

# U=U: issues in clinical practice

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# Declarations of interest

None

UNDETECTABLE = UNTRANSMITTABLE



**U=U\***  
UNDETECTABLE  
viral load means HIV IS  
UNTRANSMITTABLE  
[www.i-base.info/u-equals-u](http://www.i-base.info/u-equals-u)  
\* Undetectable = Untransmittable



**U = U**  
Undetectable  
means  
Untransmittable

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- Swiss statement
- HPTN052
- Partner
- Opposites Attract
- Partner 2

# Data summary

	Sample	Study design	No. condomless sex acts	No. new HIV diagnoses PL = phylogenetically linked		
	M-M = male-male M-F = male-female			Total	PL	PL & HIV+ partner suppressed
<b>HPTN052 (2011)</b>	1763 sero-different couples; 98% M-F	2-arm RCT: HIV+ partner early or delayed ART		78 total: 19 on early ART, 59 on delayed ART	46 total: 3 on early ART, 43 on delayed ART	0
<b>Partner 1 (2018)</b>	1166 sero-different couples; 888 analysed; 62% M-F	Observational	55,193 total; 34,214 male-female; 20,979 male-male	11	0	0
<b>Partner 2 (2018)</b>	972 serodifferent M-M; 783 analysed	Observational	76,991	15	0	0
<b>Opposites Attract (2018)</b>	358 serodifferent M-M couples	Observational	12,447 when HIV+ partner suppressed & HIV- not on PrEP	3	0	0

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- Transform sexual and reproductive lives
- Dismantle HIV stigma
- Encourage testing and engagement in care
- Remove fear

# Case 1

- 45 male, diagnosed HIV positive 2013
- Started Eviplera January 2014

Date	Viral Load copies/mL	CD4 cells/mm <sup>3</sup> (%)
March 2014	762	451 (22%)
June 2014	<40	603 (25%)

Nadir CD4	Highest Viral Load
431 cells/mm <sup>3</sup> , Jan 2014	41352 copies/mL, Jan 2014

# Case 1

- Routine clinical review June 2018, no new concerns
- RMP 1 year, HIV negative



# Case 1

What would you tell him about U=U?

- A. The risk of transmission is negligible
- B. The risk of transmission is extremely low as long as his viral load remains undetectable
- C. The risk of transmission is zero as long as long as he remains on his ART

# BHIVA U=U in practice questionnaire

ANSWER CHOICES	Responses	
I tell everyone that the risk of transmission is extremely low	8.30%	21
I tell everyone that the risk of transmission is next to zero	21.74%	55
I tell everyone that the risk of transmission is zero	37.15%	94
I tell everyone that the risk of transmission is virtually impossible	9.88%	25
I tell everyone that the risk of transmission is negligible	11.07%	28
Other	11.86%	30
<b>TOTAL</b>		<b>253</b>

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# Language matters

- Be clear and consistent about risk
- “From a practical standpoint the risk is zero”, Dr Anthony Fauci, NIAID
- Knowledge slow to filter from the scientific community
  - ACTG A5257, reported in 2016
    - ART 48/52 – 91% VL<50copies/mL
      - 38% thought they were highly infectious
      - 90% thought they were somewhat infectious



## **BHIVA encourages universal promotion of Undetectable=Untransmittable (U=U)**

- Discuss U=U proactively at all appropriate points of care
- Consistent and unambiguous terminology, such as “zero risk”
- Explain the evidence behind U=U emphasizing the importance of excellent adherence

# Case 1

- 6 month review – recalled to clinic due to viral load

Date	Viral Load copies/mL	CD4 cells/mm <sup>3</sup> (%)
June 2018	<40	652 (28%)
January 2019	187copies/mL	

- Full adherence, no missed or late doses, meeting calorie requirement

# Case 1

- Drug history
  - No new medication
  - St John's Wort herbal tea
- Patient distraught
  - What about U=U?

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- What value is suppressed viral load?
- When are you U=U?

Study	Baseline Viral Load		Follow up	
	<50copies/mL	<200copies/mL	<50copies/mL	<200copies/mL
Opposites Attract		267 (78%)		258 (75%)
Partner			94%	6%
Partner 2	754 (97%)	774 (99%)	1523 couple years (96%)	1593 couple years (100%)

## UK guideline for the use of HIV Post-Exposure Prophylaxis Following Sexual Exposure, 2015

- PEPSE is no longer recommended if the source is on ART with a **confirmed** and **sustained** (>6 months) undetectable plasma HIV VL (<200 c/mL) (1B).



BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP) 2018

### 4.1 Evidence for safety and efficacy in men who have sex with men (MSM): recommendations

2. We recommend that PrEP with on-demand or daily oral TD-FTC should be offered to HIV-negative MSM having condomless anal sex with partners who are HIV positive, unless the partner has been on ART for at least 6 months and their plasma viral load is <200 copies/mL. (1A)



# Case 1

What about our patient?

- Stopped St John's Wort and re-suppressed after 1 month
- No new resistance mutations
- RMP remains HIV negative

# Case 2

- 32 male, virologically suppressed on Triumeq for 3 years.
  - CD4 803cells/mm<sup>3</sup>(39%)
- 4 semi-regular male partners in last 3 months
  - 3 HIV negative
  - Condomless anal and oral sex
  - Aware of U=U
- Attends clinic upset as asymptomatic urethral Gonorrhoea positive NAAT

## Case 2

What will you tell him about U=U?

- A. The risk of HIV transmission remains zero despite STI diagnosis
- B. The risk of HIV transmission has become very small with concurrent STI diagnosis
- C. The risk of HIV transmission is greatly increased by concurrent STI diagnosis

# BHIVA U=U in practice questionnaire

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<b>Other</b>	<b>11.86%</b>	<b>30</b>
<b>TOTAL</b>		<b>253</b>

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- “I tell them the risk is zero except if other STIs present this may increase risk”

Study	STI prevalence in HIV positive partner during follow up		STI prevalence in HIV negative partner during follow up		Transmissions
	MSM	Heterosexual male/female	MSM	Heterosexual male/female	
Partner	59 (18%)	16 (6%)	56 (17%)	16 (6%)	0
Opposites Attract	115 (34%)	-	85 (25%)	-	0
Partner 2	214 (27%)	-	185 (24%)	-	0 (6090 condomless sex acts reported whilst STI present)

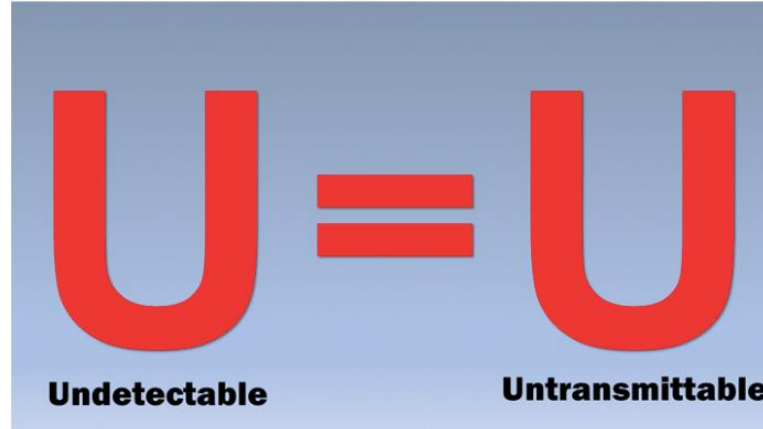


**JAMA Network™**

HIV viral load and  
Transmissibility of HIV infection  
Undetectable Equals  
Untransmittable

Robert Eisinger, PhD, Carl  
Dienflénbach PhD, Anthony  
Fauci MD, January 2019

**NIH** Director's Blog



“For HIV, Treatment is Prevention”  
NIH Director Dr Francis Collins  
January 2019

# THE LANCET

Providers should discuss U=U  
with all patients living with HIV

Sarah Calabrese, Kenneth  
Meyer  
George Washington University  
February 2019



**End to Aids in sight as huge study finds  
drugs stop HIV transmission**

**Paper says risk between male partners is zero if virus fully  
suppressed by antiretrovirals**

# Acknowledgments

- Professor Jonathan Ross
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