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:
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
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
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

<table>
<thead>
<tr>
<th>Health Authority / Region</th>
<th>Point of Care Testing</th>
<th>Standard Laboratory Testing</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>New Diagnosis</td>
<td># Tests Done</td>
<td>Diagnosis Rate</td>
</tr>
<tr>
<td>VCHA</td>
<td>118</td>
<td>15,982</td>
<td>0.7%</td>
</tr>
<tr>
<td>NHA</td>
<td>6</td>
<td>358</td>
<td><strong>1.7%</strong></td>
</tr>
<tr>
<td>FHA</td>
<td>2</td>
<td>324</td>
<td>0.6%</td>
</tr>
<tr>
<td>VIHA</td>
<td>0</td>
<td>226</td>
<td>0.0%</td>
</tr>
<tr>
<td>IHA</td>
<td>0</td>
<td>139</td>
<td>0.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>126</strong></td>
<td><strong>17,029</strong></td>
<td><strong>0.7%</strong></td>
</tr>
</tbody>
</table>
INSTI™ HIV Test Adoption History in Europe and Canada

**INSTI™ Units**

Europe:
- 2013: 356,901
- 2014: 451,879

Canada:
- 2013: 78,815
- 2014: 80,401
US and Canadian POCT Trends

  - 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

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](http://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 CANADA. Tel: 902.494.1155 Email: [jgahagan@dal.ca](mailto: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)
INSTIT 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

<table>
<thead>
<tr>
<th>Test</th>
<th>Primary</th>
<th>Secondary</th>
<th>Latent</th>
<th>Tertiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDRL</td>
<td>78</td>
<td>100</td>
<td>95</td>
<td>71</td>
</tr>
<tr>
<td>RPR</td>
<td>86</td>
<td>100</td>
<td>98</td>
<td>73</td>
</tr>
<tr>
<td>FTA-Abs</td>
<td>84</td>
<td>100</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>TP-PA</td>
<td>76</td>
<td>100</td>
<td>97</td>
<td>94</td>
</tr>
<tr>
<td>EIA</td>
<td>93</td>
<td>100</td>
<td>100</td>
<td>ND</td>
</tr>
<tr>
<td>INSTI</td>
<td>82.5</td>
<td>100</td>
<td>95.5</td>
<td>ND</td>
</tr>
</tbody>
</table>

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: typell 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

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

1 sample
1 minute
2 results

- 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

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

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:

<table>
<thead>
<tr>
<th>Country</th>
<th>Distance (km)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benin</td>
<td>7.5</td>
</tr>
<tr>
<td>Bolivia</td>
<td>11.8</td>
</tr>
<tr>
<td>Chad</td>
<td>22.9</td>
</tr>
<tr>
<td>Haiti</td>
<td>8.0</td>
</tr>
<tr>
<td>Madagascar</td>
<td>15.5</td>
</tr>
<tr>
<td>Niger</td>
<td>26.9</td>
</tr>
<tr>
<td>Tanzania</td>
<td>4.7</td>
</tr>
<tr>
<td>Uganda</td>
<td>4.7</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>8.6</td>
</tr>
</tbody>
</table>

Selected from the 2004 World Health Report, p.22

### Inequity of Access to Diagnostics

<table>
<thead>
<tr>
<th>Pregnant women with syphilis</th>
<th>% who access ANC</th>
<th>% who access ANC early in pregnancy</th>
<th>% tested for syphilis</th>
<th>% given test results</th>
<th>% treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>75%</td>
<td>50%</td>
<td>25%</td>
<td>18%</td>
<td>15%</td>
<td>15%</td>
</tr>
</tbody>
</table>
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

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
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
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%

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

Adapted from Jafari et al.\(^7\)

*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.

## 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

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**Source:** Disease Control Priorities


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

http://www.who.int/reproductivehealth/topics/rtis/Diagnostic_Landscape_2017.pdf
# Target Product Profile: Dual HIV-Syphilis Test

## 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

<table>
<thead>
<tr>
<th></th>
<th>HIV Infection</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference Test/Gold Standard</td>
<td>ELISA/EIA</td>
<td>TPPA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Minimal</th>
<th>Optimal</th>
<th>Minimal</th>
<th>Optimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Sensitivity</td>
<td>&gt;98%</td>
<td>&gt;99%</td>
<td>&gt;85%</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>Clinical Specificity</td>
<td>&gt;98%</td>
<td>&gt;99%</td>
<td>&gt;95%</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>Quantitation</td>
<td>None: Qualitative Test</td>
<td>None: Qualitative Test</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### MINIMAL AND OPTIMAL OPERATIONAL CHARACTERISTICS FOR COMBINED HIV/SYPHILIS ASSAY

<table>
<thead>
<tr>
<th></th>
<th>Minimal</th>
<th>Optimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Specimen</td>
<td>Fingerstick capillary blood (maximum 50μL)</td>
<td>Fingerstick capillary blood (maximum 20μL)</td>
</tr>
<tr>
<td>Sample Preparation</td>
<td>Minimal sample processing; no more than 1 operator step</td>
<td>Integrated</td>
</tr>
<tr>
<td>Steps performed by healthcare worker between sample preparation and result</td>
<td>No more than 3 operator steps (only one of which is timed), excluding waste disposal</td>
<td>Operator step (none of which is timed), excluding waste disposal</td>
</tr>
<tr>
<td>Additional 3rd party consumables</td>
<td>None, except for sample collection</td>
<td>None, except for sample collection</td>
</tr>
<tr>
<td>Cold Chain</td>
<td>None required at any point in supply chain or storage</td>
<td>None required at any point in supply chain or storage</td>
</tr>
<tr>
<td>Kit</td>
<td>All materials required for assay and reagents, including buffers or other consumables to diagnose one patient, included in individually packaged, self-contained kit</td>
<td>All materials required for assay and reagents, including buffers or other consumables to diagnose one patient, included in individually packaged, self-contained kit</td>
</tr>
<tr>
<td>Kit Stability and storage conditions</td>
<td>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)</td>
<td>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)</td>
</tr>
</tbody>
</table>

www.idc-dx.org
ASSURED Tests for improving Access to STI testing

\[
\begin{align*}
A &= \text{Affordable} \\
S &= \text{Sensitive} \\
S &= \text{Specific} \\
U &= \text{User-friendly} \\
R &= \text{Rapid and robust} \\
E &= \text{Equipment-free} \\
D &= \text{Deliverable}
\end{align*}
\]

- ✓ Affordable
- ✓ Accurate
- ✓ Accessible
Trade-off between Access vs Sensitivity

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

<table>
<thead>
<tr>
<th>OraQuick Test</th>
<th>Professional Use</th>
<th>Over-the-Counter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum Recommended Performance for the lower bound of 2-sided 95% CI</td>
<td>Actual Performance</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>98%</td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td>98%</td>
<td></td>
</tr>
</tbody>
</table>

*95%CI = 95% Confidence Interval*
## FDA Approval: OraSure HIV Test

<table>
<thead>
<tr>
<th>Accuracy</th>
<th>Professional Use</th>
<th>Over-the-Counter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum Recommended Performance: lower bound of 2-sided 95% CI</td>
<td>Actual Performance</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>98%</td>
<td>99.3% (98.4-99.7%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>98%</td>
<td>99.8% (99.6-99.9%)</td>
</tr>
</tbody>
</table>

**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
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.

- 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.

* 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.

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

<table>
<thead>
<tr>
<th></th>
<th>Comparison with HIV ELISA</th>
<th>Comparison with TPPA/TPHA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
<td>Specificity (%)</td>
</tr>
<tr>
<td>SD Bioline</td>
<td><strong>99.0</strong> (98.0-99.5)</td>
<td><strong>99.0</strong> (98.0-99.5)</td>
</tr>
<tr>
<td>Chembio</td>
<td><strong>99.6</strong> (98.8-99.9)</td>
<td><strong>97.9</strong> (96.7-98.7)</td>
</tr>
<tr>
<td>MedMira</td>
<td><strong>99.5</strong> (99.4-99.8)</td>
<td><strong>98.3</strong> (97.2-99.0)</td>
</tr>
</tbody>
</table>

N=1,514 specimens
Performance of HIV Component of the Dual HIV syphilis tests

Performance of Syphilis Component of the Dual HIV syphilis tests

Performance of the ChemBio DPP Trep-Non Trep Combo Test

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

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

NA, not applicable.

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


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

Global Targets for eMTCT HIV/Syphilis

As of 2017:
- Cuba (2015)
- Thailand (2016)
- Belarus (2016)
- Moldova (Syphilis only, 2016)
- Armenia (HIV only, 2016)

- Access ANC: 95%
- Tested for HIV & Syphilis: 90%
- Treated: 95%
 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**

<table>
<thead>
<tr>
<th>Number of times going to HC</th>
<th>Activity</th>
<th>Number of days spent</th>
</tr>
</thead>
</table>
| 1st Contact                 | - Filling out documents  
                            - (ANC service)  
                            - Anti-tetanus vaccine | 1 |
| 2nd y 3rd Contact           | Processing of Social security insurance | 8 |
| 4th Contact                 | ANC service – paper work for lab tests | 1 |
| 5th Contact                 | - Laboratory – sampling  
                            - Use of venous blood for HIV RT | 2 |
| 6th Contact                 | - ANC – tests results provided  
                            - Pen G not available in ANC services  
                            - Partners not treated  
                            - No monitoring of patients in treatment | 15 |

Approximately 27 days have passed between the time when the patient came for the first time until the time when the patient received treatment.

Data Connectivity: Automated reporting from POC tests/readers

Connectivity

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

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.
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

• 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

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
Syphilis Outbreak

FIGURE 1: Monthly number of infectious syphilis cases per year, by sex and RHA.

(data from January 01, 2013 to August 31, 2017)
Social Networks: Syphilis cases and locations where they met new sexual partners over the last 12 months.

House Parties 48.1%

Work 10.4%

Hotels/Bars 22.6%

Outdoors 9.4%

Shapes: Circle=Male, Triangle=Female, Square=Locations
Colours: Purple=City/Towns Red=Smaller Remote Communities Yellow=Location
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!