Systematic review of orogenital HIV-1 transmission probabilities

Rebecca F Baggaley,[1]* Richard G White[2] and Marie-Claude Boily[1]

Accepted	23 June 2008
Background	The objective was to assess the risk of HIV transmission from orogenital intercourse (OI).
Methods	Systematic review of the literature on HIV-1 infectiousness through OI conducted according to MOOSE guidelines for reviews of observational studies. The PubMed database and bibliographies of relevant articles were searched to July 2007.
Results	Of the titles, 56 214 were searched from which 10 potentially appropriate studies were identified; two additional studies were identified through bibliographies and one through discussion with experts. There were 10 included studies, providing estimates of transmission probabilities per-partner ($n=5$), incidence per-partner ($n=3$), per-study participant ($n=3$, following initially seronegative individuals whose partners are of unknown serostatus) and per-act ($n=3$). Only four of 10 studies reported non-zero estimates: two per-partner estimates (20%, 95% CI: 6–51, $n=10$ and a model-based estimate, 1%, range 0.85–2.3%), one per-study participant estimate (0.37%, 95% CI: 0.10–1.34%) and one per-act estimate (0.04%, 95% CI: 0.01–0.17%). Upper bounds for the 95% CI for zero estimates tended to be relatively large due to the small study sample sizes: 9.0, 12.1 and 2.8% for per-partner; 4.7, 9.6 and 1.8 per 100 person-years for incidence per-partner; 4.4% per-study participant and 0.45 and 0.02% for per-act. Given the small number of studies, a meta-analysis was not considered appropriate.
Conclusions	There are currently insufficient data to estimate precisely the risk from OI exposure. The low risk of transmission evident from identified studies means that more and larger studies would be required to provide sufficient evidence to derive more precise estimates.
Keywords	HIV, oral sex, orogenital intercourse, infectivity, transmission probability

[1] Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College London, London, UK.
[2] Infectious Disease Epidemiology Unit, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK.
* Corresponding author. Department of Infectious Disease Epidemiology, Imperial College London, St Mary's Campus, Norfolk Place, Paddington, London W2 1PG, UK. E-mail: r.baggaley@imperial.ac.uk

Introduction

The risk of HIV transmission through orogenital intercourse (OI) has yet to be precisely quantified. Various case reports suggest that the risk of OI transmission is not nil but much lower than from vaginal and anal intercourse (AI).[1] While some of these reports may have been misattributed to OI transmission through underreporting of higher risk behaviours such as AI,[2] this is unlikely to be true for all cases of

reported OI transmission. It is important to quantify this probability because some confusion about the risks associated with these practices remains. Based solely on the evidence from case reports, current guidelines tend to be very cautious and suggest 100% condom use and use of dental dams.[3] More precise information on the actual risk would help clinicians to advise their patients on the relative risks. This may be especially important as the relative contribution of OI may have increased because other higher risk activities, such as unprotected receptive AI (URAI), have become less common. More precise transmission probability estimates would improve predictions of the contribution of OI exposure to HIV incidence that has previously been estimated to be up to 8% in some populations in industrialized countries.[4–6]

The risk of OI transmission is difficult to assess. Most studies focused on men who have sex with men (MSM), and since many men have varied sexual practices, risks of transmission from low-risk sexual practices such as OI have been difficult to detect. Furthermore, there is a range of OI practices that likely carry different risks, but risks for specific OI practices are difficult to quantify because many individuals practice multiple types of OI (as well as higher risk activities such as vaginal and anal sex). Here, we define OI to include both insertive and receptive penile-oral sex between males and between males and females, as well as vaginal-oral sex between females and between male and females, but to exclude oroanal contact. While Rothenberg *et al.* reviewed case reports and epidemiological association studies up to the beginning of 1998 reporting OI risk for HIV transmission,[1] ours is the first study systematically to review the evidence on transmission probability estimates for receptive and insertive unprotected OI.

Methods

The systematic review was undertaken following MOOSE guidelines for reviews of observational studies.[7]

Search strategy

The PubMed database was searched to July 2007 using the following search terms and Boolean operators, for matches under any field: (HIV OR LAV OR HTLV III OR HTLV-III OR AIDS OR human immuno-deficiency virus OR human T-lymphotropic virus III OR acquired immunodeficiency) AND {infectious-ness OR infectivity OR probability OR contact OR contacts OR partner OR partners OR wives OR spouses OR husbands OR couples OR discordant OR [transmission AND (heterosexual OR homosexual OR risk OR female OR male OR anal)]}. Titles and available abstracts were scanned for relevance, iden-tifying papers requiring further consideration. Biblio-graphies of relevant articles were checked and experts in the field were approached in order to identify additional relevant publications.

Selection criteria and data extraction

Due to the small number of studies on OI transmis-sion probability estimates, the review included empir-ical studies and also statistical model-based estimates (Bernouilli models) using datasets involving partners with multiple exposure types [e.g. OI, URAI and unprotected insertive AI (UIAI)], aiming to delineate the contribution of each sexual activity to the overall transmissions observed in the sample.[8,9] Four types of estimate were included: (i) per-act (one OI act); (ii) per-partner (multiple OI acts over the total dura-tion of a sexual partnership with an infected indi-vidual); (iii) per-partner incidence (multiple OI acts over a specified duration within a sexual partnership with an infected individual) and (iv) per-seronegative study participant (studies following up initially HIV negative individuals reporting unprotected OI expo-sure as their sole risk factor, with one or more part-ners of positive or unknown serostatus). There was no other restriction by study design or language of publication. Each relevant publication was examined by two investigators (R.F.B., R.G.W.) to extract available information on estimates and study and participant characteristics. Two of the three authors contacted replied; authors of one study provided additional information.

Quantitative data synthesis

For uniformity, all confidence intervals (CIs) were recalculated using the Wilson 'score' method without continuity correction[10,11] except for Samuel *et al.*[8] and Vittinghoff *et al.*,[9] which reported lowest and highest estimates from a sensitivity analysis based on various model assumptions, and the per-partner incidence estimate from de Vincenzi 1994,[12] where the number of person-years exposure was not stated and, there-fore, the published CI are shown.

Results

Of the titles 56 214 were searched from which 10 potentially appropriate studies were identified; two additional studies were identified through bibliogra-phies and one through discussion with experts. There were 10 included studies that provided five per-partner, three per-partner incidence, three per-study participant and three per-act estimates (with further estimates subdivided by direction of transmission and type of OI act). A flowchart summary of the search is shown in Figure 1. Three publications were excluded. Results from two prospective studies reported in Kingsley *et al.*[13] and Raiteri *et al.*[14] were superseded by Detels *et al.*[15] and Raiteri *et al.*,[16] respectively, which reported results with longer durations of follow-up in each case. Winkelstein *et al.*[17] was excluded because there was no previous HIV
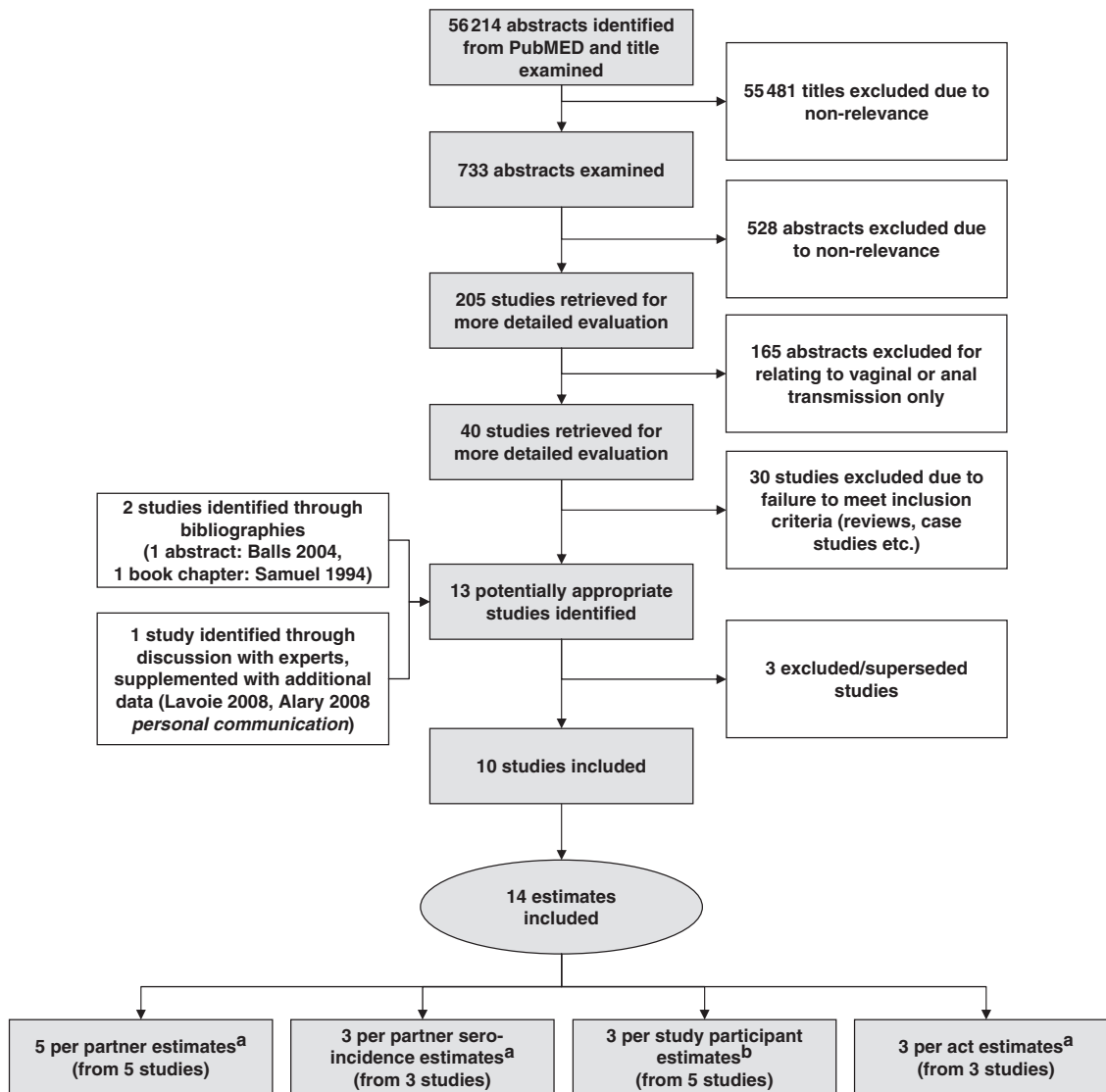
Figure 1 Flowchart summarizing the results of the search on HIV-1 transmission probabilities relating to orogenital sex up to July 2007. 'Studies' may refer to published articles or abstracts. [a]Counting principal estimate by del Romero *et al.* 2002 only (and not subdivisions by direction of transmission and type of act). [b]Counting only the estimate by Balls *et al.* 2004 and Page-Shafer *et al.* 2002 restricted to participants reporting exposure to a seropositive partner or partner of unknown serostatus

negative test to exclude those with URAI exposure from 2 years earlier (HIV prevalence was as high as 18.2% among those with no OI or AI contact in the last 2 years).

Forest plots summarizing estimates for each transmission probability type are presented in Figure 2. Details for each study are shown in Table 1. All studies were from industrialized countries and most reported zero seroconversions (Table 1). All but two studies reported no unprotected sexual activity other than unprotected OI, but subjects often practised protected vaginal or AI. Vittinghoff *et al.*[9] and Samuel *et al.*[8] were able to derive model based estimates using data from MSM with various risk factors including URAI and UIAI. Samuel *et*

al. inferred the unknown HIV status of index partners from MSM prevalence data.[8] None of the MSM who exclusively reported OI as a risk factor seroconverted in Vittinghoff *et al.*'s study.[9] Vittinghoff *et al.* calculated a per-act risk for infected or unknown serostatus partners because there were too few cases of OI contact with known infected partners in their dataset. Raiteri *et al.* followed a cohort of HIV discordant lesbian couples who reported oroanal as well as orogenital contact; there were no seroconversions.[16]

There were five non-zero estimates (two per-partner,[8,18] two per-study participant[15,22] and one per-act[9]). The two non-zero per-partner estimates were 1% (range 0.85–2.3%) for receptive OI (ROI)[8]

(a)

	Study participants	Description of exposure
Giesecke et al. 1992	Heterosexual/MSM couples	Fellatio
de Vincenzi 1994	Heterosexual couples	Unprotected fellatio (with protected vaginal or AI)
Samuel et al.1994	MSM	All OI
Raiteri et al. 1998	Lesbian couples	All OI (and other sexual practices such as OAI for some couples)
del Romero et al. 2002	Heterosexual couples	All OI

(b)

	Study participants	Description of exposure
de Vincenzi 1994	Heterosexual couples	All OI
Raiteri et al. 1998	Lesbian couples	All OI (and other sexual practices such as OAI for some couples)
del Romero et al. 2002	Heterosexual couples	All OI

(c)

	Study participants	Description of exposure
Detels et al.1989	MSM	All OI (plus no AI in previous 12 months)
Page-Shafer et al. 2002, Balls et al. 2004[a]	MSM	Exposure to ejaculate of an HIV positive or unknown serostatus partner
Lavoie et al. 2007, Alary 2008	MSM	ROI with ≥1 HIV positive and/or casual partners but no AI in previous 6 months

(d)

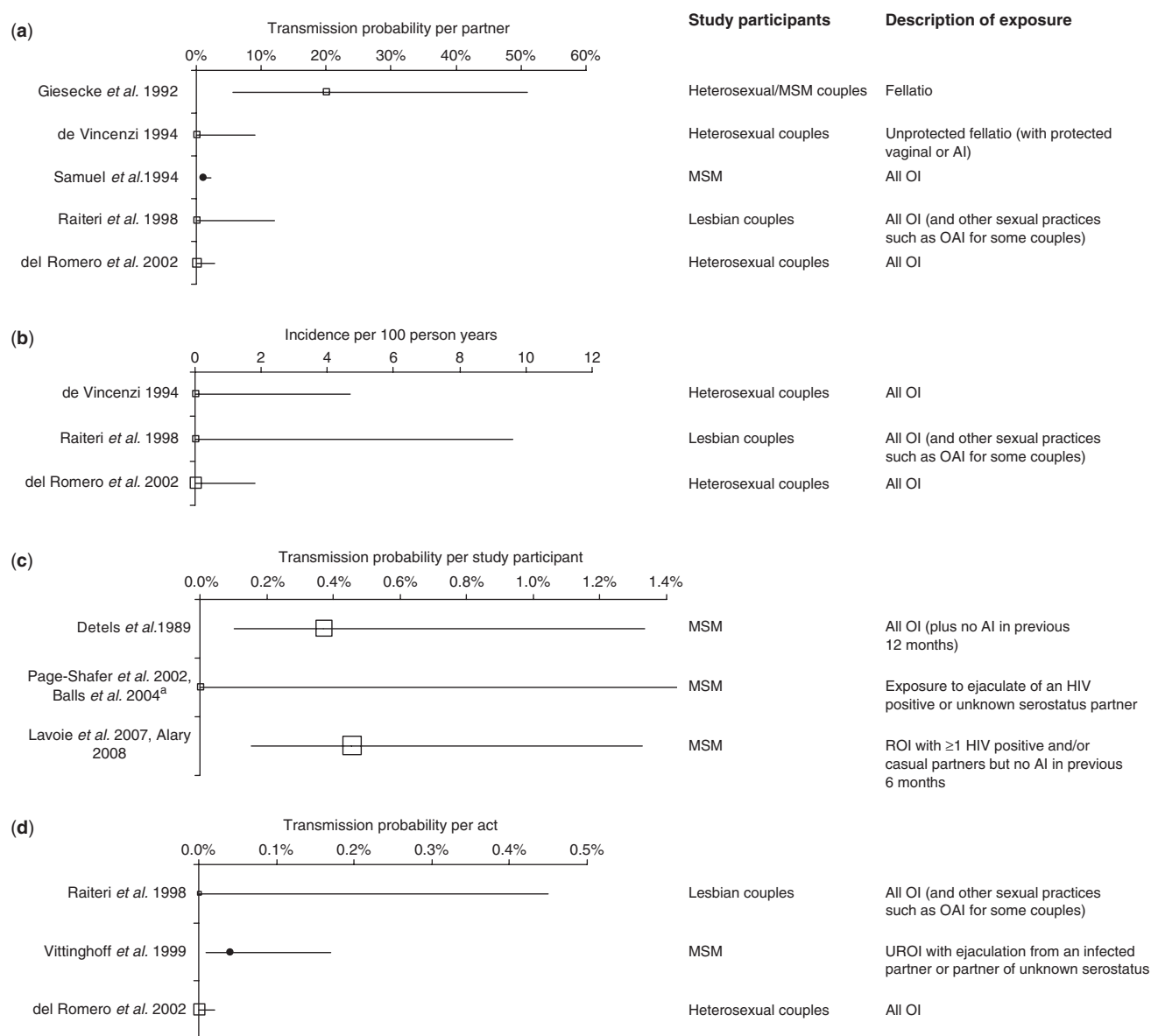|	Study participants	Description of exposure
Raiteri et al. 1998	Lesbian couples	All OI (and other sexual practices such as OAI for some couples)
Vittinghoff et al. 1999	MSM	UROI with ejaculation from an infected partner or partner of unknown serostatus
del Romero et al. 2002	Heterosexual couples	All OI

Figure 2 Summary of studies estimating HIV transmission probabilities for orogenital sex. Estimates are grouped as (a) transmission probability per-partner; (b) incidence per 100 person-years of exposure; (c) transmission probability per-study-participant and (d) transmission probability per-act. Bars represent 95% CIs except for Samuel et al.,[8] and Vittinghoff et al.,[9] which represent highest and lowest estimates using various models and assumptions. Sizes of boxes are proportional to sample sizes, except for Samuel et al.,[8] and Vittinghoff et al.,[9] which are denoted by circles because no sample size is available. OAI, oro-anal intercourse. [a]Estimate used is 0.00 (0/83, 0.00–4.42)—sample restricted to 19% of men reporting an HIV positive or unknown serostatus partner

and 20% (95% CI: 5.7–51.0%) for fellatio.[18] The very high estimate by Giesecke et al. was based on only 10 heterosexual and homosexual discordant couples where the seronegative partner reported no concurrent or subsequent seropositive partner, no intravenous drug use and only OI exposure over follow-up.[18] The high estimate may be due to underreporting of higher risk activity, or simply due to chance. Vittinghoff et al. reported a 0.04% risk per-act from men-to-men for unprotected ROI (UROI).[9] Two per-

study participant studies among MSM reported non-zero transmission probabilities for all OI[15] and ROI[22] in the absence of practising AI in the previous 12 and 6 months, respectively, but the number of partners and their serostatus were not determined. Therefore, as the exposure and the risk of infection depend on HIV prevalence in the population, these results cannot be generalized to other settings. Similar limitations apply to Vittinghoff et al.'s estimate, which reflects a risk per-act with sexual partners of infected or

Table 1 Transmission probabilities for orogenital intercourse—all types

Study	Setting/study design/population/date/gender	Description of exposure	Direction of transmission	Transmission probability (%) (x/n, 95% CI)	Duration of exposure (DE), duration of partnership (DP) or duration of follow-up (DF); stage of HIV infection, other risk factors, uncontrolled cofactors
Per-partner					
Giesecke et al. 1992[18]	Sweden prospective 1989–1990 Index patients diagnosed in Sweden and their partners identified through partner notification—discordant couples identified from a pool of heterosexual and homosexual couples.	Fellatio	NS	20.0 (2/10, 5.7–51.0)	DF: <2 years DE: <2 years 100% monogamy; HIV disease stage not stated; other risk factors for infection not stated.
de Vincenzi 1994[12]	European Study Group prospective 1987–1991 Stable heterosexual discordant couples percentage of partners female not stated	Unprotected fellatio with protected vaginal or AI	M-to-F and F-to-M	0.0 (0/39, 0.0–9.0)[a]	DF: median 24 months for the entire cohort ($n=256$) 1994
Samuel et al. 1994[8]	US prospective 1984 onwards MSM from SFMHS Series of mathematical Bernoulli models assuming independent risks for transmission for RAI, IAI and ROI	ROI	M-to-M	1.0 (range: 0.85–2.3, $n=410$)	Dataset included 410 men with multiple types of exposure (AI, OI), with 46 seroconversions during follow-up. Number of exposures to HIV estimated from prevalence data[17]. Range of estimates shown here is produced from different models and varying assumptions.
Raiteri et al. 1998[16]	Italy prospective 1992–1997 Stable HIV discordant lesbian couples (10 index cases and 28 partners)	All OI (and other sexual practices such as OAI for some couples)	F-to-F	0.0 (0/28, 0.0–12.1)	DF: median 10 months (range: 6–43; total 434 months, 849 OI exposures) DP: ⩾6 months 100% monogamy, no IDU, no heterosexual sex, no condom use
del Romero et al. 2002[19]	Spain prospective 1990–2000 Heterosexual serodiscordant steady couples	All OI	M-to-F and F-to-M	0.0 (0/135, 0.0–2.8)	DF: 210 person-years (19 316 contacts) 8% index cases with AIDS; 16% with CD4 <200 cells/ml; 39% received ART during follow-up.
			M-to-F	0.0 (0/110, 0.0–3.4)	
			F-to-M	0.0 (0/25, 0.0–13.3)	
	81% of partners female	Fellatio	M-to-F and F-to-M	0.0 (0/120, 0.0–3.1)	Partners had no other risk factor for infection; no UAI or UVI.
			M-to-F	0.0 (0/96, 0.0–3.8)	
			F-to-M	0.0 (0/24, 0–13.8)	

(continued)

Table 1 Continued

Study	Setting/study design/population/date/gender	Description of exposure	Direction of transmission	Transmission probability (%) (x/n, 95% CI)	Duration of exposure (DE), duration of partnership (DP) or duration of follow-up (DF); stage of HIV infection, other risk factors, uncontrolled cofactors
		Fellatio without ejaculation in oral cavity	M-to-F and F-to-M	0.0 (0/83, 0.0–4.4)	
			M-to-F	0.0 (0/70, 0.0–5.2)	
			F-to-M	0.0 (0/13, 0–22.8)	
		Fellatio with ejaculation in oral cavity	M-to-F and F-to-M	0.0 (0/37, 0.0–9.4)	
			M-to-F	0.0 (0/26, 0.0–12.9)	
			F-to-M	0.0 (0/11, 0–25.9)	
		Cunnilingus	M-to-F and F-to-M	0.0 (0/110, 0.0–3.4)	
			M-to-F	0.0 (0/98, 0.0–3.8)	
			F-to-M	0.0 (0/12, 0–24.3)	
Per-partner sero-incidence					
de Vincenzi 1994[12]	European Study Group prospective, 1987–1991 Stable heterosexual discordant couples percentage of partners female not stated	Unprotected fellatio with protected vaginal or anal sex	M-to-F and F-to-M	0.0 Per 100 person-years (95% CI 0.0–4.7, $n = 39$)	DF: median 24 months for the entire cohort ($n = 256$)
Raiteri et al. 1998[16]	Italy prospective 1992–1997 Stable HIV discordant lesbian couples (10 index cases and 28 partners)	All OI (and other sexual practices such as OAI for some couples)	F-to-F	0.0 Per 100 person-years (95% CI 0.0–9.6, $n = 28$)	DF: median 10 months (range: 6–43; total 434 months, 6742 exposures) DP: ⩾6 months 100% monogamy, no IDU, no heterosexual sex, no condom use
del Romero et al. 2002[19]	Spain prospective, 1990–2000	All OI	M-to-F and F-to-M	0.0 Per 100 person-years (95% CI 0.0–1.8, $n = 135$)	DF: 210 person-years (19 316 contacts)
	Heterosexual serodiscordant steady couples		M-to-F	0.0 Per 100 person-years (95% CI 0.0–2.1, $n = 110$)	DF: 179 person-years (17 621 contacts)
	81% of partners female		F-to-M	0.0 per 100 person-years (95% CI 0.0–11.4, $n = 25$)	DF: 30 person-years (1695 contacts) 8% index cases with AIDS; 16% with CD4 <200 cells/ml; 39% received ART during follow-up. Partners had no other risk factor for infection; no UAI or UVI.

Per seronegative study participant with partners of unknown serostatus

Detels et al. 1989[15]	US prospective 1984–1987 (MACS Multicenter AIDS cohort study) MSM practising OI only, seronegative at enrolment	No AI in previous 12 months (median 8 partners in previous 12 months)	M-to-M	0.37 (2/542, 0.10–1.34)[c]	DF: range 6–24 months No AI in previous 12 months
Page-Shafer et al. 2002[20] and Balls et al. 2004[21] (abstract)	US cross-sectional (person-years of exposure inferred from participants' reported previous negative HIV tests and patterns of risk behaviour) 1999-finish date not stated MSM HIV testers, tested for recent HIV infection[b]	All participants (median 3 fellatio partners in previous 6 months [IQR (1–10)] Restricted to 19% of men reporting an HIV positive or unknown serostatus partner Restricted to men reporting being exposed to the ejaculate of an HIV positive or unknown serostatus partner	M-to-M	0.00 0/439, 0–0.87)[d] 0.00 (0/83, 0.00–4.42) 0.00 (0/23, 0.00–14.31)	DE: 1519 person-years ($n = 439$) No IDU, exclusively practised fellatio in past 6 months; 6% condom use during fellatio ($n = 439$)
Lavoie et al. 2008[22] and Alary (personal communication 2008)	Canada cohort (Omega Cohort Study) MSM practising OI only (at ⩾1 of their follow-up visits), seronegative at enrolment	ROI with ⩾1 infected and/or casual partners but no AI in previous 6 months	M-to-M	0.45 (3/660, 0.15–1.33)	DF: 828.5 person-years

Per-act

Raiteri et al. 1998[16]	Italy prospective 1992–1997 Stable HIV discordant lesbian couples (10 index cases and 28 partners)	All OI (and other sexual practices such as OAI for some couples)	F-to-F	0.00 (0/849, 0.00–0.45, $n = 28$)	DF: median 10 months (range: 6–43; total 434 months) DP: ⩾6 months 100% monogamy, no IDU, no heterosexual sex, no condom use. Other F-to-F exposures, notably oroanal contact, were practised by some couples.
Vittinghoff et al. 1999[9]	US prospective 1992–1994 High risk MSM. Modified Bernoulli regression model using data from men with complex patterns of exposure [multiple types of exposure (URAI, PIAI, etc.)]. Regression of participants with multiple exposures with multiple partners, often of unknown serostatus. No seroconversions among men reporting only UROI.	UROI M-to-M with ejaculation (defined as per-act 'risk' rather than per-act 'infectivity' i.e. risk per UROI exposure from a partner who is infected or of unknown serostatus)	M-to-M	0.04 (0.01–0.17, $n = 2189$)	DF: 2633 person-years (from 2189 men with multiple sources of exposure) CI shown here calculated based on results from 100 simulated datasets created to reflect the uncertainty in the model parameters. No IDU.

(continued)

Table 1 Continued

Study	Setting/study design/population/date/gender	Description of exposure	Direction of transmission	Transmission probability (%) (x/n, 95% CI)	Duration of exposure (DE), duration of partnership (DP) or duration of follow-up (DF); stage of HIV infection, other risk factors, uncontrolled cofactors
del Romero et al. 2002[19]	Spain prospective, 1990–2000 Heterosexual serodiscordant steady couples	All OI	M-to-F and F-to-M	0.00 (0/19 316, 0.00–0.02, $n = 135$)	DF: 210 person-years
			M-to-F	0.00 (0/17 621, 0.00–0.02, $n = 110$)	DF: 179 person-years
			F-to-M	0.00 (0/1695, 0.00–0.23, $n = 25$)	DF: 30 person-years
	81% of partners female	Fellatio	M-to-F and F-to-M	0.00 (0/10 046, 0–0.04, $n = 120$)	8% index cases with AIDS; 16% with CD4 <200 cells/ml; 39% received ART during follow-up.
			M-to-F	0.00 (0/8965, 0–0.04, $n = 96$)	
			F-to-M	0.00 (0/1081, 0–0.35, $n = 24$)	Partners had no other risk factor for infection; no UAI or UVI.
		Fellatio without ejaculation in oral cavity	M-to-F and F-to-M	0.00 (0/6545, 0–0.06, $n = 83$)	
			M-to-F	0.00 (0/5905, 0–0.07, $n = 70$)	
			F-to-M	0.00 (0/640, 0–0.60, $n = 13$)	
		Fellatio with ejaculation in oral cavity	M-to-F and F-to-M	0.00 (0/3501, 0–0.11, $n = 37$)	
			M-to-F	0.00 (0/3060, 0–0.13, $n = 26$)	
			F-to-M	0.00 (0/441, 0–0.86, $n = 11$)	
		Cunnilingus	M-to-F and F-to-M	0.00 (0/9270, 0–0.04, $n = 110$)	
			M-to-F	0.00 (0/8656, 0–0.04, $n = 98$)	
			F-to-M	0.00 (0/614, 0–0.62, $n = 12$)	

F-to-F—female-to-female transmission; F-to-M—female-to-male transmission; IQR—interquartile range; IOI—insertive orogenital intercourse; M-to-F—male-to-female transmission; M-to-M—male-to-male transmission; IAI—insertive anal intercourse; NS—not stated; OAI—oroanal intercourse; PIAI—protected insertive anal intercourse; SFMHS—San Francisco Men's Health Study; UAI—unprotected anal intercourse; UVI—unprotected vaginal intercourse.

Unless specified, exposure refers to all types of OI.

[a]While Rothenberg et al.'s review[1] states that 50 couples practised unprotected OI but protected vaginal intercourse and AI in The European Study Group, we have been unable to confirm this with study authors and so have used 39 as the sample size, as quoted in the paper.[12]

[b]Using a sensitive/less sensitive enzyme immunoassay strategy.[25]

[c]Authors suspected that one of the seroconversions may have occurred after RAI exposure directly preceding the period of follow-up: 'if one assumes that the interval between infection and appearance of antibody may extend beyond 6 months in some individuals, as has been reported.[23,24]

[d]Upper 95% CI given as 0.8% in Balls et al.[21] but recalculated as 0.009 using the Wilson 'score' method without continuity correction[10] as recommended by Newcombe.[11]

unknown serostatus and, therefore, very likely under-estimates transmission probability per-act per infected partner for UROI.[9] No study among heterosexuals reported transmission by OI, except possibly Giesecke et al., where the characteristics of the 10 couples were not stated (59 homosexual and 71 heterosexual couples comprised all discordant couples identified by the study).[18] Due to the differences across studies and uncertainty regarding the quality of the estimates due to small sample sizes and misclassification biases due to difficulties in isolating OI as the only source of exposure, it was deemed inappropriate to pool study estimates by transmission types.

Discussion

Very few studies reporting HIV transmission prob-abilities through OI or reporting sufficient data to calculate it were found. This may be due to the difficulty in identifying individuals with OI as their sole exposure, the tendency to ascribe any transmis-sion events that occur to any higher risk exposure that is identified, such as AI, and the assumption that the associated risk is very low. Although transmission risk per-act or per-partner through any type of OI activity remains poorly quantified and despite the high estimate from Giesecke et al.,[18] our review suggests a low but non-zero transmission probability.

Where OI exposure with no other HIV risk factors is reported, there are the possibilities of both social desirability bias and recall bias leading to under-reporting of higher risk behaviour, which may lead to overestimation of transmission probability estimates. Celum et al. stated that in their study most men reporting UROI also reported protected AI and that for such studies that rely on self-reported behavioural data, 'some seroconverters may not have recognized condom failure and others may have over-reported condom use, which could result in over-attribution of HIV transmission to oral sexual exposure'.[26] In a MSM cohort study, Keet et al. reported that of 20 men denying receptive AI (RAI) in the 6–9 months prior to seroconversion in written questionnaires, 11 later reported this practice in face-to-face interviews.[2] Conversely, transmission probability estimates from discordant couple studies such as de Vincenzi[12] may be low and underestimate infectiousness because index partners are likely to be in the incubation period, after the period of high infectiousness during primary infection.

Different types of OI are likely to have different risks for HIV transmission. The report of a working group of the UK Chief Medical Officers' Expert Advisory Group on AIDS suggested that, 'it would seem reasonable to assume that ejaculation increases the extent of exposure to HIV and that avoiding it may help reduce the risk of HIV transmission'.[27]

Again, there are insufficient data to investigate this assumption. Del Romero et al. provide per-partner estimates by type of act and direction of transmission, but there were no seroconversions in this study.[19]

Studies reporting risk per-study participant, where number of partners and the serostatus of partners for each participant were often not available, were included in this review because of the limited number of studies reporting any type of OI risk estimate. However, such studies may suffer additional reporting bias, as seroconversions from study participants with no risk factor other than OI are notable because such events are rare and, therefore, their occurrence may increase the likelihood of reports from cohorts men-tioning them. For per-act infectiousness, Vittinghoff et al. could only quantify the OI risk per partner infected or of unknown serostatus, which would be an underestimate of risk per infected partner.[9]

Given the small number of studies, a meta-analysis was not considered appropriate as many zero esti-mates might have occurred because of the small sample size, the low risk of transmission through OI and the increased influence of misclassification biases. The low risk of transmission means large and expensive studies would be required to provide useful evidence to supply more precise estimates. Such esti-mates are important for prevention and counselling of individual patients. The relative contribution of OI to HIV transmission, despite its inherent low infec-tiousness, may be substantial if the frequency of unprotected OI is increasing relative to higher risk sexual practices, which may be protected.[1,28,29] Never-theless, the fact that infected study participants with solely this exposure have remained difficult to iden-tify may suggest that indeed the contribution of OI to HIV incidence remains low. The contribution of OI to HIV incidence needs close monitoring and oppor-tunities for further transmission probability studies should be identified and utilized in order to give greater understanding of this neglected mode of transmission.

Acknowledgements

KEY MESSAGES

- It is important to assess risk of HIV transmission from OI (between men, between men and women and between women) but very few studies have been published which look at this.

- Given the lack of information, summary estimates for risk, be it risk per act of OI or risk per partner where OI is practised, cannot be made.

- More and larger (therefore expensive) studies would be required to derive more precise estimates.

- However, despite the few data, it appears that risk of HIV transmission through orogenital sex is very low but not zero—individuals should protect themselves using condoms or dental dams to minimize this small risk.

References

[1] Rothenberg RB, Scarlett M, del Rio C, Reznik D, O'Daniels C. Oral transmission of HIV. *AIDS* 1998;**12**:2095–105.

[2] Keet IP, Albrecht van Lent N, Sandfort TG, Coutinho RA, van Griensven GJ. Orogenital sex and the transmission of HIV among homosexual men. *AIDS* 1992;**6**:223–26.

[3] Centers for Disease Control and Prevention DoHaHS, HIV/AIDS Questions and Answers: Can I get HIV from oral sex? Available at: http://www.cdc.gov/hiv/resources/qa/qa19.htm (Accessed December 21, 2007).

[4] Dillon B, Hercht FM, Swanson M *et al*. Primary HIV infection associated with oral transmission. 7th Conference on Retroviruses and Opportunistic Infections Chicago, February 2000 [Abstract 473]. 2000.

[5] Gilbart VL, Evans BG, Dougan S. HIV transmission among men who have sex with men through oral sex. *Sex Transm Infect* 2004;**80**:324.

[6] Richters J, Grulich A, Ellard J, Hendry O, Kippax S. HIV transmission among gay men through oral sex and other uncommon routes: case series of HIV seroconverters, Sydney. *AIDS* 2003;**17**:2269–71.

[7] Stroup DF, Berlin JA, Morton SC *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;**283**: 2008–12.

[8] Samuel MC, Mohr MS, Speed TP, Winkelstein W. Infectivity of HIV by anal and oral intercourse among homosexual men. Estimates from a prospective study in San Francisco. In: Kaplan EH, Brandeau ML (eds). *Modeling the AIDS Epidemic: Planning, Policy and Prevention*. New York: Raven Press, 1994. pp. 423–38.

[9] Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *Am J Epidemiol* 1999;**150**:306–11.

[10] Wilson EB. Probable inference, the law of succession, and statistical inference. *J Am Stat Assoc* 1927;**22**:209–12.

[11] Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med* 1998;**17**:857–72.

[12] de Vincenzi I. A longitudinal study of human immunodeficiency virus transmission by heterosexual partners. European study group on heterosexual transmission of HIV. *N Engl J Med* 1994;**331**:341–46.

[13] Kingsley LA, Detels R, Kaslow R *et al*. Risk factors for seroconversion to human immunodeficiency virus among male homosexuals. Results from the Multicenter AIDS Cohort Study. *Lancet* 1987;**1**:345–49.

[14] Raiteri R, Fora R, Sinicco A. No HIV-1 transmission through lesbian sex. *Lancet* 1994;**344**:270.

[15] Detels R, English P, Visscher BR *et al*. Seroconversion, sexual activity, and condom use among 2915 HIV seronegative men followed for up to 2 years. *J Acquir Immune Defic Syndr* 1989;**2**:77–83.

[16] Raiteri R, Baussano I, Giobbia M, Fora R, Sinicco A. Lesbian sex and risk of HIV transmission. *AIDS* 1998;**12**:450–51.

[17] Winkelstein W Jr, Lyman DM, Padian N *et al*. Sexual practices and risk of infection by the human immunodeficiency virus. The San Francisco Men's Health Study. *JAMA* 1987;**257**:321–25.

[18] Giesecke J, Ramstedt K, Granath F, Ripa T, Rado G, Westrell M. Partner notification as a tool for research in HIV epidemiology: behaviour change, transmission risk and incidence trends. *AIDS* 1992;**6**:101–07.

[19] del Romero J, Marincovich B, Castilla J *et al*. Evaluating the risk of HIV transmission through unprotected orogenital sex. *AIDS* 2002;**16**:1296–97.

[20] Page-Shafer K, Shiboski CH, Osmond DH *et al*. Risk of HIV infection attributable to oral sex among men who have sex with men and in the population of men who have sex with men. *AIDS* 2002;**16**:2350–52.

[21] Balls J, Evans J, Dilley J *et al*. No incident HIV infections among MSM who practice exclusively oral sex. International Conference on AIDS, Bangkok, Thailand 2004; Oral Poster Presentation WePpC2072, 2004.

[22] Lavoie E, Alary M, Remis RS *et al*. Determinants of HIV seroconversion among men who have sex with men living in a low HIV incidence population in the era of highly active antiretroviral therapies. *Sex Transm Dis* 2008;**35**:25–9.

[23] Allain JP, Laurian Y, Paul DA, Senn D. Serological markers in early stages of human immunodeficiency virus infection in haemophiliacs. *Lancet* 1986;**2**:1233–36.

[24] Wolinsky S, Rinaldo C, Farzadegan H *et al*. Polymerase chain reaction (PCR) detection of HIV provirus before HIV seroconversion (abstract). IVth International

Conference on AIDS, Stockholm, Sweden, June 12–16, 1988.

[25] Janssen RS, Satten GA, Stramer SL *et al*. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA* 1998;**280**:42–48.

[26] Celum CL, Buchbinder SP, Donnell D *et al*. Early human immunodeficiency virus (HIV) infection in the HIV Network for Prevention Trials Vaccine Preparedness Cohort: risk behaviors, symptoms, and early plasma and genital tract virus load. *J Infect Dis* 2001; **183**:23–35.

[27] Review of the evidence on risk of HIV transmission associated with oral sex. Report of a working group of the UK Chief Medical Officers' Expert Advisory Group on AIDS. June 12, 2000. Available at: www.dh.gov.uk (Accessed December 5, 2007).

[28] Edwards S, Carne C. Oral sex and the transmission of viral STIs. *Sex Transm Infect* 1998;**74**:6–10.

[29] Samuel MC, Hessol N, Shiboski S, Engel RR, Speed TP, Winkelstein W Jr. Factors associated with human immunodeficiency virus seroconversion in homosexual men in three San Francisco cohort studies, 1984-1989. *J Acquir Immune Defic Syndr* 1993;**6**:303–12.