Viral load and transmission
Does U=U?

Simon Collins
HIV i-Base
www.i-Base.info
**HIV transmission**

Big changes in last few years:

- Treatment as Prevention (TasP) & PrEP
  - Does U=U? Am I uninfectious?
  - What does it mean to be undetectable?
  - Your health now and in the future, your relationships, your Quality of life
  - Evidence (vs stigma and fear)
Does U=U?
Am I uninfectious?

- Easy vs complex answers?
- Residual prejudice/concern etc?
- Limits of science?
- Legal issues: criminalisation and liability for health workers?
- Historical approach to condoms?
- Risk in life?
- Evidence: PARTNER and other studies
U=U

UNDetectable = UNTransmittable

A PERSON LIVING WITH HIV WHO HAS AN UNDETECTABLE VIRAL LOAD DOES NOT TRANSMIT THE VIRUS TO THEIR PARTNERS.

The International AIDS Society is proud to endorse the U=U consensus statement of the Prevention Access Campaign.

www.preventionaccess.org/undetectable
If your viral load is undetectable, it means you can't pass HIV to others. Treatment = Prevention! on.nyc.gov/staysure #PlaySure #TasP

HIV treatments can make the virus undetectable, meaning it cannot be passed on

#TestWeekScot

www.preventionaccess.org/undetectable
PEOPLE WITH HIV ON EFFECTIVE TREATMENT DO NOT SEXUALLY TRANSMIT HIV
UNDetectable = UNtransmittable

www.preventionaccess.org/undetectable
Timeline

1998 ART stops mother to baby transmission [2]
2000 Rakai Study (Observational) [3]
2008 Swiss Statement: zero risk (Evidence review) [4]
2011 HPTN 052: 1 vs 27 (Randomised: low risk) [5]
2014 PARTNER: zero/44,000 (Observational: high risk) [6]
2016 PARTNER published – zero/58,000 [6]
2016 U=U + wide endorsements

Timeline

1998 ART stops mother to baby transmission [2]
2000 Rakai Study (Observational) [3]
2011 HPTN 052: 1 vs 27 (Randomised: low risk) [5]
2014 PARTNER: zero/44,000 (Observational high risk) [6]
2016 PARTNER published – zero/58,000 [6]
2016 U=U + wide endorsements

US DHHS guidelines (Dec 1998)

Expert opinion.

“Factors that would lead one to initiate early therapy include … possibly decreasing the risk of viral transmission.”
Timeline

1998 ART stops mother to baby transmission [2]
2000 Rakai Study (Observational) [3]
2011 HPTN 052: 1 vs 27 (Randomised: low risk) [5]
2014 PARTNER: zero/44,000 (Observational: high risk) [6]
2016 PARTNER published – zero/58,000 [6]
2016 U=U + wide endorsements

“Despite adherence problems … the use of combination ART … during pregnancy results not only in improved maternal health, but also in rates of transmission that approach zero"
Timeline

1998 ART stops mother to baby transmission [2]
2000 Rakai Study (Observational) [3]
2011 HPTN 052: 1 vs 27 (Randomised: low risk) [5]
2014 PARTNER: zero/44,000 (Observational: high risk) [6]
2016 PARTNER published – zero/58,000 [6]
2016 U=U + wide endorsements

Rakai study:
~ 400 +ve/–ve couples in Uganda for 30 months: no infections when VL less than 400 c/mL.

Large observational study
(Quinn et al, NEJM 2000)
Timeline

1998 ART stops mother to baby transmission [2]
2000 Rakai Study (Observational) [3]
2008 Swiss Statement: zero risk (evidence review) [4]
2011 HPTN 052: 27 vs 1 (Randomised: low risk) [5]
2014 PARTNER: zero/44,000 (Observational: high risk) [6]
2016 PARTNER published: zero/58,000 [6]
2016 U=U + wide endorsements

Swiss Statement (Vernazza et al, 2008)

Data review and expert opinion – driven by criminalisation in Switzerland.

“similar to kissing”

“an HIV positive person on effective HIV treatment (ART) cannot transmit HIV through sexual contact”

So long as:

• on ART and adherent
• undetectable VL
• no STIs
• risk <1 in 100,000 (<0.001%)
Timeline

1998 US guidelines - early ART

1998 ART stops mother to baby transmission

2000 Rakai Study (Observational) [3]


2011 HPTN 052: 27 vs 1 (Randomised: low risk) [5]

2014 PARTNER: zero/44,000 (Observational: high risk) [6]

2016 PARTNER published – zero/58,000 [6]

2016 U=U + wide endorsements

Randomised studies = "Gold standard evidence"
HPTN 052
(Cohen et al, 2011)

Randomised ~ 1700 +ve/-ve couples to early ART vs waiting

- all linked infections in couples waiting for ART (+ single case with detectable VL)
- study stopped early
- protection over 4 yrs
HPTN 052

1700 HIV+ CD4>350

Randomisation

ART
N=1*

No ART
N=27

* Very early ART when VL was still detectable
Timeline

1998 US guidelines - early ART \[1\]
1998 ART stops mother to baby transmission \[2\]
2000 Rakai Study (Observational) \[3\]
2008 Swiss Statement: zero risk \[4\]
2011 HPTN 052: 27 vs 1 (low risk) \[5\]
2014 PARTNER – zero/44,000 (high risk) \[6\]
2016 PARTNER published – zero/58,000 \[6\]
2016 U=U + wide endorsements

Best evidence: PARTNER

• >800 couples not using condoms.
• Detailed sexual questionnaires.
• Already not using condoms (for years)
• One third were gay male couples.
• Calculated absolute real risks.
• STI were common in gay men.
• Undetectable = less than 200 copies/mL
PARTNER study

800 HIV+/- couples not using condoms.

Follow over time, collect info on risk.

After 58,000 times without condoms:
ZERO linked transmissions
Conclusions

- Zero transmissions without condoms when VL undetectable in all studies.
- No published case reports since Swiss Statement in 2008.
- PARTNER includes random blips between undetectable results.
- Includes VL >50 to 200 copies/mL.
- Includes STI - 30% of gay couples.
Questions?

My viral load is undetectable
that means I can’t
*sexually* pass it
on to my “FRIENDS”

www.preventionaccess.org/undetectable
Additional slides

Transmission....
Different types of evidence

• Expert opinion - NOT evidence!
• Case reports – small studies
• Systematic review – comparing studies
• Observational data – large cohorts when randomised studies are not possible
• Randomised clinical trials (RCTs)
  Double-blind, placebo controlled
## HIV negative partners: Characteristics

<table>
<thead>
<tr>
<th></th>
<th>MSM couples (n=282)</th>
<th>Heterosexual couples (n=445)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M -ve (n=245)</td>
<td>W -ve (n=240)</td>
</tr>
<tr>
<td><strong>At study entry</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>40 (32-47)</td>
<td>45 (37-50)</td>
</tr>
<tr>
<td>Yrs CL sex, median (IQR)</td>
<td>1.5 (0.5-3.5)</td>
<td>2.7 (0.6-6.9)</td>
</tr>
<tr>
<td><strong>During follow up</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years in the study, median (IQR)</td>
<td>1.1 (0.7-1.9)</td>
<td>1.5 (1.0-2.0)</td>
</tr>
<tr>
<td>Diagnosed with STI, %</td>
<td>16%</td>
<td>5%</td>
</tr>
<tr>
<td>CL sex with other partners, %</td>
<td>34%</td>
<td>3%</td>
</tr>
<tr>
<td>CL sex acts/year, median (IQR)</td>
<td>43 (18-79)</td>
<td>37 (14-77)</td>
</tr>
<tr>
<td>Estimated total number CL sex acts</td>
<td>16,400</td>
<td>14,000</td>
</tr>
</tbody>
</table>
### HIV positive partners: Characteristics

<table>
<thead>
<tr>
<th></th>
<th>MSM couples (n=282)</th>
<th>Heterosexual couples (n=445)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>W +ve (n=245)</td>
<td>M +ve (n=240)</td>
</tr>
<tr>
<td>At study entry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>42 (36-47)</td>
<td>40 (34-46)</td>
<td>45 (40-49)</td>
</tr>
<tr>
<td>Years on ART, median (IQR)</td>
<td>5 (2-11)</td>
<td>7 (3-14)</td>
<td>10 (4-15)</td>
</tr>
<tr>
<td>Self-reported adherence &gt;=90%, %</td>
<td>97%</td>
<td>94%</td>
<td>94%</td>
</tr>
<tr>
<td>Self report undetectable VL, %</td>
<td>94%</td>
<td>86%</td>
<td>85%</td>
</tr>
<tr>
<td>CD4&gt;350 cells/mm³, %</td>
<td>90%</td>
<td>88%</td>
<td>84%</td>
</tr>
<tr>
<td>During follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Having missed ART for more than 4 consecutive days, %</td>
<td>2%</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Diagnosed with STI, %</td>
<td>16%</td>
<td>4%</td>
<td>5%</td>
</tr>
</tbody>
</table>
What does it mean to be undetectable?

• Your health now?
• Your health in the future?
• Partners and relationships?
• Stigma and discrimination?
• Legal issues?