Evidence for U=U: PARTNER studies & the prevention access campaign

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Interests to declare

No financial conflict of interest

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I am community rep on PARTNER steering committee and i-Base are signed on to U=U campaign.
Timeline and evidence

1998 vs 2008 vs 2018

• Difficult to think pre-2016
• But at BHIVA 2018, most/some doctors do not tell all/some patients...
There should be no doubt that a person with sustained, undetectable levels of HIV in their blood CANNOT transmit HIV to their sexual partners.”

BHIVA statement (2017)
Prof Chloe Orkin, BHIVA chair
Personal views

- Current views – 100%? (or close)
- Translate to personal life
Timeline

1998  ART stops mother to baby transmission [1]
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) [6]
2016  PARTNER published – zero/58,000 [6]
2016  U=U campaign
2017  Opposites Attract [7]

1. Beckerman et al. IAS, 1988
2. DHHS, 1998;
3. Quinn et al, NEJM 2000;
5. Cohen et al NEJM 2011;
6. Rodgers et al. CROI 2014 and JAMA 2016;
Different types of evidence

• Observational data – large cohorts when randomised studies are not possible
• Randomised clinical trials (RCTs)
• Systematic review – comparing studies
• Case reports – small studies
• Expert opinion
Opinion vs evidence

- **Expert opinion - NOT evidence**

There is currently no evidence that HIV transmission occurs when viral load is undetectable.
Challenge since 2008 is whether HIV transmission can occur – so far not been proven.
In absence of evidence, having an opinion against U=U is either out-of-date or just prejudice.
References

HTB article:
“The evidence for U=U (Undetectable = Untransmittable): why negligible risk is zero risk”

www.i-base.info/htb/32308

Or just Google: “U=U”

Small observational study treating HIV positive pregnant women with triple therapy ART for their own best care.

“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”
“Factors that would lead one to initiate early therapy include … possibly decreasing the risk of viral transmission.”
Quinn et al, NEJM 2000

Rakai study:
~ 400 +ve/–ve couples in Uganda for 30 months: no infections when VL less than 1500 copies/mL.

Large observational study. Pre-ART, low condom use, no STI effect, new cases all uncircumcised men.
Swiss Statement
(Vernazza et al, 2008)

Evidence review – driven by criminalisation in Switzerland.
Also: “We were telling everyone to use condoms when we had no evidence they needed to”.

“an HIV positive person on effective HIV treatment (ART) cannot transmit HIV through sexual contact”
• on ART and adherent
• undetectable VL
• no STIs
• risk <1 in 100,000 (<0.001%)
HPTN 052 (Cohen et al, 2011)
Pilot from 2005, enrolled 2007-2010

96% reduction

Randomised ~ 1700 +ve/-ve couples to early ART vs waiting.
Study stopped early – ethics.
All linked infections in couples waiting for ART (+ single case with detectable VL).
Durable over 4 yrs (2017).
HPTN 052: reported 2011: (enrolled 2007-2010)

1700 couples: HIV+ CD4>350

Randomised 1:1

Expected ~ 200 infections: 8% vs 13%
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ART

N=1*

No ART

N=27

~ 4 years follow up

* Very early ART when VL was still detectable
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Best evidence: PARTNER 2014 -2016

~ 900 HIV+/- couples not using condoms.

Follow over time, collect info on risk.
After 58,000 times without condoms: ZERO linked transmissions

Rodgers et al. CROI 2014 and IAS July 2016.
PARTNER [1, 2, 3]

• ~900 couples not using condoms (1/3 gay men).
• 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
• Protected anonymity

# Partner - UK sites

<table>
<thead>
<tr>
<th>UK sites</th>
<th>London centres</th>
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</thead>
<tbody>
<tr>
<td>Birmingham: Birmingham Heartlands Hospital</td>
<td>Royal Free Hospital</td>
</tr>
<tr>
<td>Brighton: Lawson Unit, Royal Sussex Country Hospital</td>
<td>St. Stephens Centre/Kobler clinic</td>
</tr>
<tr>
<td>Bristol: Southmead Hospital</td>
<td>Royal London Hospital</td>
</tr>
<tr>
<td>Cardiff: Cardiff Royal Infirmary</td>
<td>Homerton Hospital</td>
</tr>
<tr>
<td>Coventry: Coventry and Warwickshire Hospital</td>
<td>North Middlesex Hospital</td>
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<tr>
<td>Edinburgh: Western General Hospital</td>
<td>King’s College Hospital</td>
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<tr>
<td>Leicester: Leicester Royal Infirmary</td>
<td>St. Thomas Hospital</td>
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<tr>
<td>Manchester: North Manchester Hospital</td>
<td>Mortimer Market Centre</td>
</tr>
<tr>
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<td>St. Mary’s Hospital</td>
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</tbody>
</table>

*2010-2018*
PARTNER 2014

• Intensive involvement of nurses (Tina Braun, CHIP)
• Recruiting and retaining couples depended on close connections with researchers.
• Enrolment slower than predicted, but steady.
• Sometimes driven by one rather than both partners
• Often difficult if relationships were short-term
• High participant interest in outcome
• High community involvement throughout
The PARTNER 2 Study: a study for sero-different gay couples

Understanding the risk of HIV transmission when the HIV+ partner is on therapy

If you would like to consider joining the study, please mention this to one of the clinic staff participating in PARTNER.
Rate of HIV transmission according to sexual behaviour reported by the negative partner

Rate of within couple transmission (per 100 CYFU)

- Any sex (CYFU=894)
- Anal sex (CYFU=374)

10 year risk (%) of within couple transmission

- estimated risk
- 95% confidence interval

Rodgers et al. CROI Feb 2014
Rate of HIV transmission according to sexual behaviour reported by the negative partner

Any sex (CYFU=894)

Anal sex (CYFU=374)

- estimated risk
- 95% confidence interval

Rodgers et al.
CROI Feb 2014
PARTNER timeline

2009  Protocol, funding and planning - Rate 0.5/100 CYFU
2010 Sep – first enrolled participants
2014 Feb - Preliminary results at CROI
2014 March – Launch of PARTNER 2
2014 May – Final data collection
2014-15 Paper rejected by several journals, JAMA accept but take 18 months to publish with repeated analyses.
2016 Apr – JAMA accept – then delay to IAS (July)
2018 – PARTNER 2 results
Zero HIV transmissions in the PARTNER study

i-Base: >35,000 facebook views in first week
Prevention Access Campaign

Launched in July 2016 by Bruce Richman and other researchers and activists.

Driven by problems with “96% reduced risk”, use of “reduced”, “negligible” but not 0.

Pressure for scientist to shift focus from minimal (if any) risk.

Mainstream campaign – IAS, BHIVA, US CDC: EFFECTIVELY ZERO = ZERO
Pepole with HIV on effective treatment do not sexually transmit HIV
Undetectable = Untransmittable

www.preventionaccess.org
International AIDS Society

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

Simon Collins (i-Base.info)

NHIVNA conference, Brighton 2018
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
U=U Statement

Since 2016 more than 670 organisations signed the U=U statement.

From more than 60 countries

Statement update in Jan 2018:
EFFECTIVELY ZERO = ZERO

Challenge: is transmission is possible?
www.preventionaccess.org
Se o preconceito é uma doença, a informação é a cura.

I = I

Indetectável = Intransmissível

Cientistas declaram: pessoas que vivem com HIV, estão em tratamento regular e têm carga viral indetectável há mais de 6 meses não transmitem o vírus sexualmente.

Para maiores informações acesse o site: giv.org.br

www.preventionaccess.org
“Bằng chứng khoa học là rõ ràng. Một người có tải lượng virus không phát hiện được trong máu của họ không có nguy cơ lây nhiễm cho bạn tính của họ.”

- Bản tuyên bố của NAM aIDSMAP (Thống Hải năm 2017)
Ain’t no viral load…
Ain’t no risk of HIV
PARTNER 2 timeline

2014 March – launch PARTNER 2
~900 gay couples only
• March 2014 to May 2018
• Provide similar level of confidence for gay men
  Even though actual risk is believed to be zero
2018 May – Final data collection

2018 – PARTNER 2 results at IAS 2018
Personal views

• How important is PARTNER 2?
• Any changed views during today
• Increased confidence to talking about U=U?
Conclusions

• Zero transmissions without condoms when VL undetectable in all studies.
• No published cases in ten years.
• U=U based on of upper range of acceptable risk
• Still not talked about by all health workers to all HIV positive patients
• PARTNER 2 results due July 2018.
Thanks:
Tina Braun
Roy Trevelion
Michelle Ross
Angelina Namiba
Garry Brough
Prof Chloe Orkin
PARTNER study

Questions?
Additional slides

Transmission....
What does it mean to be undetectable?

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

Has your doctor talked to you about U=U?

undetectable viral load = untransmittable HIV
Randomised studies = "Gold standard evidence"

Participants

Randomise

Group 1

Results

Group 2

Results
HPTN 052 2011: (enrolled 2007-2010)

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