The Evidence for U=U

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Undetectable = Untransmittable Outline

- Review of the Science
  - What are the origins of U=U?
  - Prior to antiretroviral therapy (ART), how did we learn lower viral load = lower risk?
  - What supports starting ART to lower transmission risk?
  - What supports U=U in the real world?
  - What supports U=U in MSM?

- Frequently Asked Questions
What Are the Origins of U=U?

1998: Studies of HIV transmission from mother to baby: 0 transmissions when on ART
  Beckman et al (Int Conf AIDS 1998)

1998: U.S. guidelines include “possibly decreasing transmission” as rationale for starting ART
  DHHS guidelines 1998

2000: Study of HIV transmission in sero-different partners in Uganda
  Quinn et al 2000
2000: Without Antiretroviral therapy
No Transmissions When Viral Load <1500

- 415 couples in Uganda studied for up to 30 months
- Lower viral load, lower risk
- No transmissions when viral load was <1500

Quinn NEJM 2000
What Supports Starting Antiretroviral Therapy to Lower Risk?

2001-2008: Swiss Commission Statement summarizing observational trials: “Suppressed does not transmit” (with caveats)
Vernazza et al 2008

2011: Large Randomized Trial: Starting Antiretroviral Therapy to Decrease HIV Infection (HPTN 052)
Cohen et al. NEJM 2011

2015: Final Analysis Of Same Trial (HPTN 052)
Cohen et al. IAS 2015
Cohen et al. NEJM 2016
2011: Antiretroviral Therapy Decreases HIV Transmission in a Randomized Trial (HPTN 052)

Sexually-Active Sero-Different Couples with CD4 Count 350-550 (1763 couples)

Immediate ART Arm (886 couples)

Delayed ART Arm (877 couples)

Fewer HIV-related Clinical Events

Fewer HIV Transmissions

2015: Final Analysis of HPTN 052--No Transmissions If Undetectable

- 36% of transmissions occurred outside of partnership (“unlinked”)

- No “linked” transmissions when partner on ART 3 months and virally suppressed

- Caveats: ~0 MSM, High Condom Use

8 Transmissions when Partner on ART

4: Partner Had Treatment Failure

4: Partner Had Started ART within 90 Days

Cohen MS, et al. IAS 2015
**2016-2017: What supports U=U in the Real World and in MSM?**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Condomless Sex Acts</th>
<th>Transmissions within Partnership</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PARTNER</strong></td>
<td>888 couples, 38% MSM</td>
<td>58,000</td>
<td>0</td>
</tr>
<tr>
<td><strong>Opposites Attract</strong></td>
<td>343 couples, 100% MSM</td>
<td>17,000</td>
<td>0</td>
</tr>
</tbody>
</table>

Rodger et al. JAMA 2016; 316: 171-81  
Bavinton et al, IAS 2017: TUAC 0506LB
“The science really does verify and validate U=U.” Anthony S. Fauci, M.D., Director, NIAID, NIH Speech at United States Conference on AIDS (September, 2017)

“People who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner.” CDC (September, 2017)

“It is time, to end the fears!” “I really think these community members who were active on U=U did a great job.” Pietro Vernazza, author of Swiss Commission Statement (November, 2017)
FAQ: U=U

- How long after starting antiretroviral therapy does U=U?
- What if you or a partner misses doses or stops therapy?
- What about sexually transmitted infections (STIs)?
- What about people with injection drug use?
How Long After Starting ART Is Safe?: No Infections After 6 Months in Partners-PrEP

- Randomized, placebo-controlled trial in sero-different heterosexual partners with partner starting ART
  - 3 infections in first six months vs. 0 after six months
- 6 Months May Be Conservative
  - Older HIV Regimens
  - No Infections after 90 days in HPTN 052

Mujugira, J AIDS 2016;72:579-84
What If I/My Partner Misses Doses Or Stops Antiretroviral Therapy (ART)?

- When do people become detectable off ART?
  - Risk increases significantly after one week (2x odds).
  - Can be as soon as 48hrs (Genberg et al. AIDS 2012)
    - Risk of transmission is still very low if only missing several days

- If you/partner stops for longer than several days:
  - Other prevention strategies remain available: PrEP, condoms
    - Continue until undetectable
What Do We Know about Sexually Transmitted Infections? Injection Drug Use?

Sexually Transmitted Infections:
- No transmissions if undetectable (6-17% with STIs in PARTNER)
  (Rodgers et al. JAMA 2016; 316: 171-81)

Injection Drug Use:
- Limited data (only 2% with injection drug use in PARTNER)
- PrEP is effective for prevention (Choopanya K. et al. Lancet 2013)
UNDetectable = UNtransmittable
Additional Slides
Some Patients Linked to Care Are Not Always Suppressed

- ~14,500 patients at 6 HIV clinics in the U.S. followed 3 years
- 90% were Prescribed ART
- Half of patients had 1 or more viral loads >1,500 copies
  - ¼ of study person-time

Marks, AIDS 2015, 29:947-954