

AN UPDATED SYSTEMATIC REVIEW AND META-ANALYSIS¹

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BACKGROUND

- Anal intercourse (AI) drives HIV epidemics in men-who-have-sex-with-men (MSM) and numerous studies have reported common AI practice in heterosexual populations,^{2,3} potentially making it an important source of HIV transmission for this group.
- Quantifying HIV transmission risk per act of anal intercourse (AI) is important for effective targeting of safe sex messages, for developing and implementing HIV prevention technologies and to inform mathematical models.

OBJECTIVES

To update previous reviews^{4,5} (of studies published up to February 2012) of HIV transmission risk through AI, and to explore how this risk varies by gender, setting and other study characteristics.

METHODS

- We searched Medline and Embase to February 2018 for new studies reporting HIV transmission risk per AI sex act.
- We pooled study estimates of per act risk through receptive AI (URAI) and insertive AI (UIAI) both unprotected by condoms, using random effects models.
- We conducted subgroup analyses by gender (heterosexual, MSM), study design and whether antiretroviral therapy (ART) had been introduced by the time of the study.

RESULTS

- We reviewed 5336 titles. Two new relevant studies were identified, one of which met inclusion criteria, adding three new cohorts and increasing the number of individuals/partnerships included from <1870 used in previous meta-analyses to 14,277.
- Four studies, all from high-income countries, were included (see Figure).
- The revised pooled HIV risk was higher for URAI (1.25%, 95%CI 0.55-2.23, N=5, I²=87%) than for UIAI (0.17%, 95%CI 0.09-0.26, N=3, I²=0%).
- The sole heterosexual URAI estimate⁶ (3.38%, 95%CI 1.85-4.91), from a study of 72 women published in a peer-reviewed journal, was significantly higher than the MSM pooled URAI estimate (0.75%, 95%CI 0.56-0.98, N=4, p<0.0001) and higher than the only other heterosexual estimate identified (0.4%, 95%CI 0.08-2.0%, based on 59 women, excluded for being a pre-2013 abstract⁷) (see Figure).
- Pooled per-act URAI risk varied by study design (retrospective-partner studies: 2.56%, 95%CI 1.20-4.42, N=2: one MSM, one heterosexual; prospective studies of individuals: 0.71, 95%CI 0.51-0.93, N=3: all MSM, p<0.0001).
- URAI HIV risk was lower for studies conducted in the ART era (0.75%, 95%CI 0.52-1.03%) than pre-ART (1.67%, 95%CI 0.44-3.67%) but not significantly so (p=0.537). Only study design was independently associated with URAI transmission risk estimate (p=0.055).

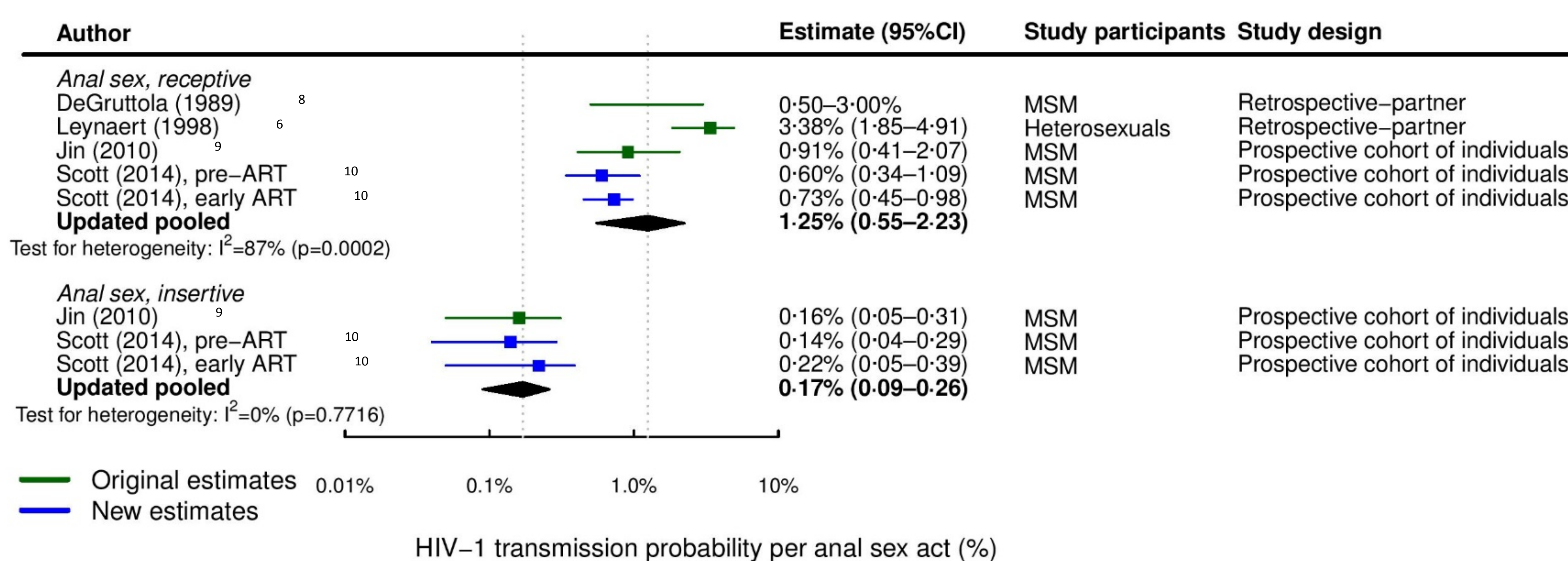
TABLE Subgroup analysis: pooled per-act HIV transmission probability estimates for unprotected receptive and insertive anal intercourse, stratified by gender, study design and plausible extent of ART use.

Estimate type	Pooled estimate, % (95%CI)	p ^a	I ^{2,b} (%)	N	p-value ^a
Unprotected receptive anal intercourse					
Gender					
Women	3.38 (1.85-4.91)	1.000	0.0%	1	
MSM	0.75 (0.56-0.98)	0.278	<0.1%	4	p<0.0001
Study design					
Retrospective-partner	2.56 (1.20-4.42)	0.1296	56.5%	2	
Prospective cohort of individuals	0.71 (0.51-0.93)	0.722	0.0%	3	p<0.0001
Plausible extent of ART use by sexual partners					
0%	1.67 (0.44-3.67)	<0.0001	87.6%	3	
>0%	0.75 (0.52-1.03)	0.650	0.0%	2	p=0.537
Pooled estimate	1.25 (0.55-2.23)	0.0002	87.3%	5	
Unprotected insertive anal intercourse					
Plausible extent of ART use by sexual partners					
0%	0.14 (0.04-0.29)	1.000	0.0%	1	
>0%	0.18 (0.09-0.31)	0.604	0.0%	2	p=0.955
Pooled estimate	0.17 (0.09-0.26)	0.7716	0.0%	3	

a a "P" is the p-value for heterogeneity of the pooled estimate; "p-value" is the metaregression p-value defining the significance of the difference in pooled estimates between the two subgroups.

b I² lies between 0% and 100%; 0% indicates zero observed heterogeneity and larger values show increasing heterogeneity.

FIGURE Forest plot of studies estimating per-act HIV transmission probability through anal intercourse. "Original estimates" refers to studies included in either previous review.^{2,3} I² lies between 0% and 100%; 0% indicates zero observed heterogeneity and larger values show increasing heterogeneity.



CONCLUSION

- Risk of HIV transmission through AI remains high (1.25%, 95%CI 0.55-2.23% for URAI; 0.17%, 95%CI 0.09-0.26% for UIAI). HIV is at least 10-fold more transmissible through anal than vaginal sex in high income settings (unprotected receptive VI: 0.08%, 95%CI 0.06-0.11%¹¹).
- Transmissibility appears to have remained high despite ART use having increased in the HIV-infected population.
- Prevention messages should emphasise this high risk.
- Further studies, particularly among heterosexual populations and in resource-limited settings, are required to elucidate whether AI risk differs by gender, region and following ART scale-up at the population level.

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