Evaluation of New HIV Testing Technologies in a Clinical Setting with High Incidence: Rationale, Study Design and Preliminary Results from Project DETECT

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Special Studies and Diagnostics Team

The views expressed in this presentation are those of the authors and do not necessarily represent those of the Centers for Disease Control and Prevention
Project DETECT:
Diagnostic Evaluation To Expand Critical Testing Technologies
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A research contract with University of Washington and Public Health - Seattle & King County funded by CDC

**CDC**
- Kristina Bowles
- Pollyanna Chavez
- Elizabeth DiNenno
- Kevin Delaney
- Steven Ethridge
- John Lacey
- Silvina Masciotra
- Michele Owen
- Marc Pitasi
- Laura Wesolowski

**UW**
- Andy Cornelius
- Lindsey Legg
- Janine Maenza
- Sarah McDougal
- Vanessa McMahan
- Joanne Stekler
- George Ure

**Public Health – Seattle & King County**
- Alfred Iqbal
- David Katz (also UW)
- Candice Le
- Paul Swenson
- STD Clinic staff and leadership
Background and Need

- HIV testing is the gateway to care and treatment
- Need to know which tests to recommend given changing testing landscape
- DHAP monitors new tests to keep guidelines current

- We need to compare tests head-to-head
Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50% Positive Cumulative Frequency

and Owen et al, J Clin Micro 2008
Sequence of Test Positivity Relative to WB (plasma)

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Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50% Positive Cumulative Frequency


Luo et al, J Clin Virol 2013
Background and Need

- DETECT is a prospective evaluation in a clinical setting looking at unprocessed specimens (oral fluid, whole blood) with plans to evaluate:
  - A new oral fluid rapid test (DPP)
  - New fingerstick rapid tests (Determine, INSTI)
  - A new HIV-1/HIV-2 differentiation test (Geenius) (using Fingerstick, EDTA WB and Plasma)
  - Simplified nucleic acid tests (using WB and potentially plasma)
DETECT objectives

1. Evaluate test sensitivity and specificity:
   - ~600 established positive specimens
   - ~50-60 seroconverters
   - Nearly 6000 HIV-negative specimens

2. Evaluate seroconversion sensitivity via serial follow-up for whole blood, oral fluid and plasma

3. Evaluate risk characteristics of those identified in seroconversion

4. Assess transmission risks for seroconverters compared to participants with newly diagnosed and previously diagnosed infection
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Project DETECT: Study components

Part 1: Identify highest risk persons and HIV-infected clients

Behavioral Survey

Low risk clients
standard testing

High Risk participants

Part 2: Head to head evaluation of novel HIV tests (n=6,000)

Low Risk participants with positive HIV test

Referrals into the study with positive HIV test

1. Behavioral Survey
2. Testing with 6 novel POC tests

600 established positives

Part 3: Document seroconversion – 70 day follow up

>100 Participants with discordant POC test results (at least 50 with early infection)

9 visits with testing:
- 6 novel POC tests
- collection of more specimens: OF, DBS plasma
- last visit: survey

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Project DETECT: Visit Flow

Discuss study and obtain oral consent
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Link study and clinic IDs
Project DETECT: Visit Flow

Discuss study and obtain oral consent

Link study and clinic IDs

Read 25 – 40 min

IF DISCORDANT:
Save this sampletainer
Project DETECT: Visit Flow

Discuss study and obtain oral consent

Link study and clinic IDs

IF DISCORDANT:
Save this sampletainer

Read 25 – 40 min

[DPP OMT 2]

10 mL

10 mL

4 mL

10 mL

10 mL
Project DETECT: Visit Flow

Discuss study and obtain oral consent

Link study and clinic IDs

IF DISCORDANT:
Save this samplétainer

Read 25 – 40 min

For STORAGE only

Read 20 – 40 min
Project DETECT: Visit Flow

1. Discuss study and obtain oral consent
2. Link study and clinic IDs
3. IF DISCORDANT: Save this samplentainer
   - Read 25 – 40 min
4. Read 20 – 40 min
5. Participant completes survey
Project DETECT: Visit Flow

Discuss study and obtain oral consent

Link study and clinic IDs

IF DISCORDANT: Save this samptainer

Read 25 – 40 min

[For STORAGE only]

For STORAGE only

4 mL

10 mL

10 mL

10 mL

Read 20 – 40 min

Read 20 – 40 min

Read 20 – 40 min

Read 20 – 40 min

Prepare for overnight drying

Participant completes survey

4 mL

For STORAGE only

[DPP WB]

[DPP OMT]

[DPP OMT]

For STORAGE only

4 mL

For STORAGE only

IF DISCORDANT:

Save this samptainer

4 mL

Read 21 – 30 min

Read 10 – 45 min

Read 0 – 1 min

4 mL

4 mL

4 mL

4 mL

4 mL

4 mL
Project DETECT: Visit Flow

Discuss study and obtain oral consent → Link study and clinic IDs → IF DISCORDANT: Save this samplentainer → Read 25 – 40 min

[Image: Diagram showing the process]

Participants complete survey → IF ANY positive POC result: Run POC Geenius → Read 15 – 20 min

[Image: Diagram showing the process]

For STORAGE only

[Image: Diagram showing the process]
How do you do 12 tests with one patient at the same time?

- Very carefully...
Project DETECT: Specimen Storage

Place specimen bag in clinic refrigerator

- **CLINIC Bag**
  - EIA Syphilis
  - 10 mL

- **Concordant STUDY Bag**
  - 10 mL
  - 10 mL
  - STORAGE

- **Discordant STUDY Bag**
  - 10 mL
  - 10 mL
  - STORAGE
  - POC
  - [DPP OMT 2]
  - [DPP WB]

- [POC]

- We retain approximately 9ml of Plasma, and at least two matched OMT specimens
PHSKC Clinical Care

DatStat Web-based Kiosk
- Behavior & medical hx
- Entered by patient

PHSKC Lab
- Lab test results
- Entered by lab

Clinic Charts
- Clinical exam
- Recorded by clinician

Epic
- Exam & lab results

STD Clinic Data
Merge in SAS

Part 1

Aggregate data comparing Part 2 participants to all clinic patients

Part 2

Study test results (G1)

Study test results (G2-G3)

Study CASIs (Part 2)
- Consent, behavior, & medical hx
- Entered by patient

Study-Clinic ID Link
- Entered by study staff

Study Charts
- Consent, contact info, visit

Study CASIs (Part 3)
- Behavior & medical hx
- Entered by patient

Study test results (Part 3)
- Entered by study staff

Clinic-Study Data 1
- Clinic & Study Survey Part 2 merged via Link

Part 2 Dataset
To CDC

Part 3

Clinic-Study Data 2
- Clinic-Study 1 & Part 3 Data merged via Study IDs

Part 3 Dataset
To CDC

Part 2

Lab Tracking
Specimens to CDC

Part 3

Clinic-Study Data 2
- Clinic-Study 1 & Part 3 Data merged via Study IDs

Part 3 Dataset
To CDC

Lab Tracking
Specimens to CDC

PII removed, except Clinic ID and date of service

PII not included

To CDC
Earliest results

- Soft launch of testing and enrollment procedures began in September 2015
  - Through February 2016
    - 182 Offered participation
    - 143 accepted (79%)
      - All presumed HIV-negative and at high risk for infection
    - 3 persons with laboratory results indicative of early HIV infection and
    - 1 person with known established HIV-infection referred to the project
Earliest results

- Of 147 total tested
  - 137 concordant negative
  - 4 concordant positive (3 ART Naïve)
  - 6 with discordant results (3 AHI referrals plus 3 with reactive results on only 1 test)
  - 4 enrolled in follow-up (2 with results considered likely to be false-positive declined)
Our first Part 3 participant: Interesting, NOT seroconversion

<table>
<thead>
<tr>
<th>Test</th>
<th>Day of follow-up</th>
<th>0</th>
<th>3</th>
<th>7</th>
<th>10</th>
<th>14</th>
<th>21</th>
<th>28</th>
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<th>56</th>
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<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>DPP Oral</td>
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<td>N</td>
<td>N</td>
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<td></td>
<td>N</td>
<td>N</td>
<td>N</td>
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<td>N</td>
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<td>N</td>
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<tr>
<td>Oraquick FS</td>
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<td>N</td>
<td>N</td>
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<td>N</td>
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<td>N</td>
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<td>N</td>
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<tr>
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<td></td>
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<td>N</td>
<td>N</td>
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<td>N</td>
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<td>N</td>
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<td>N</td>
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<td>N</td>
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<td>N</td>
</tr>
<tr>
<td>Insti WB</td>
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<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
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</tr>
<tr>
<td>Insti FS</td>
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<td>P</td>
<td>N</td>
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<td>P</td>
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<tr>
<td>Determine Combo</td>
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<tr>
<td>Determine FS</td>
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<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
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</tr>
</tbody>
</table>
### Example 2 - Much more interesting seroconversion data

<table>
<thead>
<tr>
<th>Test</th>
<th>Day of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Oraquick Oral</td>
<td>N</td>
</tr>
<tr>
<td>DPP Oral</td>
<td>N</td>
</tr>
<tr>
<td>Oraquick WB</td>
<td>N</td>
</tr>
<tr>
<td>Oraquick FS</td>
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<td>P</td>
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</tr>
<tr>
<td>Determine Combo WB</td>
<td>P</td>
</tr>
<tr>
<td>Determine FS</td>
<td>NA</td>
</tr>
</tbody>
</table>
## Example 2 – Geenius, Multispot and 4\textsuperscript{th} gen screening data

<table>
<thead>
<tr>
<th>Test</th>
<th>Day of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Geenius WB</td>
<td>HIV Neg</td>
</tr>
<tr>
<td>Geenius Bands detected WB</td>
<td>ND</td>
</tr>
<tr>
<td>Geenius FS</td>
<td>NA</td>
</tr>
<tr>
<td>Geenius Bands FS</td>
<td>NA</td>
</tr>
<tr>
<td>BioRad Combo S/CO</td>
<td>1.66</td>
</tr>
<tr>
<td>Multispot</td>
<td>N</td>
</tr>
</tbody>
</table>
More on Example 2

- Tested BioRad Combo reactive, MS negative on 11/17/2015, VL >39,000
- By 11/20, BioRad Combo reactive, Western blot negative, VL >370,000

<table>
<thead>
<tr>
<th>Reported Symptom</th>
<th>Onset Date</th>
<th>End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>11/8/2015</td>
<td>12/03/2015</td>
</tr>
<tr>
<td>Nausea</td>
<td>11/12/2015</td>
<td>11/27/2015</td>
</tr>
<tr>
<td>Vomiting</td>
<td>11/12/2015</td>
<td>11/29/2015</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>11/12/2015</td>
<td>11/27/2015</td>
</tr>
<tr>
<td>Fever</td>
<td>11/14/2015</td>
<td>11/19/2015</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Last three UAI partners</th>
<th>Date of last reported UAI</th>
<th>Participant reported status of partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11/5/2015</td>
<td>HIV negative</td>
</tr>
<tr>
<td>2</td>
<td>9/15/2015</td>
<td>HIV negative</td>
</tr>
<tr>
<td>3</td>
<td>11/6/2015</td>
<td>HIV negative</td>
</tr>
</tbody>
</table>
Summary of our early results

- Our earliest results have provided useful information
  - We identified 1 individual who was serially false-positive on only one test
  - We have identified 3 individuals in the earliest stages of infection
    - 2 started treatment and their results are likely affected by this
    - 1 did not remain engaged in the study

- We are re-building our repository of specimens for future diagnostics evaluations
  - Serial false-positive specimens and seroconversion panels, as well as true positive specimens on and off therapy
Next Steps

- Ramp up enrollment of highest risk persons to identify newly infected persons at the POC
  - Hope to add POC NAT testing in FY 2017
    - an incentive to test and more rapid identification of early infections
  - Now 2 research assistants working full time on the project, which should double capacity
  - Implementing same-day referrals at the disclosure appointment for persons with early infection

- Expand recruitment of persons with known HIV-infection to stabilize sample size for estimates of test sensitivity
Thanks Again!

CDC
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<td>NA P  P  P  P  P  P  P  P  P  N</td>
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<td>Insti WB</td>
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<tr>
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Example 4 – Not so interesting seroconversion data

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<td>P  P</td>
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<td>NA  P</td>
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<td>P  P</td>
</tr>
<tr>
<td>Determine FS</td>
<td>NA  P</td>
</tr>
</tbody>
</table>
Background/Need

A new Oral fluid test – Chembio DPP

Tests CBOs may be using

Insti HIV-1/HIV-2
A 60-second, CLIA-waived blood test

Determine Antigen/Antibody test
Background/Need

Tests CBOs may be using

Insti HIV-1/HIV-2
A 60-second, CLIA-waived blood test

Determine Antigen/Antibody test

Tests (soon to be?) available in clinics/labs

A new HIV-1/HIV-2 differentiation test

Several Point-of-Care Nucleic Acid Tests