

Risk of HIV Transmission with Low Levels of Viremia

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Disclaimer

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Undetectable = Untransmittable



Risk of HIV Transmission with Undetectable Viral Load

Statements from CDC



A person with HIV who takes HIV medicine as prescribed and gets and stays virally suppressed or undetectable can stay healthy and will not transmit HIV to their sex partners.

Risk of HIV Transmission With Undetectable Viral Load by Transmission Category

Transmission Category	Risk for People Who Keep an Undetectable Viral Load
Sex (oral, anal, or vaginal)	Studies have shown no risk of transmission
Pregnancy, labor, and delivery	1% or less [†]
Sharing syringes or other drug injection equipment	Unknown, but likely reduced risk
Breastfeeding	Substantially reduces, but does not eliminate risk.

HIV Treatment is Prevention

Summary of Principal Data

Study	Methodology	Definition of Undetectable (HIV RNA level)	Approximate # CLS Acts	# Transmissions When Undetectable*	Estimated HIV Transmission Risk
HPTN 052	ART early vs delayed for partner with HIV (1,763 serodifferent couples)	<400 copies/mL	-	<u>Zero</u>	93-96% risk reduction
Partner 1	888 serodifferent couples (548 MF couples, 350 MM couples); 1,238 CYFU	<200 copies/mL	58,000	<u>Zero</u>	95% CI 0.0-0.3/100 CYFU (0.0-0.84 for MM couples)
Partner 2	783 serodifferent couples (all MM); 1,596 CYFU	<200 copies/mL	77,000	<u>Zero</u>	95% CI 0.0-0.23/100 CYFU
Opposites Attract	343 serodifferent couples (all MM); 591 CYFU	<200 copies/mL	17,000	<u>Zero</u>	95% CI 0.0-0.62/100 CYFU

*Genetically linked transmissions in which person with HIV had undetectable viral load
 Abbreviations: MM = male-male, MF = male-female, CLS = condomless sex acts, CYFU = couple years of follow up

Key Points About “U=U”

- **Powerful message that can reduce stigma**
- Important to continue STI prevention counseling
- Outstanding question: what is the risk of transmission with low levels of viremia?

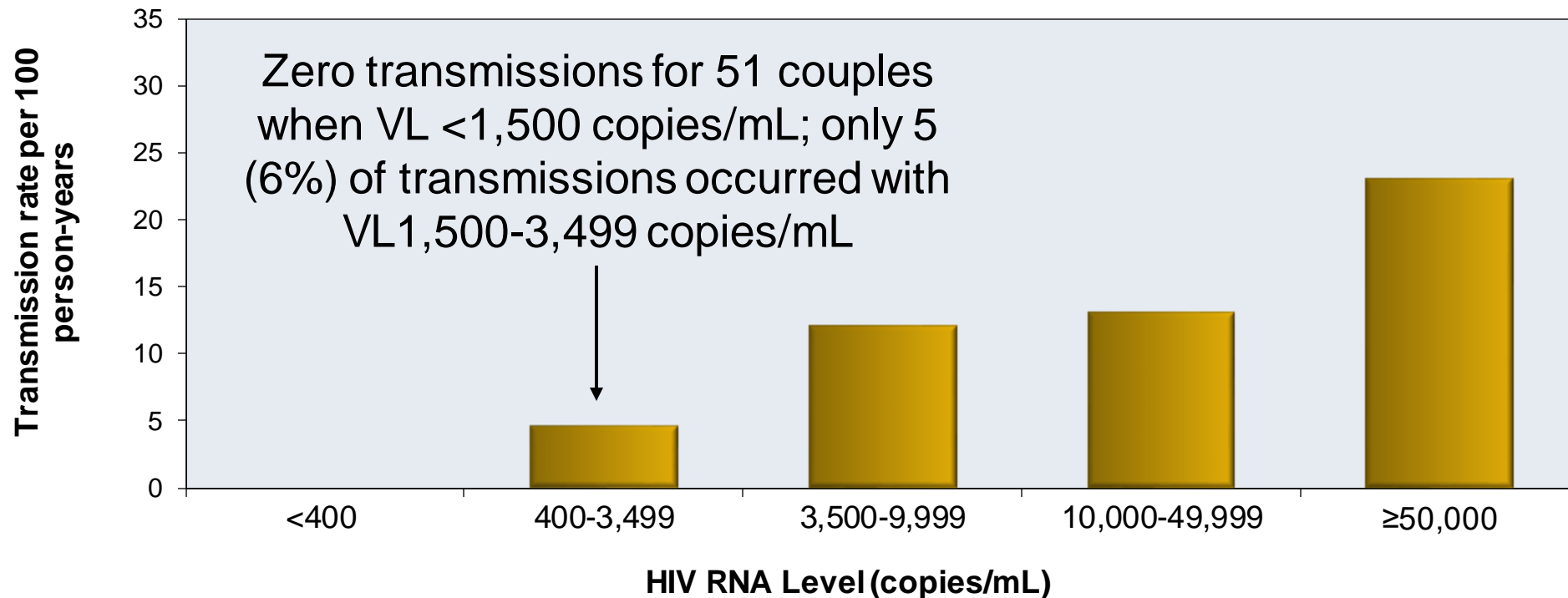
Viral load does not equal Value $V \neq V$

The Third **U** = **UNIVERSAL**

Revisiting Older Data

The Rakai Study, NEJM 2000

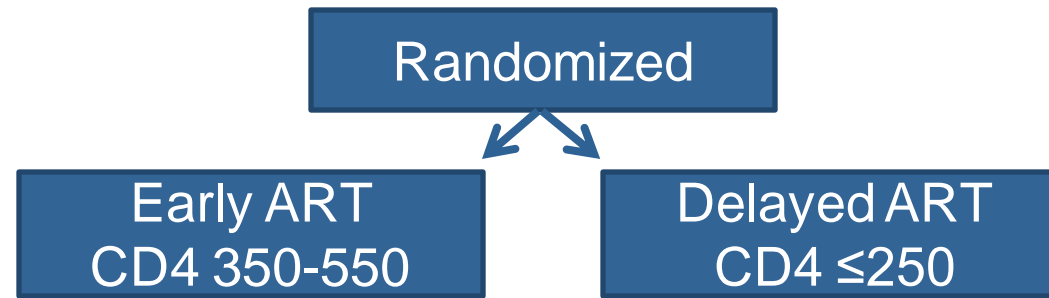
- Community-based study of 15,127 persons in rural district of Uganda
- 415 serodifferent, heterosexual couples; 90 seroconversions



“The viral load is the chief predictor of the risk of heterosexual transmission of HIV-1, and transmission is rare among persons with levels of less than 1500 copies of HIV-1 RNA per milliliter.”

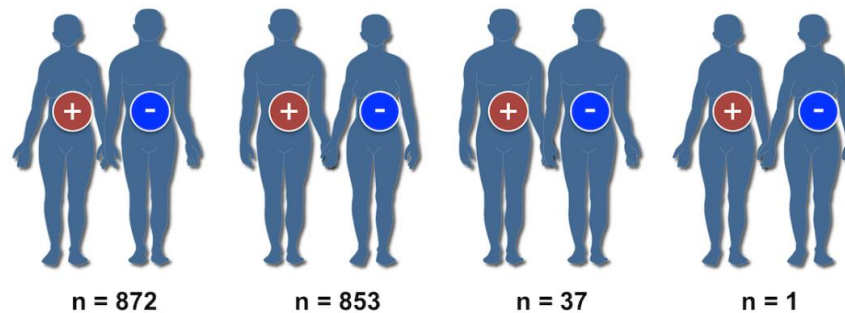
HPTN 052: HIV Treatment as Prevention

- Sexually active couples, partner with HIV had baseline CD4 350-550 cell/mm³

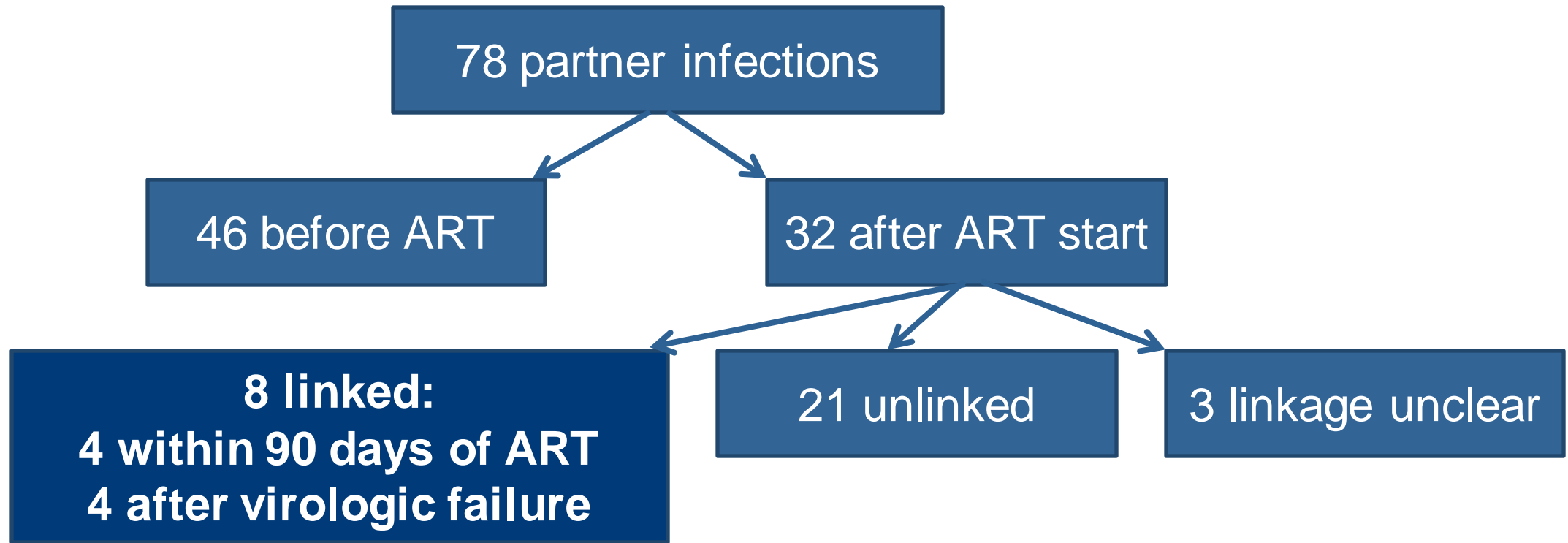


- Primary outcome: genetically-linked partner infections

1,763 HIV Serodiscordant Couples (97% heterosexual)



HPTN 052: HIV Treatment as Prevention



- 0 linked infections when partner with HIV had stable viral load <1,000 copies/mL
- 1 linked infection with viral load 617 copies/mL (50 days prior to estimated transmission date)

New review: what is the documented risk of HIV transmission with low levels of viremia?



The risk of sexual transmission of HIV in individuals with low-level HIV viraemia: a systematic review



Laura N Broyles, Robert Luo, Debi Boeras, Lara Vojnov

Summary

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Background The risk of sexual transmission of HIV from individuals with low-level HIV viraemia receiving antiretroviral therapy (ART) has important public health implications, especially in resource-limited settings that use alternatives to plasma-based viral load testing. This Article summarises the evidence related to sexual transmission of HIV at varying HIV viral load levels to inform messaging for people living with HIV, their partners, their health-care providers, and the wider public.

Methods We conducted a systematic review and searched PubMed, MEDLINE, Cochrane Central Register of Controlled Trials, Embase, Conference Proceedings Citation Index-Science, and WHO Global Index Medicus, for work published from Jan 1, 2010 to Nov 17, 2022. Studies were included if they pertained to sexual transmission between serodiscordant couples at various levels of viraemia, the science behind undetectable=untransmittable, or the public health impact of low-level viraemia. Studies were excluded if they did not specify viral load thresholds or a definition for low-level viraemia or did not provide quantitative viral load information for transmission outcomes. Reviews, non-research letters, commentaries, and editorials were excluded. Risk of bias was evaluated using the ROBINS-I framework. Data were extracted and summarised with a focus on HIV sexual transmission at varying HIV viral loads.

Findings 244 studies were identified and eight were included in the analysis, comprising 7762 serodiscordant couples across 25 countries. The certainty of evidence was moderate; the risk of bias was low. Three studies showed no HIV transmission when the partner living with HIV had a viral load less than 200 copies per mL. Across the remaining four prospective studies, there were 323 transmission events; none were in patients considered stably suppressed on ART. Among all studies there were two cases of transmission when the index patient's (ie, patient with previously diagnosed HIV infection) most recent viral load was less than 1000 copies per mL. However, interpretation of both cases was complicated by long intervals (ie, 50 days and 53 days) between the transmission date and the most recent index viral load result.

Interpretation There is almost zero risk of sexual transmission of HIV with viral loads of less than 1000 copies per mL. These data provide a powerful opportunity to destigmatise HIV and promote adherence to ART through dissemination of this positive public health message. These findings can also promote access to viral load testing in resource-limited settings for all people living with HIV by facilitating uptake of alternative sample types and technologies.

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Risk of HIV Sexual Transmission with Low Levels of Viremia on ART

Systematic Review 2023

- 8 studies of sexual transmission in serodifferent couples that included VL data
- Certainty of evidence: “moderate;” risk of bias: “low”
- 4 cohort studies, 3 RCTs, 1 cross-sectional analysis; total 7,762 couples
- Only 2 transmissions with most recent VL <1,000; however, long intervals (50 days and 53 days) between last VL check and estimated transmission date
- *Overall, no definitive evidence of HIV transmission with VL <600, and “incredibly rare” occurrence of possible transmission with VL 600 to 1,000*

	Study name	Countries	Study type	Years	Sex of Couples	# of Couples	# of Linked Transmissions
Bavinton (2018)	Opposites attract	Australia, Brazil, Thailand	Cohort	2012-16	100% MM	358	0
Cohen (2016)	HPTN 052	9 countries	RCT	2005-10	97% MF, 3% unspecified	1763	43 delayed ART 3 with early ART
Fideli (2001)		Zambia	Nested case-control within prospective cohort	1994-2000	100% MF	318	109 couples with transmission and 209 with no transmission*
Mujugira (2016)	Partners PrEP	Kenya, Uganda	Analysis of couples in placebo arm of RCT	2008-2012	100% MF	1573	55 no ART; 3 prescribed ART**
Quinn (2000)	Rakai	Uganda	RCT	1994-1998	100% MF	415	90
Rodger (2016)	PARTNER	14 European countries	Cohort	2010-14	62% MF, 38% MM	1166	0
Rodger (2019)	PARTNER2	14 European countries	Cohort	2010-17	100% MM	972	0
Tovanabutra (2002)		Thailand	Cross-sectional	1992-98	100% MF	493	44% of partners seropositive at enrolment***

*No transmissions when partner with HIV had VL <1,000; 92% of transmissions occurred with VL >10,000

**All 3 within 6 months of ART initiation; 1 could have occurred with VL <1,000, but substantial uncertainty exists (VL 600's to 800's, but 53 days between last VL and likely transmission event)

***No transmission occurred with VL <1,000 copies/mL

“There is almost zero risk of sexual transmission of HIV with viral loads of less than 1000 copies per mL. These data provide a powerful opportunity to destigmatise HIV and promote adherence to ART through dissemination of this positive public health message.”

Questions for Discussion

- How do you discuss U=U with patients/clients?
- How do you counsel individuals who take ART but have low-level viremia? How will the systematic review data inform this counseling?
- What data are we still missing?
 - Inclusion of transgender and non-binary individuals in studies
 - Injection drug use/needle sharing
 - Needle stick injury (PEP)
 - Risk with concomitant bacterial STI
 - Innate HIV controllers (low viral load without ART)
 - What else???

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