Dr Suneeta Soni
Brighton and Sussex University Hospitals NHS Trust
Dr Suneeta Soni
Brighton and Sussex University Hospitals
NHS Trust

<table>
<thead>
<tr>
<th>Speaker Name</th>
<th>Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td>April 2015</td>
</tr>
</tbody>
</table>
The Latest in STI Diagnostics

DR. SUNEETA SONI
CLAUDE NICOL CLINIC, BRIGHTON
Number of STI diagnoses among MSM: England, 2004-2013

- Data from routine GUM service returns; New HIV diagnoses sourced from HIV & AIDS New Diagnoses & Deaths Database
- * First episode; ** Includes diagnoses of primary, secondary & early latent syphilis
- Chlamydia data from 2012 onwards are not comparable to data from previous years (please see ‘Notes’ slide for more details)
- Data type: service data
Number of STI diagnoses among MSM by HIV status: England, 2013

- Data from routine GUM service returns
- * First episode; ** Includes diagnoses of primary, secondary & early latent syphilis
- HIV diagnosed includes those who were diagnosed with HIV more than 6 weeks prior to their STI infection
- Data type: service data
HIV clinic 2015

- Blood results
- Any problems?
- Adherence check
- New medications
- FRAX score
- Qrisk
- Alcohol and party drugs
- Eligible for study?
- HARS form

20 minutes

STI SCREEN!!!
Diagnostic pathway

Specimen collection

Laboratory test

Inform of results

Near patient test

Treatment of patient and partners
Assessment of best single sample for finding chlamydia in women with and without symptoms: a diagnostic test study

*BMJ* 2012; 345 doi: http://dx.doi.org/10.1136/bmj.e8013 (Published 12 December 2012)
Cite this as: *BMJ* 2012;345:e8013

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Assessment of self taken swabs versus clinician taken swab cultures for diagnosing gonorrhoea in women: single centre, diagnostic accuracy study

*BMJ* 2012; 345 doi: http://dx.doi.org/10.1136/bmj.e8107 (Published 12 December 2012)
Cite this as: *BMJ* 2012;345:e8107

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Schoeman et al

Stewart et al
Assessment of best single sample for finding chlamydia in women with and without symptoms: a diagnostic test study

Self-taken vulvovaginal swabs better at detecting chlamydia than endocervical swabs
Equivalent for detection of gonorrhoea

Stewart et al
**Table 3** The sensitivity and specificity of self-taken and nurse-taken swabs for the detection of CT and GC

<table>
<thead>
<tr>
<th>Method of collection</th>
<th>Sensitivity (95% CI)</th>
<th>p Value (no of true positives)</th>
<th>Specificity (95% CI)</th>
<th>p Value (no of true negatives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal GC* (n = 262)</td>
<td>Nurse 94.9% (82.7 to 99.4)</td>
<td>1.00 (39)</td>
<td>90.1% (85.4 to 93.7)</td>
<td>0.30 (223)</td>
</tr>
<tr>
<td></td>
<td>Patient 92.3% (79.1 to 98.4)</td>
<td>0.50 (17)</td>
<td>87.9% (82.9 to 91.9)</td>
<td>0.006 (245)</td>
</tr>
<tr>
<td>Pharyngeal GC* (n = 262)</td>
<td>Nurse 88.2% (63.6 to 98.5)</td>
<td></td>
<td>91.8% (37.7 to 94.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patient 100% (80.5 to 100)</td>
<td></td>
<td>87.8% (33.0 to 91.6)</td>
<td></td>
</tr>
<tr>
<td>Rectal CT† (n = 258)</td>
<td>Nurse 80.0% (63.1 to 91.6)</td>
<td>0.13 (35)</td>
<td>99.6% (97.5 to 100)</td>
<td>0.25 (223)</td>
</tr>
<tr>
<td></td>
<td>Patient 91.4% (76.9 to 98.2)</td>
<td></td>
<td>98.2% (95.5 to 99.5)</td>
<td></td>
</tr>
</tbody>
</table>

*Nurse and patient-taking swabs (tested by AC2) compared with GC culture results.
†Nurse and patient-taking swabs (tested by AC2) compared with clinic strand displacement assay (SDA) result.
CT, C trachomatis; GC, N gonorrhoeae.
## Acceptability of self taken samples for STIs in MSM

<table>
<thead>
<tr>
<th>Paper</th>
<th>Year</th>
<th>Place</th>
<th>Study</th>
<th>N</th>
<th>Acceptability (men)</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown L</td>
<td>2006</td>
<td>Birmingham, UK</td>
<td>Randomised to Non invasive testing (NIT) pathway (no rectal swabs, clinician taken throat swabs (SOC): men and women</td>
<td>101</td>
<td>90% NIT Experience better than expected 69% NIT not uncomfortable</td>
<td>Significantly reduced time in clinic, improved patient experience</td>
</tr>
<tr>
<td>Lampinen TM</td>
<td>2003</td>
<td>Vancouver, Canada</td>
<td>Clinician taken v self taken anal cytology MSM</td>
<td>222</td>
<td>Overall 4.48/5</td>
<td>Excellent concordance</td>
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<tr>
<td>Cranston R</td>
<td>2004</td>
<td>San Francisco, USA</td>
<td>Home anal cytology following biopsy MSM</td>
<td>102</td>
<td>NA</td>
<td>10% declines 20% non return of specimens</td>
</tr>
<tr>
<td>Freeman AH</td>
<td>2009</td>
<td>San Francisco, USA</td>
<td>Self taken v clinician taken pharyngeal samples in MSM</td>
<td>480</td>
<td>Ease 4.03/5  Comfort 2.64/5 Willing 4.31/5 Prefer 3.05/5</td>
<td>99.4% concordance</td>
</tr>
<tr>
<td>Van der Helm J</td>
<td>2006</td>
<td>Netherlands</td>
<td>Self taken v clinician taken rectal samples in MSM (also women)</td>
<td>1458</td>
<td>94% would use again 97% would return if standard 94% easy 91% comfortable</td>
<td>98% concordance</td>
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<tr>
<td>Sexton ME</td>
<td>2009</td>
<td>Washington DC, USA</td>
<td>Self taken v clinician taken pharyngeal &amp; rectal swabs in MSM</td>
<td>374</td>
<td>NA</td>
<td>Anecdotal 7/374 had difficulties with procedures</td>
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<td>Soni S</td>
<td>2009</td>
<td>London, UK</td>
<td>Review of self taken swabs offered in HIV OPD</td>
<td>100</td>
<td>100% all HIV (only 21 MSM)</td>
<td>Addresses barriers to STI testing in HIV clinics</td>
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<td>Wayal S, Phase-1</td>
<td>2006</td>
<td>Brighton, UK</td>
<td>Self taken v clinician taken swabs and questionnaire MSM</td>
<td>301</td>
<td>Pharyngeal swab 76% Rectal Swab 82%</td>
<td>T-76% R-82%</td>
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<tr>
<td>Fisher M, Phase-2</td>
<td>2009</td>
<td>Brighton, UK</td>
<td>Home sampling for STIs from GUM, HIV and outreach</td>
<td>574</td>
<td>Overall acceptance rate = 75%</td>
<td>Overall uptake/return = 35%</td>
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<td>Dodge B</td>
<td>2010</td>
<td>Indianapolis, USA</td>
<td>Qualitative/quantitative evaluation of rectal sampling in MSM</td>
<td>75</td>
<td>72% happy to do rectal swab again</td>
<td>81% prefer MSM venue 16% called for results</td>
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Acceptability of self-taken swabs range 69%-100%
Sampling technique is important for optimal isolation of pharyngeal gonorrhoea

M Mitchell¹, V Rane¹, C K Fairley¹,², D M Whiley³,⁴, C S Bradshaw¹,²,⁵, M Bissessor¹, M Y Chen¹,²


swabbing a larger surface area
applying more swab pressure
swabbing the right anatomical sites

Patients should be able to self swab but they need to be told how!
Overall prevalence of CT and GC was 17.4%, mainly rectal.
Pooling self-taken pharyngeal, urine and rectal samples into a single sample for analysis

Comparable sensitivities Pooled swab v single site
Using Genprobe Aptima Combo assay

<table>
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<th>Sensitivity (%)</th>
</tr>
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<td>Pooled Specimen</td>
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<tr>
<td>Gonorrhoea</td>
<td>92.9</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>93.1</td>
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Cost saving potential for MSM and women?
Similar MSM study using BDQx assay, Brighton 2015

Sultan et al. ISSTDR Vienna 2013
Diagnostic pathway

Specimen collection → Laboratory test → Near patient test → Inform of results → Treatment of patient and partners
Diagnostic pathway

Specimen collection

Laboratory test

Near patient test

Inform of results

Treatment of patient and partners
Chlamydia and gonorrhoea

Diagnosed using dual NAAT
Confirm GC with supplementary test if low prevalence population
Gonococcal resistance is a real threat, resistance testing relies on culture of organism
CT and GC are mainly non-genital and asymptomatic
LGV is endemic and circulating strains that are asymptomatic
Cepheid GeneXpert

Turnaround 90 minutes
Highly sensitive and specific
2 GC targets
Cepheid GeneXpert

Highly sensitive and specific
2 GC targets
Turnaround 90 minutes

GeneXpert Infinity - 80 samples
Dean St. pilot:
  ◦ Test to treatment time reduced – 8 days to 1 day
  ◦ Informing to treatment time remained 1 day

Whitlock et al. Sex Transm Infect 2014;90:474
How rapid does rapid need to be?

Willingness to wait for a rapid test result
- 59% said 20 minutes
- 20.8% said 40 minutes

Huang W et al. Sex Transm Infect 2013 Mar;89(2):108-14

What’s the point?

Convenient for patient
Convenient for clinic
Aim to reduce risk of onward transmission
Opportunity for risk reduction discussion
Atlas Velox

Near patient test

20-30min

Detection of electrochemical labels
Near patient test

20-30min

Detection of electrochemical labels


**Blind evaluation of the microwave-accelerated metal-enhanced fluorescence ultrarapid and sensitive Chlamydia trachomatis test by use of clinical samples.**

Melendez JH¹, Huppert JS, Jett-Goheen M, Hesse EA, Quinn N, Gaydos CA, Geddes CD.

The first assay targeted the C. trachomatis 16S rRNA gene, and the second assay targeted the C. trachomatis cryptic plasmid. Using pure C. trachomatis, the MAMEF assays detected as few as 10 inclusion-forming units/ml of C. trachomatis in less than 9 min, including DNA extraction and detection. A total of 257 dry vaginal swabs from 245 female adolescents aged 14 to 22 years were analyzed. Swabs were eluted with water, the
Syphilis

1906 1910
Dark ground microscopy

1943
Wasserman reaction

1957 1961
Penicillin

RPR

Fluorescent Trep Ab test

1987
ELISA

1992
Syphilis PCR

2015
Syphilis and HIV

- 1906: Dark ground microscopy
- 1910: Wasserman reaction
- 1943: Penicillin
- 1957: Fluorescent Trep Ab test
- 1961: RPR
- 1984: HIV isolated
- 1987: ELISA
- 1992: Syphilis PCR
- 1997: Viral load assay
- 2002: First rapid Ab test
- 2005: 4th generation Ag/Ab test
- 2015: 37 antiretroviral drugs licensed for use
- 2015: Development of many rapid tests – variable sensitivity
Novel Point-of-Care Test for Simultaneous Detection of Nontreponemal and Treponemal Antibodies in Patients with Syphilis

Arnold R. Castro, Javan Esfandiari, Shailendra Kumar, Matthew Ashton, Susan E. Kikkert, Mahin M. Park, and Ronald C. Ballard

How active or inactive?
Previously treated or not?
Adequately treated or not?
Neurosyphilis or not?
Trichomonas vaginalis


Epidemiological synergy of Trichomonas vaginalis and HIV in Zimbabwean and South African women.


Trichomonas vaginalis infection and human immunodeficiency virus acquisition in African women.


Infection with Trichomonas vaginalis increases the risk of HIV-1 acquisition.
Trichomonas vaginalis

Wet mount microscopy
- Trained microscopist
- Fresh sample
- Not suitable for HIV clinics

Culture is gold standard

Aptima TV NAAT

OSOM 10 minute Ag test
Mycoplasma genitalium

Known cause of male urethritis
Possible role in PID and cervicitis
No FDA approved commercial assay
Currently many “in-house” PCRs
Association between *Mycoplasma genitalium* infection and HIV acquisition among female sex workers in Uganda: evidence from a nested case–control study

*M. Genitalium* may be a co-factor in the transmission of HIV

Rectal *M. Genitalium* more prevalent in HIV-positive MSM
Macrolide resistance and azithromycin failure in a *Mycoplasma genitalium*-infected cohort, and response of azithromycin failures to alternative antibiotic regimens

Bissessor et al. *Clin Infect Disease* 23 March 2015

39% failure rate with Azithromycin 1g

High levels of pre-treatment macrolide resistance

- Urgent need for screening diagnostics
- With a resistance test
- Hologics 2016
- New multiplexes
New Multiplexes

Biorad CT/NG/MGen
Becton Dickinson CT/NG/TV
Fast Track Diagnostics CT/NG/TV
Atlas CT/NG/TV/MGen..................................................and lots more........

Current commercial platforms struggle to detect multiple targets
New assays must be rigorously tested
How many tests for the price of one?
Total solution for the detection of pathogens causing STDs

Seeplex® STI Master ACE Detection detects 25 pathogens causing sexually transmitted infection (STI) from patients' samples.

25 STIs!!!!
## Analytes

### Master Panel 1
For screening cervicitis, urethritis, trichomoniasis and PID

- *Trichomonas vaginalis*
- *Mycoplasma hominis*
- *Mycoplasma genitalium*
- *Chlamydia trachomatis* (CE0086)
- *Neisseria gonorrhoeae*
- *Ureaplasma urealyticum/pavum*

### Master Panel 2
For screening of bacterial vaginosis

- *Gardnerella vaginalis*
- *Bacteroides fragilis*
- *Mobiluncus curtisi*
- *Aptopobium vaginae*
- *Mobiluncus mulieres*

### Master Panel 3
For detection of candidiasis

- *Candida glabrata*
- *Candida tropicalis*
- *Candida parapsilosis*
- *Candida krusei*
- *Candida albicans*
- *Candida dubliniensis*

### Master Panel 4
For detection of trichomoniasis and typing of HSV

- *Trichomonas vaginalis*
- Herpes Simplex Virus 1
- Herpes Simplex Virus 2

### Master Panel 5
For diagnosis of soft-chancroid, hard-chancroid, ulcer and GBS

- *Cytomegalovirus* (CMV)
- *Treponema pallidum*
- *Haemophilus ducreyi*
- Group B *Streptococcus* (GBS)
- *Lymphogranuloma venereum* (LGV)
STI Multiplex Array - Rapid, simultaneous detection of 10 sexually transmitted infections (STIs)

STI Multiplex Array detects:

- Chlamydia trachomatis
- Neisseria gonorrhoea
- Herpes simplex 1
- Herpes simplex 2
- Treponema pallidum
- Mycoplasma hominis
- Ureaplasma urealiticum
- Mycoplasma genitalium
- Haemophilus ducreyi
- Trichomonas vaginalis

6 hour turnaround

“...will simultaneously detect all pathogens from a single patient sample...”

- which sample??
Popular Tests

Chlamydia Test
Read more £29.95 Buy now >

Chlamydia and Gonorrhoea Test
Read more £39.95 Buy now >

HIV Screen
Read more £39.95 Buy now >

Full STI Screen
Read more £149.95 Buy now >

Home sampling

Discreet Home STI Test
Quantity 1 UPDATE

Postage Option (Please select)

Total price: £85.00

NEXT
Which test have they used?

Has the test been validated?

GC -
- Is it a true positive?
- Was the test confirmed

MH and UU
- Inconclusive evidence for testing and treating

What about CT and MG?
- Is this multiplex sensitive enough?

No hepatitis screening
No extragenital testing
Take a test
Text the word TEST and your name and address to 84010
You will receive a pot
Simply pee in the pot and post back
You will get your results via a text

SH:24
Test at home
STI results by text in 7 days
Order a free test
Currently only available to residents of Southwark and Lambeth
Self-test mobile-phone networked micro-diagnostics

Access to online prescriptions for patients and partners
Your HIV clinic is a real opportunity to test for STIs......
......self sampling is largely acceptable and reliable
Your HIV clinic is a real opportunity to test for STIs……
……self sampling is widely acceptable and reliable

LOOKING FORWARD

- Rapid tests are getting quicker and more sensitive
- More efficient and therefore cheaper
- Exciting developments in diagnostics using the internet and mobile applications, home testing
Your HIV clinic is a real opportunity to test for STIs......
......self sampling is widely acceptable and reliable

LOOKING FORWARD

- Rapid tests are getting quicker and more sensitive
- More efficient and therefore cheaper
- Exciting developments in diagnostics using the internet and mobile applications along with newer technologies

CHALLENGES

- Need to learn to use these tests properly and in the right patients
- Caution with “one test fits all” approach
- Studies to understand more about home sampling and home testing
Can these tests be more functional?

- resistance testing
- genotyping
- biomarkers for level of infectivity
Diagnostic pathway

Specimen collection -> Laboratory test -> Near patient test

Inform of results -> Treatment of patient and partners
HIV clinic 2025 – nurse appointment

- Rapid VL +/- CD4
- Rapid Chlamydia, gonorrhoea +/- mycoplasma and trichomonas
- Rapid syphilis

30 minutes
HIV clinic 2025 – doctor appointment

- CD4 520 cells/µl
- VL <1 copy
- Pharyngeal and rectal GC sensitive to ceftriaxone
- Rectal chlamydia – L2 serovar
- Early syphilis re-infection – needs neurosyphilis treatment

Prescribe treatment and refer to health advisor for partner notification.
Acknowledgements

Prof. Martin Fisher
Dr. Daniel Richardson
Dr. John White
Dr. Claudia Estcourt
Dr. Nneka Nwokolo

Dr. Mike Brady
Dr. Tariq Sadiq
Dr. Sarah Alexander
Dr. John Saunders

[Sexual Health & Venereal Disease information]
“....Martin was indeed so much more than just my doctor. His inspirational work gave us confidence and determination and we counted him as a friend.”

“.....Martin was a baby doctor when I first met him what, 20 years ago, or more to become so renowned in his field. We had such a giggle when he became a Professor! I will miss our chats about football and life, he was a confidante, a friend and a brilliant doctor…”

“....he was more than my HIV specialist he became a friend if only for the short but important times we had appointments....”

Emails from Lawson Unit patients, received 22 April 2015
21st Annual Conference of the British HIV Association (BHIVA)

#BHIVA2015

21–24 April 2015

The Brighton Centre, Brighton, UK