

VIH E DESEJO DE PARENTALIDADE

Concepção Natural
Técnicas de Procriação Medicamente Assistida

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_Infeção VIH/SIDA: a situação em Portugal a 31 de dezembro de 2013

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_local / data:

Lisboa

Novembro 2014

A situação em Portugal a 31 de Dezembro de 2013

Quadro 2 – Novos casos de infeção por VIH (≥ 15 anos) diagnosticados em 2013: idade mediana à data de diagnóstico, por sexo e categoria de transmissão

	Idade mediana	DIQ	
		25%	75%
Todos os novos casos (≥ 15 anos)	40,0	32,0	51,0
Homens	41,0	32,0	52,0
Mulheres	40,0	32,0	51,0
Transmissão heterossexual	44,0	36,0	54,0
Transmissão HSH	33,0	26,0	41,0
Transmissão toxicodependência	41,0	36,0	46,0

Legenda: DIQ- Desvio interquartil

Quadro 5 – Novos casos de infeção por VIH (≥ 15 anos) diagnosticados em 2013: distribuição por categoria de transmissão e sexo

Categoria de transmissão	Nº casos		
	Total	Homens	Mulheres
Heterossexual	665	362	303
Mãe-filho	2	1	1
Toxicodependente	76	66	10
Homo e toxicodependente	2	2	-
Homo ou bissexual	330	330	-
Transfundido	a)1	a)1	0
Outro	1	1	0
Desconhecida	12	7	5
Total	1089	770	319

Legenda: a) Transfusão ocorrida fora de Portugal

A situação em Portugal a 31 de Dezembro de 2013

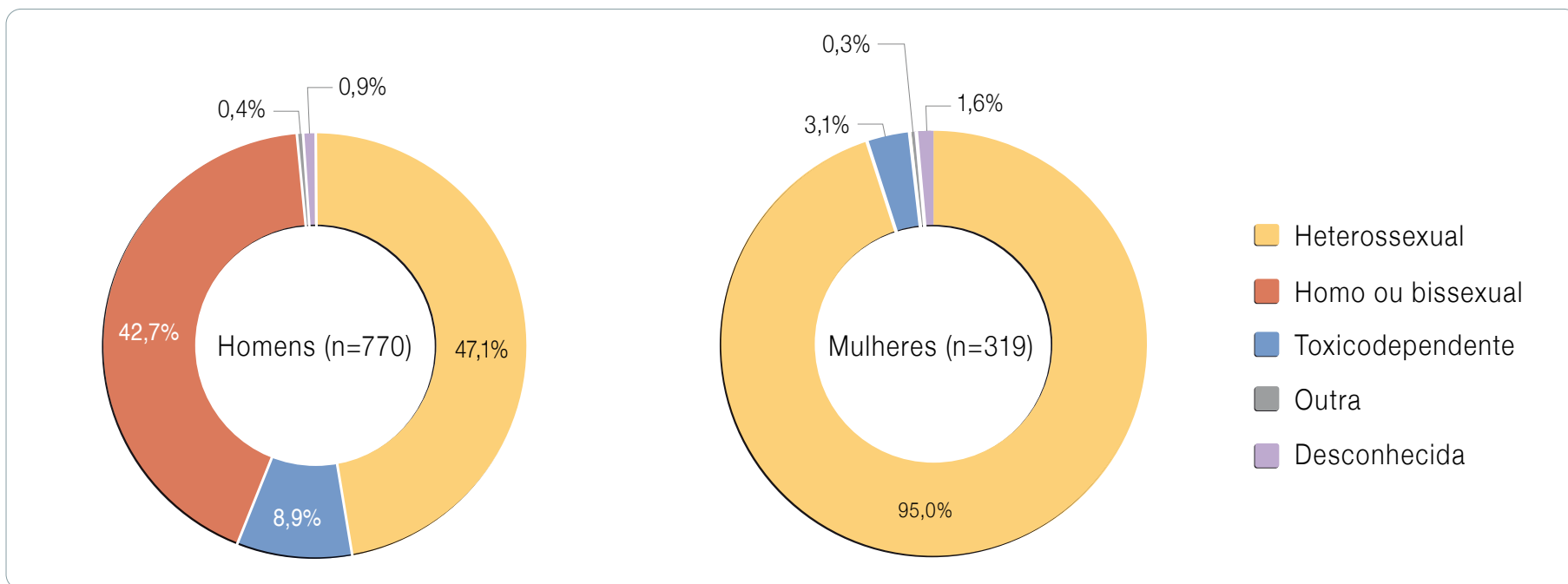


Figura 1 – Novos casos de infeção por VIH (≥ 15 anos) diagnosticados em 2013: proporção por sexo e categoria de transmissão

A situação em Portugal a 31 de Dezembro de 2013

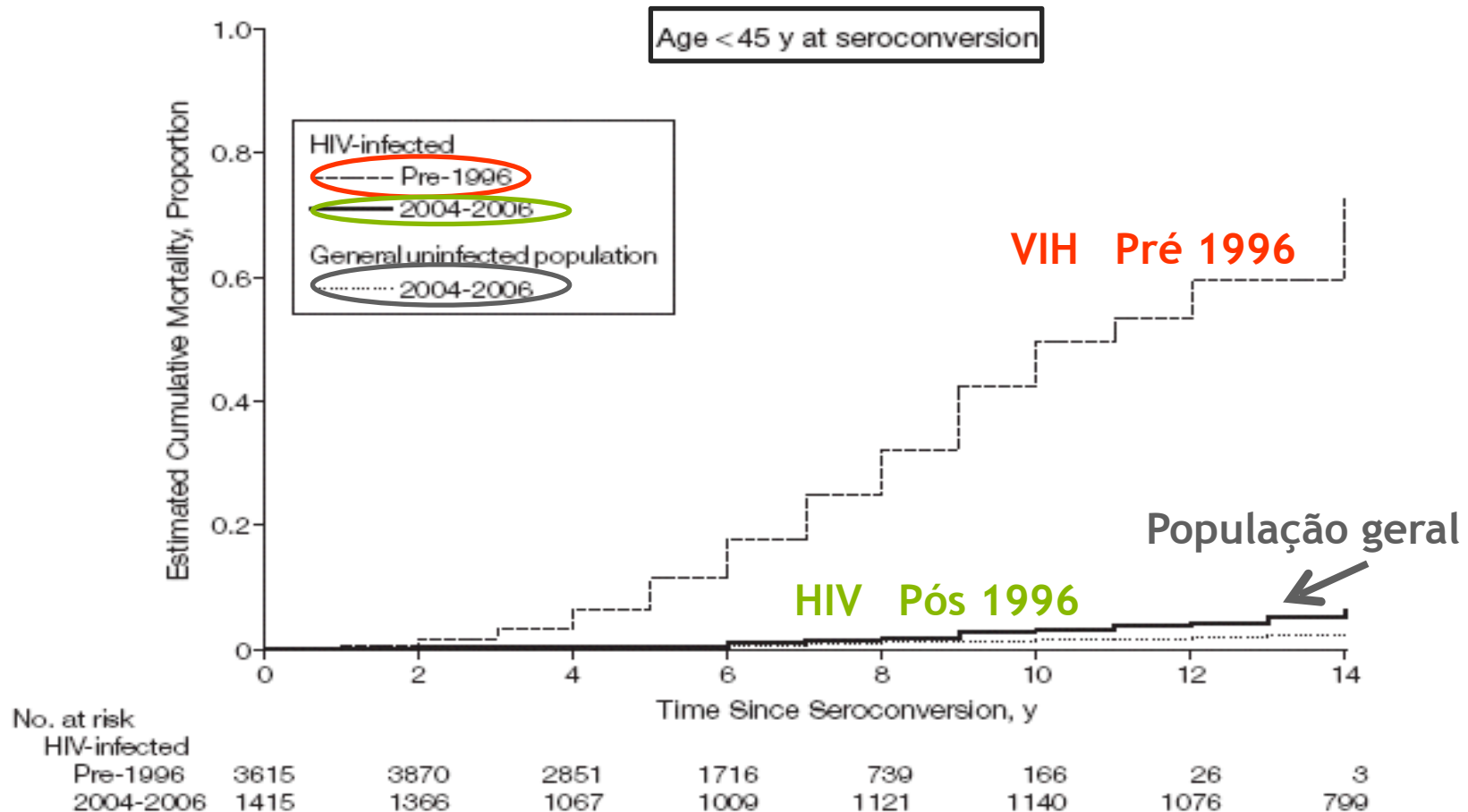
Quadro 18 – Casos de infeção por VIH (1983-2013): distribuição por grupo etário e sexo segundo o ano de diagnóstico

Grupo etário		Ano de diagnóstico											Total N	%
		≤ 2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013		
20 - 24 anos	Sub-total	^{b)} 4017	147	132	137	148	139	134	126	135	125	79	5319	11,2
	H	2815	78	69	85	99	86	101	81	91	102	64	3671	
	M	1201	69	63	52	49	53	33	45	44	23	15	1647	
25-29 anos	Sub-total	^{a)} 6572	341	256	300	285	245	203	211	162	182	138	8895	18,8
	H	4941	204	158	186	177	165	126	133	120	130	98	6438	
	M	1629	137	98	114	108	80	77	78	42	52	40	2455	
30-34 anos	Sub-total	5937	439	358	347	328	312	296	261	244	211	139	8872	18,7
	H	4633	305	263	242	202	209	198	186	153	150	90	6631	
	M	1304	134	95	105	126	103	98	75	91	61	49	2241	
35-39 Anos	Sub-total	^{b)} 4158	387	359	350	315	332	298	262	237	209	140	7047	14,9
	H	3276	291	265	248	226	246	212	182	164	150	103	5363	
	M	881	96	94	102	89	86	86	80	73	59	37	1683	
40-44 anos	Sub-total	^{b)} 2482	239	303	280	244	297	249	284	223	215	155	4971	10,5
	H	2012	164	225	209	175	211	196	213	172	153	106	3836	
	M	469	75	78	71	69	86	53	71	51	62	49	1134	

Faixa etária 20-44 anos: 74,1% dos infectados

Changes in the Risk of Death After HIV Seroconversion Compared With Mortality in the General Population

Figure. Reduction in All-Cause Mortality pre-1996 to 2006 and Comparison With That of the General Population, by Age Group



- Características demográficas e epidemiológicas da população infectada pelo VIH
- Aumento significativo da sobrevivência a longo com a terapêutica antiretroviral combinada (TARc)
- Optimização das técnicas de preparação espermática
- Risco de transmissão mãe-filho < 1%

ASRM PAGES

Human immunodeficiency virus (HIV) and infertility treatment: a committee opinion

Ethics Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

Fertility and Sterility® Vol. 104, No. 1, July 2015

Presença do VIH-1 no esperma



Partículas livres de RNA VIH-1 no líquido seminal

Partículas RNA VIH-1 adsorvidas à superfície dos linfócitos CD4+ e dos macrófagos – **Principal reservatório**

DNA proviral VIH-1 nos espermatozoides???

- Knowledge of the rates and risk factors of transmission is essential for the design and the evaluation of prevention programmes

Shattock RJ, Moore JP. **Inhibiting sexual transmission of HIV-1 infection.** *Nat Ver Microbiol* 2003;1:25-34

- The viral load is the chief predictor of the risk of transmission of HIV-1, and transmission is rare among individuals with levels of <1500 copies of HIV-1 RNA

Quinn TC et al. **Viral load and heterossexual transmission of human immunodeficiency virus type 1.** *N Engl J Med* 2000;342:921-929

- In this study involving 1763 serodiscordant couples in which HIV-1 infected participants had a CD4 count of 350 to 550 cells per cubic millimeter, there was a relative reduction of 96% in the number of linked HIV-1 transmission resulting from early initiation of antiretroviral therapy

Cohen S et al. **Prevention of HIV-1 infection with early antiretroviral therapy.** HPTN 052 Study Team. *N Engl J Med* 2011;365:493-505

Table 3 | Characteristics of couples and events occurring during follow-up according to antiretroviral treatment of index partner

	Antiretroviral treatment of index partner*			
	All couples	Without treatment	Monotherapy/ dual therapy	Combined treatment
Couples in follow-up:				
All	424	341	47	144
Male index partner (%)	351 (83)	279 (82)	33 (70)	117 (81)
Couple years	1355	863	75	417
Estimated No of coital acts	95 000	62 000	5000	28 000
Couples with sexual risk exposures during follow-up†:				
Couples with unprotected sexual contacts (%)	266 (63)	187 (55)	24 (51)	101 (70)
Couples with unprotected penile-anal contacts	26	13	4	11
Estimated No of risky sexual exposures	20 000	11 000	1600	7400
No of condom failures during intercourse	198	166	14	18
Women with bacterial vaginosis or vaginal candidiasis	61	53	9	6
Sexually transmitted infection in either partner‡	9	8	1	2
History of AIDS defining disease in index partner	55	19	13	35
First year of relationship	62	54	0	8
Index partner with primary infection	3	3	0	0
Plasma HIV RNA (undetectable/tested (%))	142/220 (65)	28/95 (29)	6/14 (43)	112/122 (92)
Median (IQR) plasma HIV RNA copies per ml	ND (ND-6900)	6402 (500-42 916)	5367 (ND-16 770)	ND
Seroconversions to HIV in follow-up:				
No of seroconversions	5	5	0	0
Percentage of couples (95% CI)	1.2 (0.4 to 2.7)	1.5 (0.5 to 3.4)	0 (0 to 7.5)	0 (0 to 2.5)
Rate per 100 couple years (95% CI)	0.4 (0.1 to 0.9)	0.6 (0.2 to 1.4)	0 (0 to 6.1)	0 (0 to 1.1)
Transmission per 1000 risk exposures (95% CI)	0.2 (0.1 to 0.6)	0.4 (0.1 to 1.0)	0 (0 to 2.2)	0 (0 to 0.5)
Natural pregnancies during follow-up:				
No of couples with any natural pregnancy	88	48	4	39
Percentage (95% CI)	21 (17 to 25)	14 (11 to 18)	9 (2 to 20)	27 (20 to 35)
No of natural pregnancies	101	50	4	47
Rate per 100 couple years (95% CI)	7.5 (6.1 to 9.0)	5.8 (4.4 to 7.6)	5.3 (1.7 to 13.8)	11.3 (8.5 to 14.8)

ND=not detectable.

*Each couple could have different therapeutic options during follow-up.

†Includes penile-vaginal or penile-anal contacts without condom and condoms breaking or slipping during intercourse.

‡Condylomata acuminata (8) and urethritis (1).

Del Romero et al. Combined antiretroviral treatment and heterosexual transmission of HIV-1: cross sectional and prospective cohort study. *BMJ* 2010;340:C2205

- Adopção

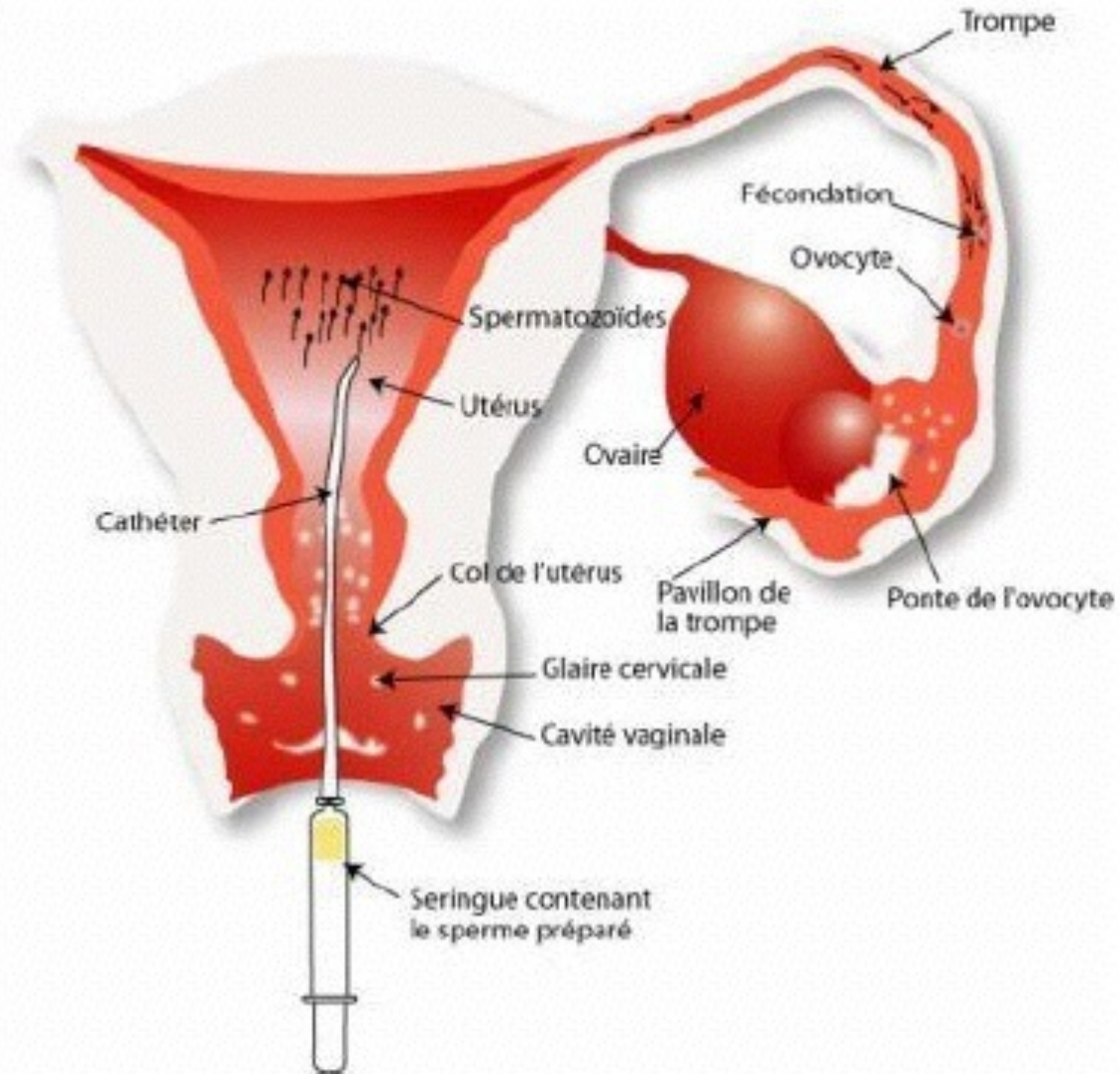
RISCO NULO

- Utilização de espermatozoides de dador

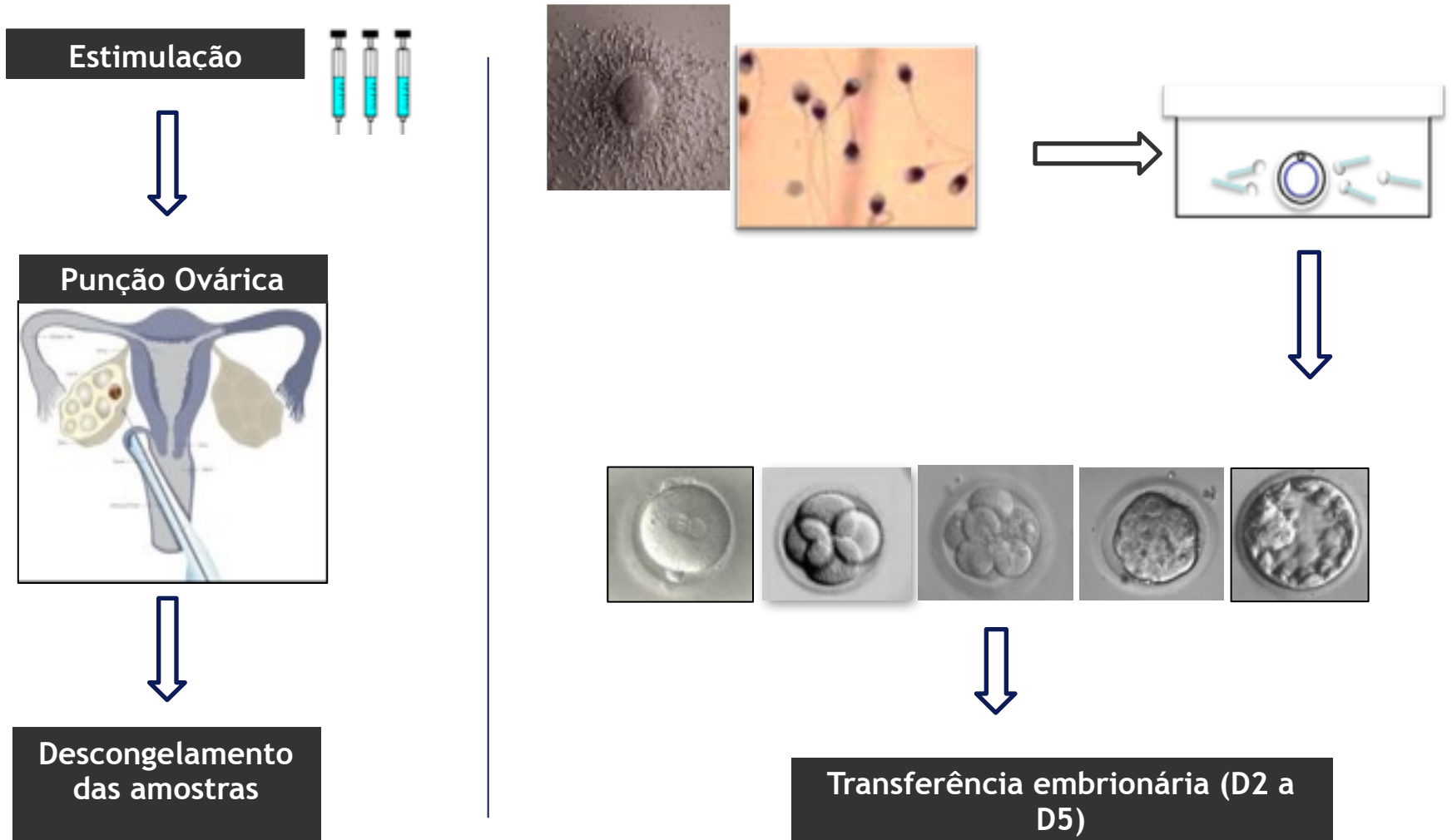
- Técnicas de PMA com espermatozoides lavados **RISCO TEÓRICO**

- Concepção natural com ou sem PrEP **RISCO ????**

INSEMINAÇÃO INTRA-UTERINA



FERTILIZAÇÃO *IN VITRO*



MICROINJEÇÃO INTRACITOPLASMÁTICA DE ESPERMATOZÓIDES

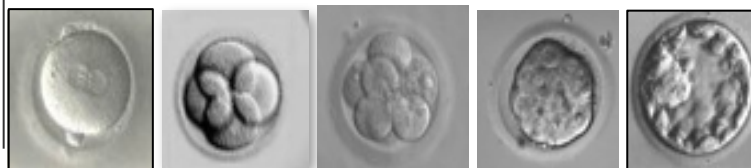
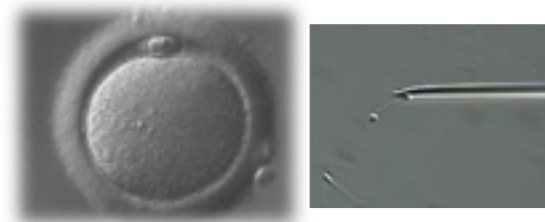
Estimulação Ovárica



Punção Ovárica



Descongelamento
das amostras
seminais



Transferência
embrionária (D2 a D5)

Efficacy and safety of intrauterine insemination and assisted reproductive technology in populations serodiscordant for human immunodeficiency virus: a systematic review and meta-analysis

Arti Barnes, M.D., M.P.H.,^a Daniel Riche, Pharm.D., B.C.P.S., C.D.E.,^b Leandro Mena, M.D., M.P.H.,^a
Thérèse Sison, B.A.,^c Lauren Barry, M.D.,^d Raveena Reddy, M.D.,^e James Shwayder, M.D.,^d
and John Preston Parry, M.D., M.P.H.^f

Characteristics of published studies on procreative therapy in serodiscordant couples with an HIV-1 infected partner.

Study	Therapy	Couples (n)	Cycles (n)	HIV+ males and females ^a	Type of study	Pregnancies		Miscarriages		Multiple gestation		Average CD4 count	Viral load
						n	% Per cycle	n	% Per pregnancy	n	% Per pregnancy		
Marina et al. 1998 (29)	IUI	63	101	63 M	Prospective cohort	31	31	3	10	8	26		
Weigel et al. 2001 (31)	ART and IUI	54	132	54 M	Retrospective cohort	30	23						
Quintana et al. 2002 (32)	IUI	15	28	15 M	Clinical retrospective	11	39			2	18	≥ 300	0
Ohl et al. 2003 (30)	ART and IUI	42	57	39 M 3 F	Clinical prospective	20	35	0	0		15	>200	69% M 92% F
Lowenstein et al. 2005 (33)	IUI	4	8	4 M	Prospective	2	25	0	0	0	0		
Ohl et al. 2005 (34)	ART and IUI	36	82	36 F	Prospective cohort	13	16	4	31	0	0	497	2,413
Terriou et al. 2005 (35)	ART	29	66	29 F	Case control	9	14	1	11	6	67	>200	
Coll et al. 2006 (12)	ART	72	100	37 M 35 F	Prospective cohort	23	23						
Manigart et al. 2006 (11)	ART and IUI	85	283	38 M 33 F 14 Both	Prospective cohort	41	14	6	15	4	10		
Bujan et al. 2007 (1) (36)	IUI	84	294	84 M	Retrospective comparative	53	18	9	17	7	13	610	633
Bujan et al. 2007 (2) (37)	ART and IUI	1,036	3,390	1,036 M	Retrospective multicenter cohort	580	17	123	21	42	7		
Savasi et al. 2007 (38)	ART and IUI	741	2,683	741 M	Prospective cohort	521	19	54	10			510	64%
Melo et al. 2008 (17)	ART	30	30	30 M	Retrospective case-control	14	47	2	14	3	21	539	2,641
Douglas et al. 2009 (39)	ART and IUI	22	45	22 F	Retrospective cohort	14	31	3	21	3	21	712	
Kashima et al. 2009 (20)	ART	27	38	27 M	Case control	17	45	3	18	5	29	377	967
Kazlauskaitė et al. 2009 (18)	IUI	19	58	9 M 10 F	Prospective	16	28	4	25	1	6	612	0
Van Leeuwen et al. 2009 (40)	IUI	61	266	61 M	Retrospective review	32	12	7	22	5	16		
Sauer et al. 2009 (41)	ART	181	420	181 M	Retrospective cohort	161	38	27	17	48	30	608.3	3,181
Nicopoulos et al. 2010 (42)	IUI	151	429	151 M	Retrospective cohort	61	14	20	33			409	36%
Prisant et al. 2010 (13)	ART	80	138	28 M 52 F	Retrospective case control	23	17					>200	
Santoulli et al. 2011 (14)	ART	144	144	87 M 57 M	Age-matched cohort study	30	21					>200	
Schuffner et al. 2011 (10)	IUI	10	10	10 M	Retrospective cohort	4	40	0	0	1	25		0
Wu et al. 2011 (43)	ART	14	22	14 M	Prospective cohort	5	23						7%
Semprini et al. 2013 (44)	IUI	587	1,993	587 M	Retrospective cohort	317	16	62	20	20	6		

^a M = number of HIV-positive men; F = number of HIV-positive women; Both = number of couples where both the man and woman are HIV positive. Data were used only for HIV serodiscordant couples. Viral load data reflects either the average viral load or the percentage with detectable viral load if the average viral load was not extractable from a publication.

Barnes. IUI and IVF in HIV-serodiscordant couples. *Fertil Steril* 2014.

Les personnes séropositives ne souffrant d'aucune autre MST et suivant un traitement antirétroviral efficace **ne transmettent pas** le VIH par voie sexuelle.

Vernezza et *al.* **Bulletin des Médecins Suisses** 2008;89:165-69

ALTERAÇÃO DE PARADIGMA

CONCEPÇÃO NATURAL

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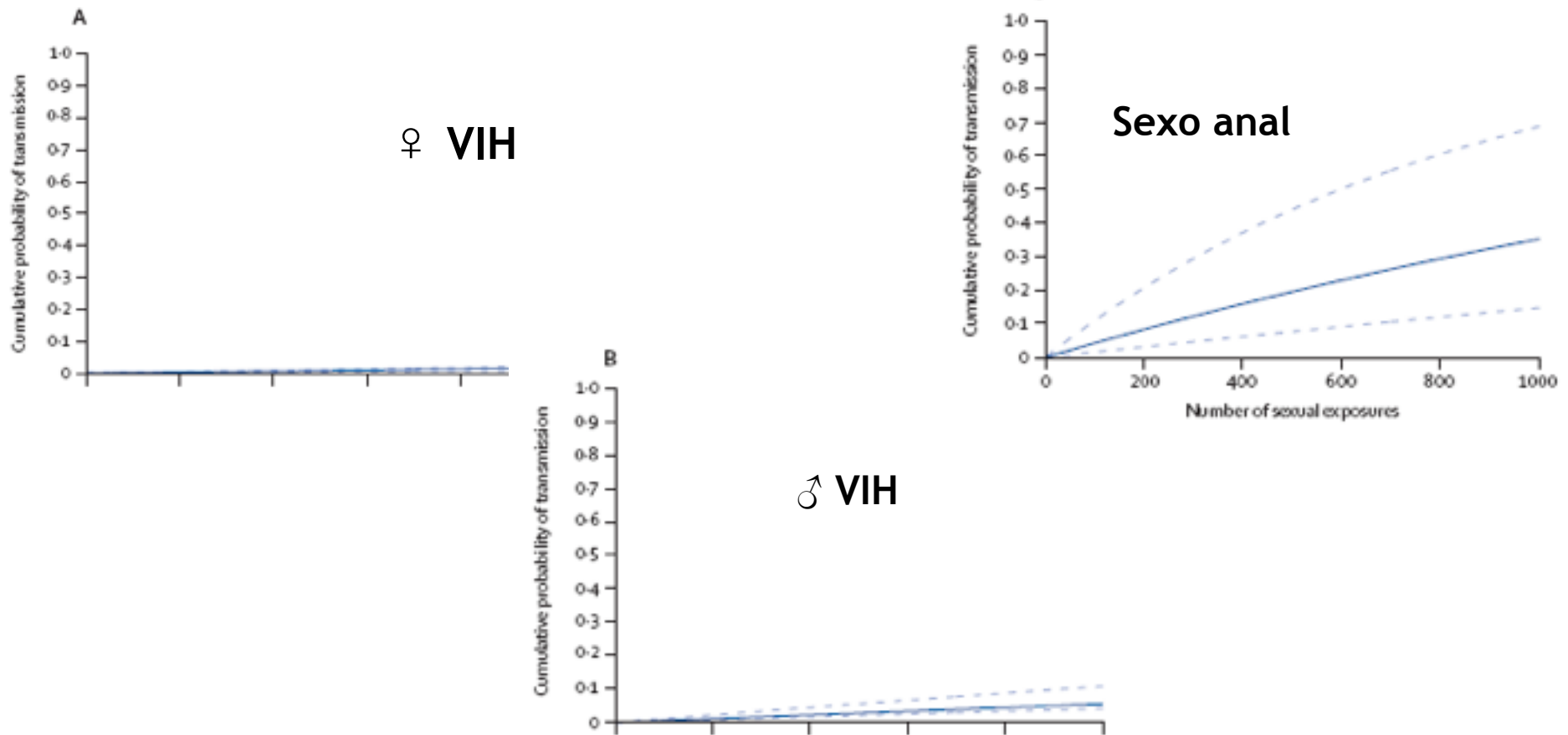


Figure 2: Relation between the cumulative risk of HIV transmission and the number of sexual exposures to HIV-infected partner who is effectively treated (viral load of 10 copies per mL)

(A) Insertive penile-vaginal transmission, (B) receptive penile-vaginal transmission, and (C) penile-anal transmission. Solid line refers to a rate ratio of 2.45 between transmission probability and viral load; broken lines are uncertainty bounds associated with the 95% CI of the rate ratio.

- Our model suggests that although the individual risk of HIV transmission per act is fairly small, the **rate of transmission over large numbers of acts might be substantial** and could be further exacerbated by viral rebounds.
- Our analyses suggest that **the risk of HIV transmission** in heterosexual partnerships in the presence of effective treatment is **low but non-zero**.

Viral load in infected partner	Sexual exposure route	Expected value	Lower bound	Upper bound
5 copies per mL	Female-to-male	164	56	471
	Male-to-female	326	111	920
	Male-to-male	2823	1060	6191
10 copies per mL	Female-to-male	215	80	564
	Male-to-female	425	159	1096
	Male-to-male	3524	1477	6871
50 copies per mL	Female-to-male	398	181	854
	Male-to-female	781	359	1635
	Male-to-male	5565	3059	8325
400 copies per mL	Female-to-male	872	517	1441
	Male-to-female	1669	1007	2674
	Male-to-male	8391	6543	9557

Table 2: Expected number of HIV seroconversions out of 10 000 serodiscordant couples in a hypothetical population over 1000 acts per partnership, with lower and upper uncertainty bounds

Wilson et al. Relation between HIV viral load and infectiousness: a model-based analysis. Lancet 2008;372:314-20

CONCEPÇÃO NATURAL

**DELINEAR, EM CONJUNTO COM O CASAL, ESTRATÉGIAS
PARA MINIMIZAR RISCO DE SEROCONVERSÃO**



- **Relações sexuais desprotegidas limitadas ao período peri-ovulatório**
- **Profilaxia pré-exposição**

Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child

Pietro L. Vernazza^a, Irma Graf^b, Ulrike Sonnenberg-Schwan^c,
Maria Geit^d and Anja Meurer^c

AIDS 2011, 25:2005–2008

- (1) Male partner has been successfully treated with undetectable HIV-RNA in plasma (<50 copies/ml) without the need of HIV-RNA testing in semen.
- (2) No report of current symptoms of genital infections and no unprotected sex with other partners.
- (3) LH-test in the urine is used to determine the optimal time of conception (36 h after LH-peak).
- (4) Administration of PrEP with tenofovir, first dose at LH-peak and second 24 h later.
- (5) After six unsuccessful attempts, a fertility evaluation was suggested.

- 46 casais
- 244 relações sexuais desprotegidas durante o estudo
- Seroconversão: 0 casos
- Taxa de gravidez: 75% após 1 ano

US PUBLIC HEALTH SERVICE

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES – 2014

CLINICAL PROVIDERS' SUPPLEMENT



Consulta de Infecçiology

Papel primordial do
infecçiology

Consulta de Medicina de Reprodução

- Excluir eventuais factores de infertilidade
- Determinar probabilidade de gravidez espontânea



Information for Clinicians

Counseling Patients about PrEP Use During Conception, Pregnancy, and Breastfeeding

PrEP use may be one of several options to help protect the HIV-negative male or female partner in a heterosexual HIV-discordant couple during attempts to conceive^{1,2}.

DHHS Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission

Panel's Recommendations on Reproductive Options for HIV-Concordant and Serodiscordant Couples

For Couples who Want to Conceive

For Both Concordant (Both Partners are HIV-Infected)/Discordant Couples:

- Expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple (AIII).
- Partners should be screened and treated for genital tract infections before attempting to conceive (AII).
- The HIV-infected partner should attain maximum viral suppression before attempting conception (AIII).

For Discordant Couples:

- Combination antiretroviral therapy (cART) for the infected partner may not be fully protective against sexual transmission of HIV.
- Periconception administration of antiretroviral pre-exposure prophylaxis (PrEP) for HIV-uninfected partners may offer an additional tool to reduce the risk of sexual transmission (CIII). The utility of PrEP of the uninfected partner when the infected partner is receiving cART has not been studied.

Discordant Couples with HIV-Infected Female:

- The safest conception option is artificial insemination, including the option of self-insemination with a partner's sperm during the peri-ovulatory period (AIII).

Discordant Couples with HIV-Infected Male:

- The use of donor sperm from an HIV-uninfected male with artificial insemination is the safest option.
- When the use of donor sperm is unacceptable, the use of sperm preparation techniques coupled with either intrauterine insemination or *in vitro* fertilization should be considered (AII).
- Semen analysis is recommended for HIV-infected males before conception is attempted to prevent unnecessary exposure to infectious genital fluid when the likelihood of getting pregnant is low because of semen abnormalities (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

- Infecção VIH considerada como doença crónica
- Exercício do direito à parentalidade biológica
- Minimizar risco de transmissão da doença ao parceiro não infectado e à criança
- Concepção natural como opção de procriação

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Assistente Hospitalar de Ginecologia e Obstetrícia
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