack of housing, poverty
- Current epidemiology – congenital syphilis, syphilis rates overall
- Health services resources – blood draw capabilities don't exist in some communities
- Current HIV POCT testing – Thompson labour ward

Other Considerations

- Concurrent HIV testing – Individual and Community readiness
- BBP testing rates
- Logistics – 'system' for testing – training, ordering, documentation, quality assurance
- Cost
- Linkage to care and public health surveillance
- Test characteristics – sensitivity, specificity, positive predictive value, negative predictive value. What is your pre-test probability?

Other Considerations

- Compromise on comprehensive testing – ‘test for one STBBI test for all’
- No ‘dils’ from POCT
- Still need to have confirmatory testing

Thanks!

Q & A Period

Type your question in the Chat section, and it will be answered by one of our presenters.

Thank you!

Upcoming webinars: Jan 29, 2018

***Webinar 3* - Reaching the Undiagnosed: Dried blood spot testing for Hepatitis C and HIV – a new approach for the rural and remote communities**

- John Kim, PHAC
- Jordan Feld, University Health Network
- Geri Bailey, Saskatoon Tribal Council

Please evaluate this webinar!