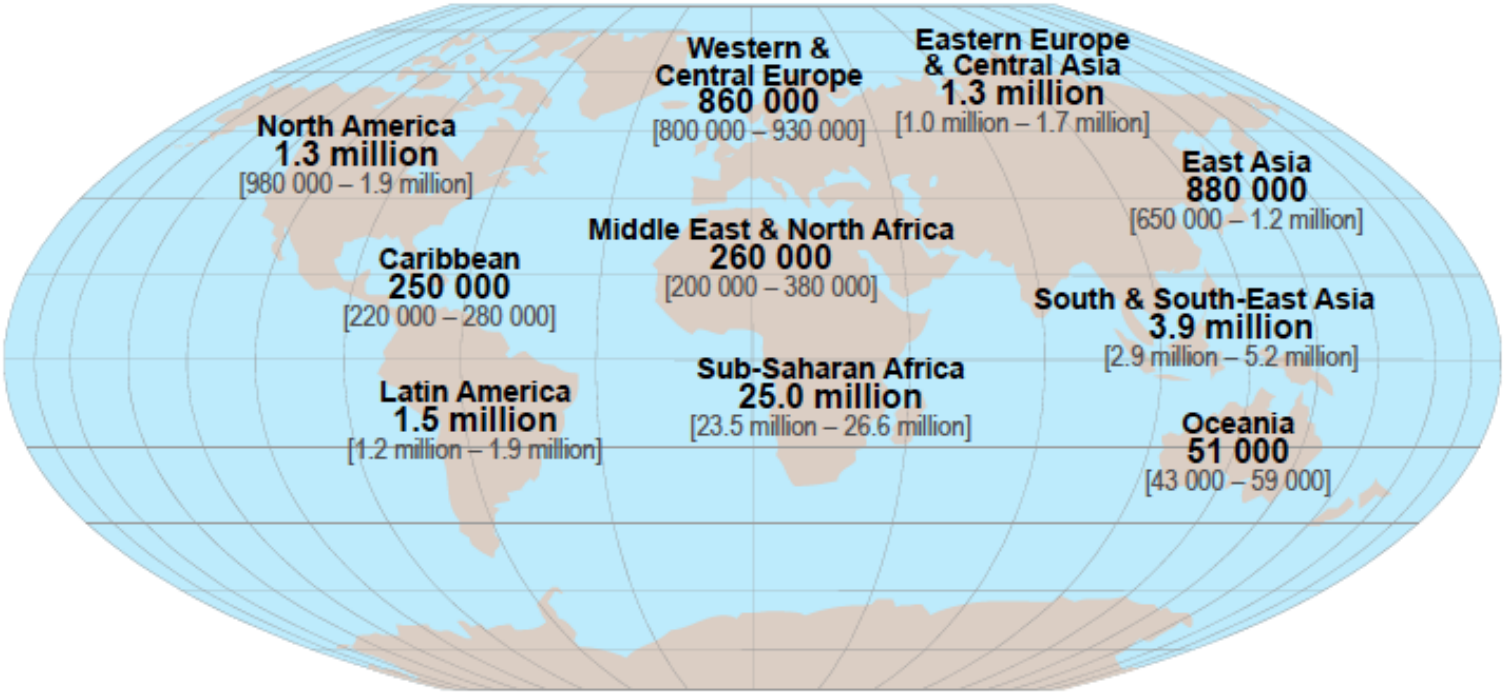
Problematiche di genere in HIV

Managing women with HIV

Cristina Mussini

Adults and children estimated to be living with HIV | 2012

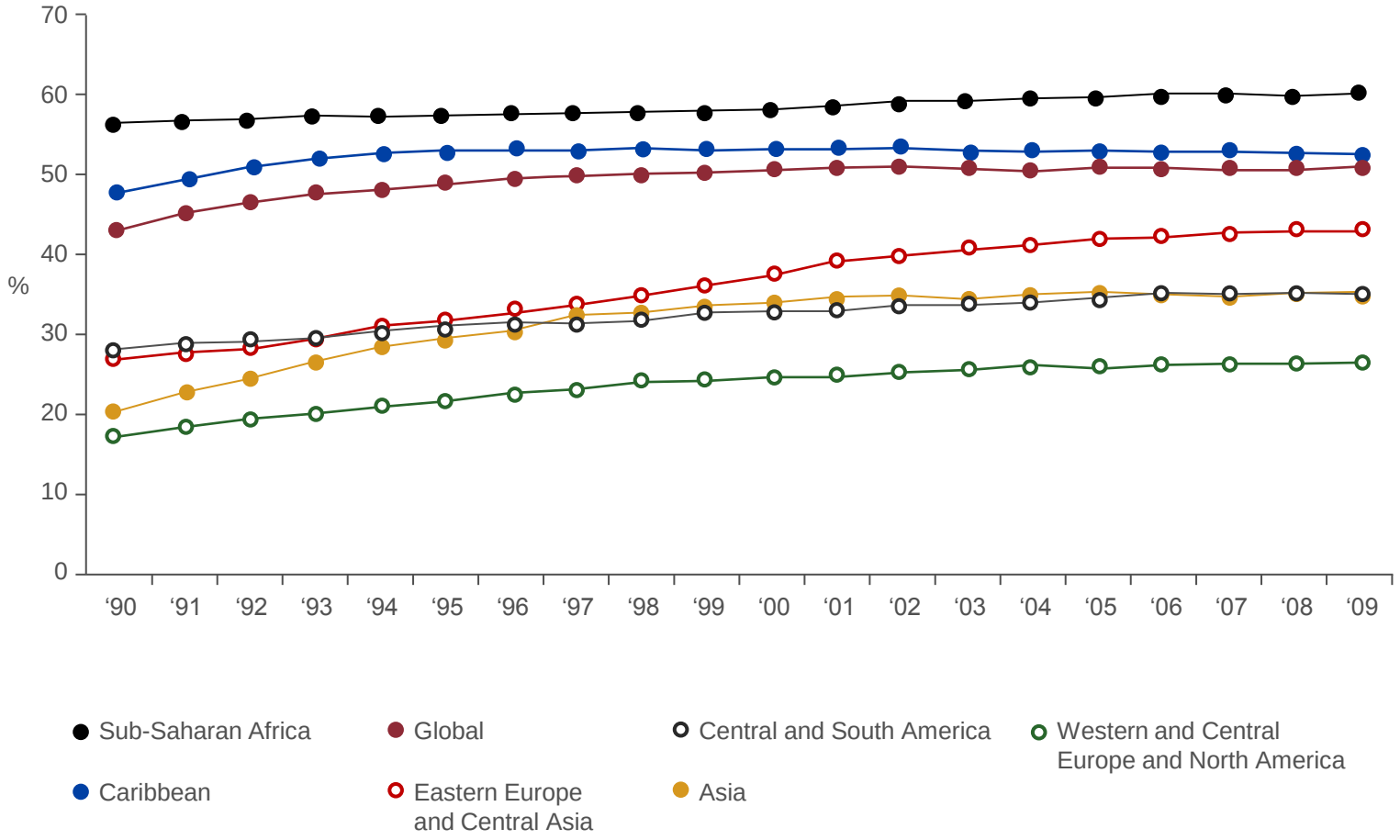


Total: 35.3 million [32.2 million – 38.8 million]

World Health Organization

UNAIDS

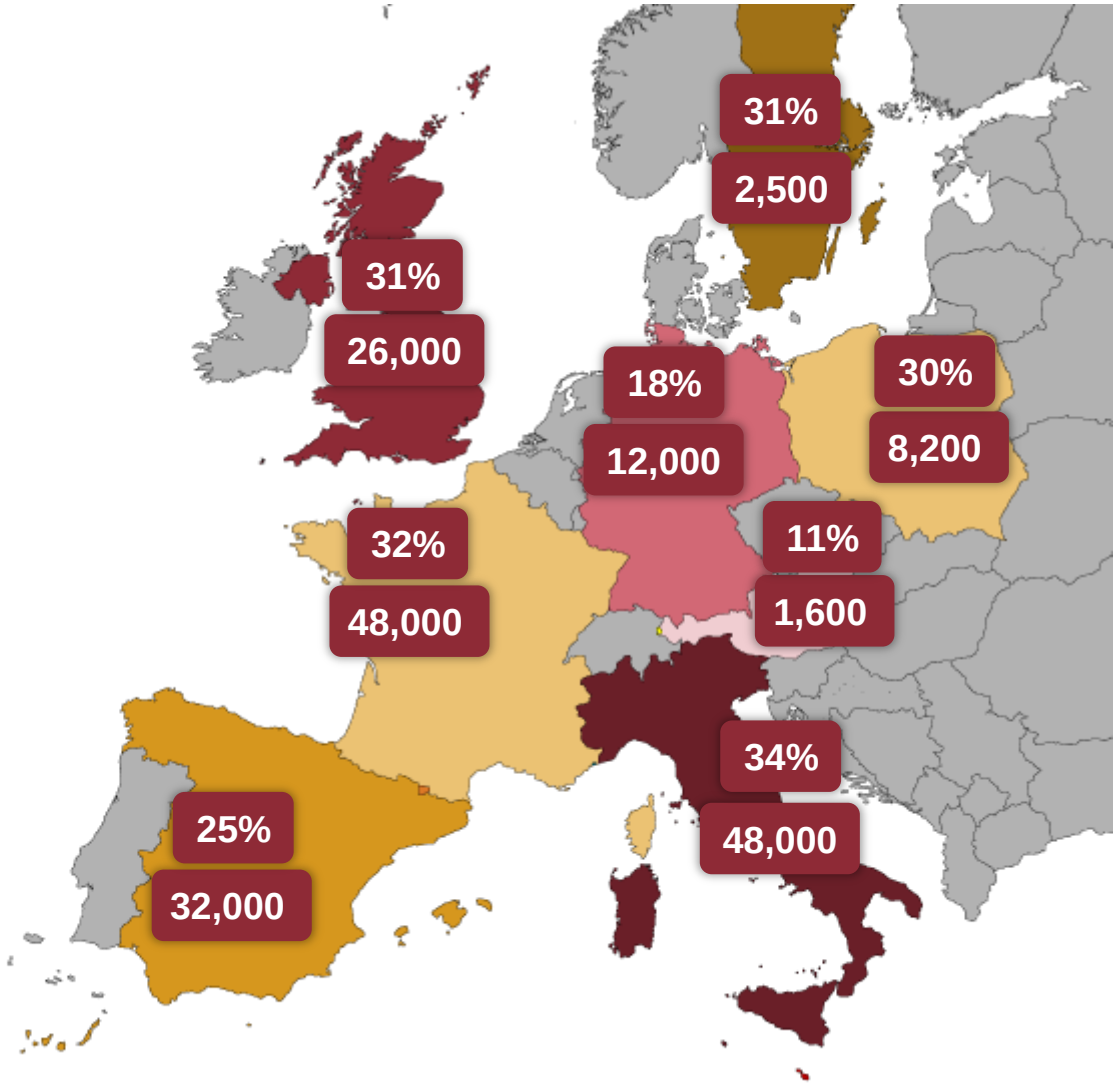
Percentage of women with HIV varies by region and over time



UNAIDS Report on the Global HIV epidemic. 2010. Available at : http://www.unaids.org/GlobalReport/documents/20101123_GlobalReport_full_en.pdf . Accessed in March 2011

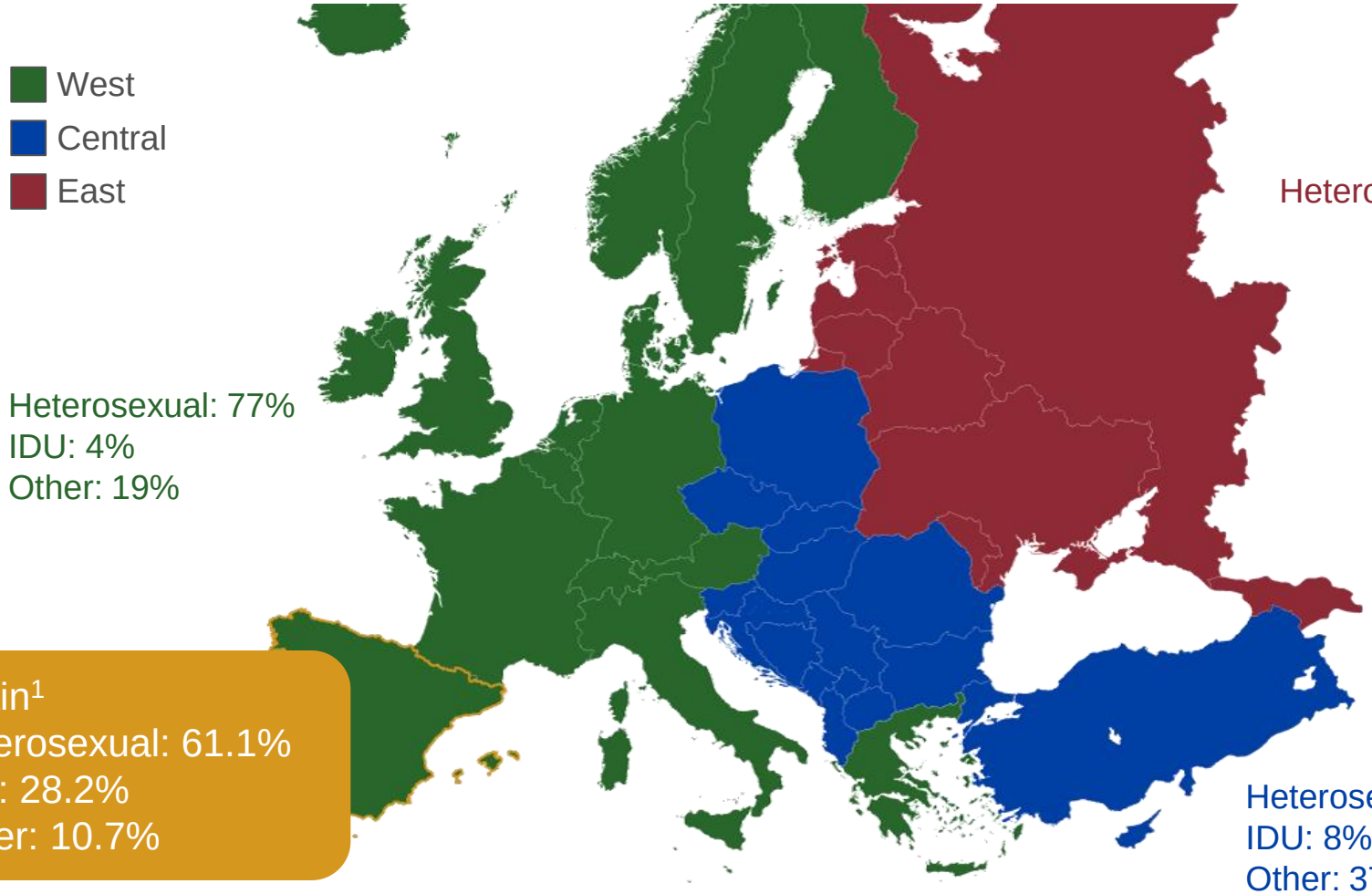
Epidemiology of women with HIV in Europe

% of people with HIV aged ≥15 years who are women by country



UNAIDS report. Available at: http://www.unaids.org/GlobalReport/documents/20101123_GlobalReport_full_en.pdf . Accessed March 2011

Main route of HIV transmission in women in West and Central Europe is heterosexual, 2007



Spain[1]
Heterosexual: 61.1%
IDU: 28.2%
Other: 10.7%

*Other includes transfusion recipients, cases of nosocomial infection and mother-to-child transmission

HIV/AIDS surveillance in Europe 2008. Available at http://ec.europa.eu/health/sexual_health/docs/ecdc_hiv_aids_surveillance_in_europe_en.pdf Accessed March 2011

1. http://www.isciii.es/htdocs/centros/epidemiologia/pdf/SPNS_Informe_semestral.pdf. June 2010 Update. Accessed March 2011

Women's vulnerability to HIV

- Biological factors[1,2]
  - Greater surface area of tissues in female sexual organs, delicate tissues that can tear easily
  - Ejaculate in direct contact with vaginal and cervical mucosal tissue
  - Ejaculate released in larger quantities with higher viral load than female secretions
- Structural factors[1,3]
  - Gender norms and inequalities (control over avoiding risk behaviour and nature of sexual interactions)
  - Violence[3]
    - Forced sex may cause damage
    - May prevent women from safe-sex negotiations, being tested, disclosing HIV status, receiving treatment

1.Pan American Health Organization. Gender and HIV. Available from: http://www.paho.org/english/ad/ge/Gender-HIV1.pdf. Accessed March 2011
2.Larkin J, et al. Medscape Womens Health 1996: 1(11):1.
3.WHO. Gender inequalities and HIV. Available from: http://www.who.int/gender/hiv_aids/en/. Accessed March 2011.

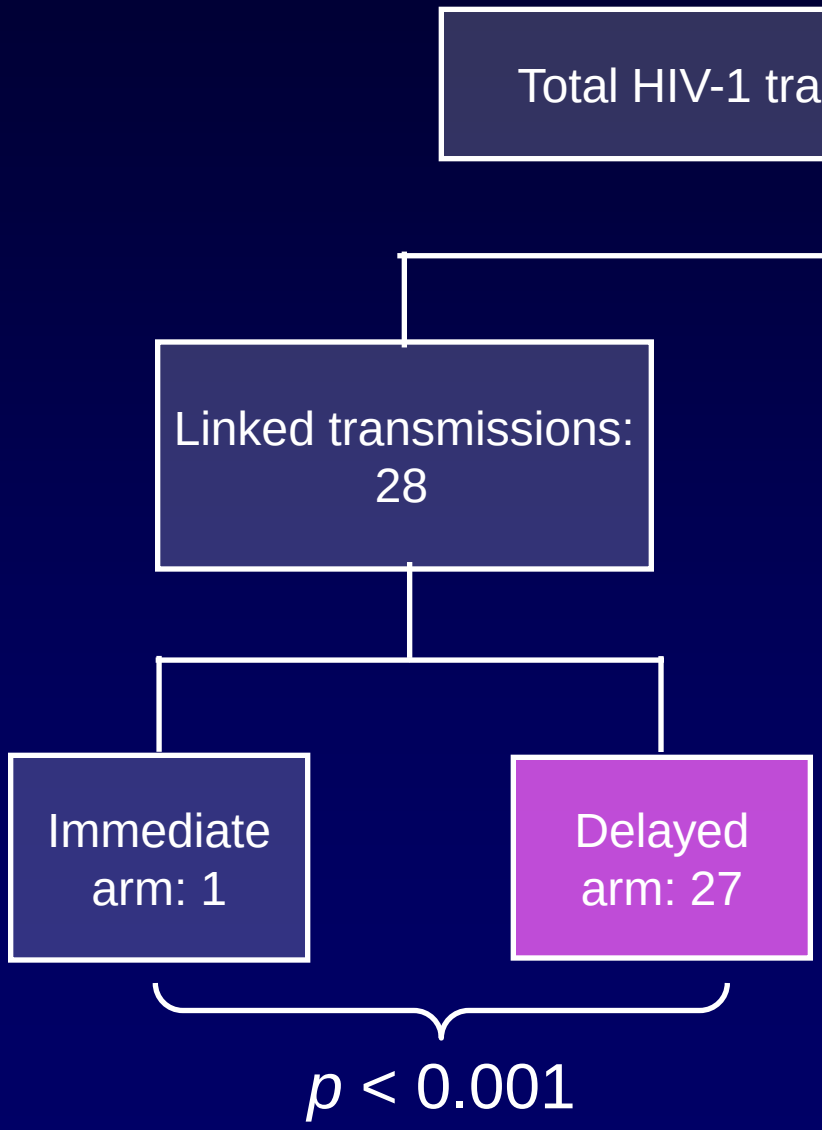
Rates of heterosexual transmission of HIV

- The likelihood of HIV transmission to women in serodiscordant couples has been reported to be more than twice that of men
  - 3.8 for women and 1.7 for men per 100 person-years were reported in one African study[1]
- A meta-analysis of studies of heterosexual discordant couples observed no incidences of transmission in patients treated with ART and with VL <400 copies/mL[2]
- Male circumcision can decrease the risk of male infection[3, 4]

1. Mugo N, et al. International Microbicides Conference Pittsburgh, 2010. Abs 8
2. Attia S, et al. AIDS 2009;23:1397–1404
3. Baeten JM, et al. J Infect Dis 2005;191:546–53
4. Quinn TC, et al. N Engl J Med 2000;342:921–29

HPTN052: Linked Transmission

Cohen M, et al
Presentation MOAX0102



- 18/28 (64%) transmissions from infected participants with CD4 > 350 cells/mm^3
- 23/28 (82%) transmissions in sub-Saharan Africa
- 18/28 (64%) transmissions from female to male partners

Percentage of patients pregnant when diagnosed with HIV can be high

- Retrospective review of PCRS charts in North Carolina revealed that **30% were pregnant at the time of HIV diagnosis**[1]
- A national observational study of pregnant women with HIV in Italy revealed that **118 of 443 patients were diagnosed while pregnant (26.6%, 95% CI 22.5–30.8)**[2]
- The Swiss Mother and Child HIV Cohort Study (MoCHiV) found that **HIV infection was diagnosed during pregnancy in 25.2%** of cases[3]
- A prospective birth cohort study of HIV-positive pregnant women conducted in nine European countries reported that 15% (185/1256) **had late-stage HIV disease at antenatal diagnosis**[4]

Torrone EA, et al. Public Health Rep 2010;125:96–102
2. Floridia M, et al. Epidemiol Infect 2006;134:1120–7
3. Aebi-Popp K, et al. J Perinat Med 2010; 38: 353–8
4. Thorne C, et al. IAS 2009. Presentation TUAC103

Switzerland: Guidelines for HIV testing in pregnancy are not being followed

- A Swiss study shows that national guidelines for serological testing in pregnant women are not being followed
- The records over 1 year (2007) for 723 pregnant women were analysed
- HIV was not tested in 30.6% of pregnant women
- There is a need for increased education of physicians

Frischknecht et al. Swiss Med Wkly 2011;140:w13138.

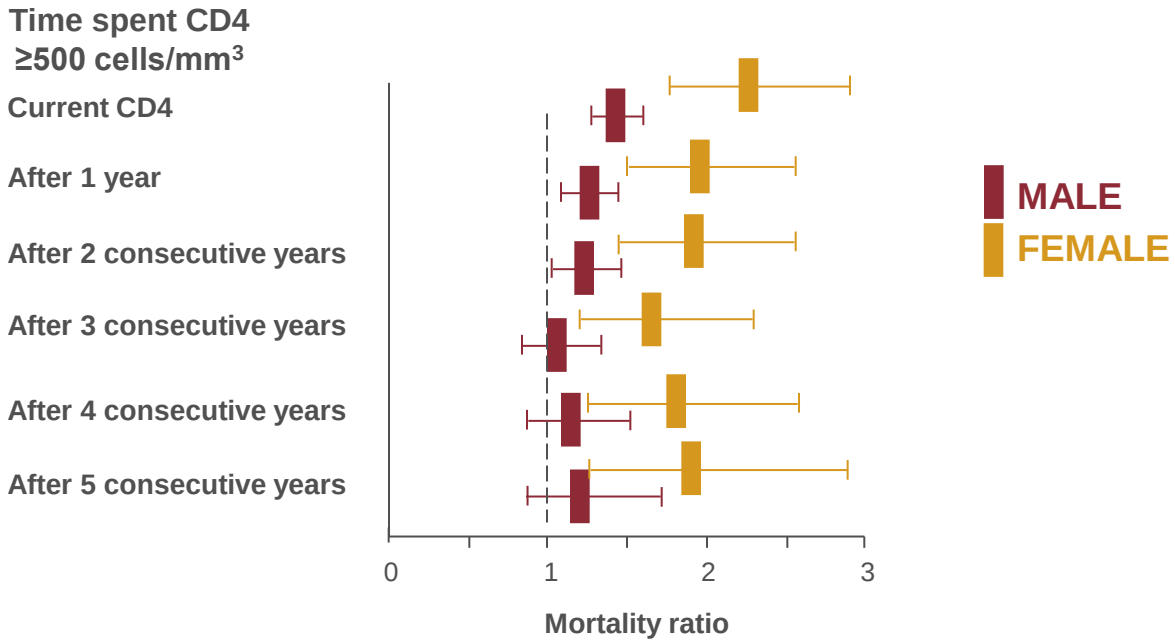
CASCADE study: Slower disease progression following HIV seroconversion in women (n=3,414 women & 3,509 men)

	Progression to AIDS				Progression to death			
	Pre-1997		1997 onward		Pre-1997		1997 onward	
	Adjusted cumulative risk	95% CI	Adjusted cumulative risk	95% CI	Adjusted cumulative risk	95% CI	Adjusted cumulative risk	95% CI
Men	1.00		1.00		1.00		1.00	
Women	0.99	0.86,1.14	0.76	0.63,0.90	0.89	0.76,1.05	0.68	0.56,0.82
***p value**	0.90		0.002		0.17		<0.001	
†p value	0.016				0.024			

*Effect of sex within calendar period; †effect of sex across calendar periods

Jarrin I, et al. Am J Epidemiol 2008;168:532–40

COHERE: Time with CD4 ≥500 cells/mm^3 allows men, but not women, to reach similar mortality rates to general population

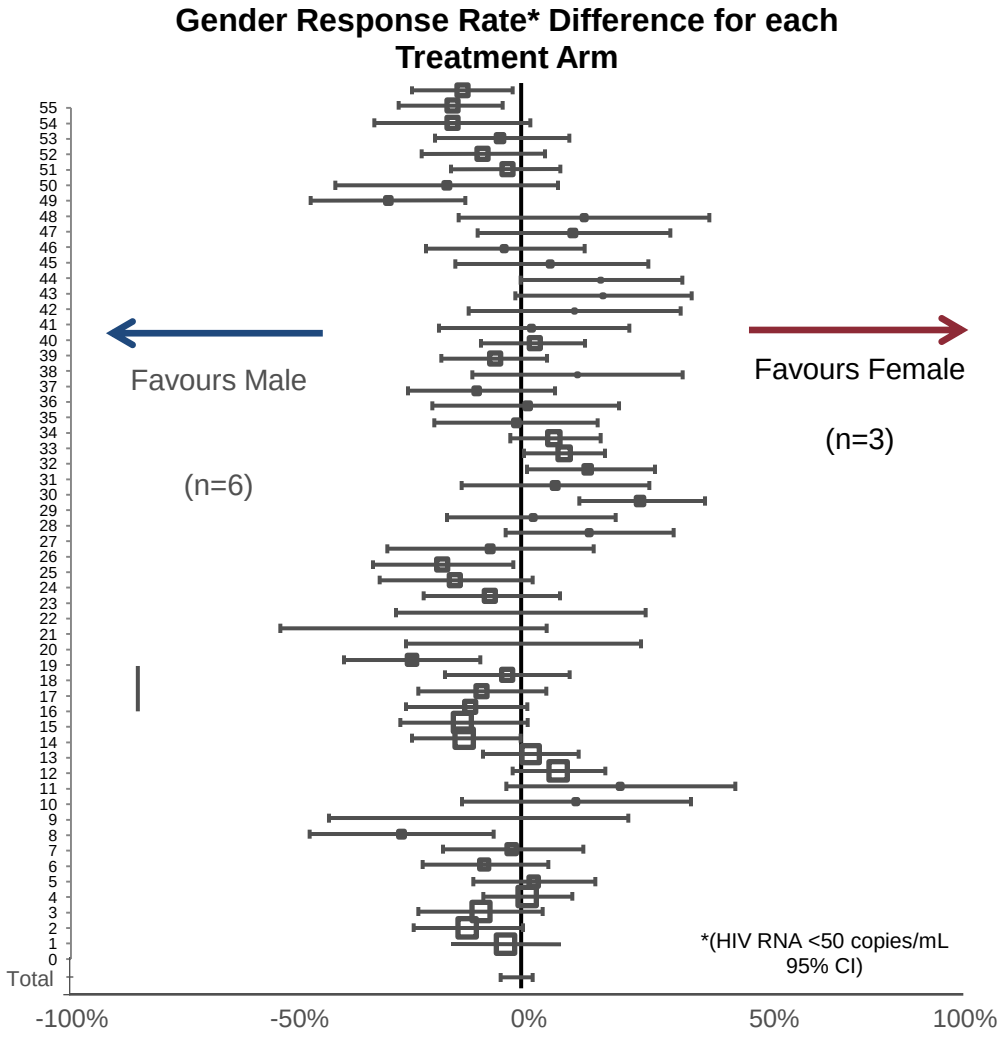


- 80,642 of the COHERE database eligible
- Death rates and standardised mortality ratios compared between men and women with CD4 ≥500 cells/mm^3
- Mortality ratios were higher in women in all CD4 strata
- Mortality rates among women did not reach similar levels to those of the general female population, even after 5 years

Adapted from Lewden C Int J Epidemiol. 2012 ;41:433-45

FDA meta-analysis: Similar efficacy of ART in women vs men

- FDA review of registrational trials from 2000–2008
- Results
  - 22,411 HIV+ subjects in 43 RCTs for 16 ARVs; 20% women
  - No significant gender differences in treatment response at week 48, discontinuations for AEs, lost to follow-up or death
  - Higher rate of discontinuations for virological failure in males (8.15%) than females (4.25%)



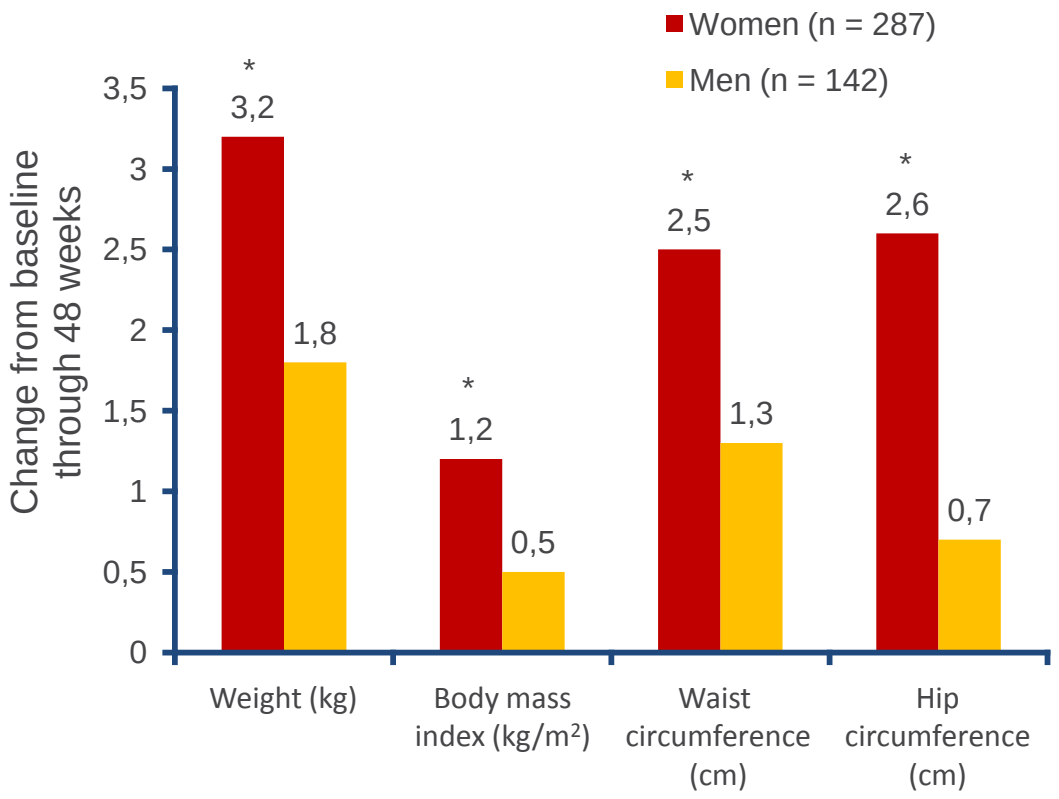
Soon G, et al. 50th ICAAC 2010. Abstract H-1812

Representation of women in randomised controlled trials in naïve patients

Trial	Trial design	Number of female patients (%)	Citation
ACTG 5142	EFV vs LPV/r	151 (20%)	Riddler SA, et al. N Engl J Med 2008;358:2095−106
ARTEMIS	LPV/r vs DRV/r	209 (30%)	Ortiz R, et al. AIDS 2008, 22:1389–1397
CASTLE	LPV/r vs ATV/r	277 (31%)	Molina JM, et al. Lancet 2008; 372(9639):646–55
STARTMRK	EFV vs RAL	105 (19%)	Lennox JL, et al. Lancet 2009; 374(9692):796–806
MERIT	EFV vs MVC	206 (29%)	Cooper DA et al. JID 2010; 201:803–813
ACTG 5202	EFV vs ATV/r TDF/FTC vs ABC/3TC	322 (17%)	Daar ES, et al. Ann Intern Med 2011 Feb 14. [Epub ahead of print]

GRACE study: Metabolic and anthropometric differences between the sexes

- In the GRACE study (darunavir/r BID over 48 weeks), median changes in triglycerides from baseline to Week 48 were greater in men than in women
- Anthropometric parameters increased for both genders over 48 weeks, but larger increases were observed for women than for men
- At Week 48, more women than men reported that their belt or waist size had increased



*p < 0.05 change from baseline to Week 48; GRACE = **G**ender, **R**ace, **A**nd **C**linical **E**xperience; /r = ritonavir

Currier et al. AIDS Patient Care and STDs 2011;25:333–9.

Impact of family obligations on adherence in women

- As well as motivators of adherence, social relationships and familial obligations can also negatively impact a woman's adherence[1,2]
  - Caring for others can take priority over own healthcare needs[1]
  - A busy daily schedule can also hinder adherence[2]

- Interventions that target these unique barriers are needed[2]

1. Ciambrone D, et al. Women Health 2006;44:61–77
2. Roberts KJ & Mann T. AIDS Care 2000;12:377–86

Factors relating to adherence in HIV-infected women

- Women have twice the odds of reporting difficulty taking HIV medications openly at home compared with gay and bisexual men[1]
  - Women are less likely to adhere to ART regimens if there are difficulties in taking medication openly at home compared to those with no difficulties[1]
- Lipodystrophy and poor body image can have negative effects on adherence[2-3]
- Depression tends to be more common in women and this is also linked to poor adherence[4,5]
  - In a multicentre, observational study of 135 patients with HIV, non-adherence was independently associated with worse depression rating scale scores (OR1.05, 95% CI1.00, 1.10)[6]

1. Sayles J et al. J Womens Health 2006;15:173–81
2. Ammassari A, et al. JAIDS 2002;31(Suppl3):S140–4
3. Huang J et al. AIDS Res Ther 2006;3:17
4. Turner B, et al. J Gen Intern Med 2003;18:248–57
5. DiMatteo R, et al. Arch Intern Med 2000; 160: 2101-7
6. Ammassari A, et al. Psychosomatics 2004;45:394–402

Contraception and HIV treatment

- HIV infection continues to increase among women of childbearing age[1]
- HIV-infected women require contraceptive measures
- Effective dual contraceptive methods are required to avoid pregnancy and decrease risk of HIV transmission
- Potential drug–drug interactions must be considered

1. Finocchario-Kessler S, et al. AIDS Behav 2010;14:1106–14

ARVs and oral contraceptives: Drug interactions

ARV drug	Effect on EE* AUC	SmPC comment
ATV/r		Oral contraceptives need to contain at least 30µg EE
LPV/r, SQV/r, DRV/r, NFV, FPV/r¥	 See individual SmPCs	Alternative or additional contraceptive measures are recommended when co-administered with oestrogen-based contraceptives
NVP	 See individual SmPCs	Alternative or additional contraceptive measures are recommended when co-administered with oestrogen-based contraceptives
EFV		Barrier contraception should always be used in combination with other methods of contraception
MVC		Can coadminister with EE
RAL		Can be co-administered without dose adjustment

*EE = Ethinylestradiol; ¥ Coadministration of FPV/r with oral contraceptives may increase the risk of hepatic transaminase elevations, alternative contraception methods are recommended

SmPCs. Available at http://www.ema.europa.eu Accessed March 2011

High rates of unplanned pregnancy

- Data from 2001 in the US showed unintended pregnancy rate **was highest among women aged 18–24 years**[1]

- A retrospective case note review of teenage mothers with HIV in 12 London hospitals between 2000 and 2007 revealed:[2]
  - Sixty seven pregnancies were recorded in 58 women
  - HIV infection was diagnosed through routine antenatal screening in 63% of cases
  - Pregnancy was unplanned in 82% of cases, with 65% of women using no contraception
  - ART was being used at conception in only 4 cases
  - Overall MTCT rate was 1.5%
  - Within 12 months of delivery, 25% of the women were pregnant again, with 88% of these pregnancies unplanned

  - In a cross sectional study of HIV in Ontario, 56% identified their last pregnancy as unintended[3]

1.Finer LB. Journal of Adolescent Health 2010; 312–14
2. Elgalib, A, et al. HIV Med 2011;12:118–23
3. Loutfy MR, et al. 1st International Workshop on HIV and Women 2011. Washington, DC. Abstract P_36

Considerations when choosing ART for pregnant women with HIV[1]

- ⇒ Efficacy of ART
- ⇒ Safety and tolerability of ART
  - Adverse effects on mother
  - Teratogenic/adverse effects on foetus
- ⇒ Resistance profile
- ⇒ Comorbidities
- ⇒ Drug–drug interactions
- ⇒ Adherence potential
- ⇒ Convenience

DHHS Perinatal Guidelines. Available at http://aidsinfo.nih.gov/contentfiles/PerinatalGL.pdf. Accessed March 2011;
2. SmPCs. Available at http://www.ema.europa.eu Accessed March 2011

EACS: Recommendations for treatment of HIV-positive pregnant women

Pregnant women should be monitored every month and as close as possible to the predicted delivery date

SCENARIO	Recommendation[1]
1. Women becoming pregnant while already on ART	1. Maintain ART, but switch drugs that are potentially teratogenic
2. Women becoming pregnant while treatment-naïve and who fulfill the criteria (CD4) for initiation of ART	2. Start ART at start of 2nd trimester is optimal
3. Women becoming pregnant while treatment-naïve and who do not fulfill the criteria (CD4) for initiation of ART	3. Start ART at start of Week 28 of pregnancy (at the latest 12 weeks before delivery); start earlier if high plasma viral load or risk of prematurity
4. Women whose follow-up starts after Week 28 of pregnancy	4. Start ART immediately

ARVs used during pregnancy should be selected only if potential benefit justifies the potential risk[2]

EACS guidelines. Available at:http://www.europeanaidsclinicalsociety.org/guidelinespdf/1_Treatment_of_HIV_Infected_Adults.pdf. Accessed March 2011; 2. SmPCs. Available at http://www.ema.europa.eu Accessed March 2011

FDA Pregnancy Categories

Class	Drug	FDA Pregnancy Category
NRTI	Emtriva (emtricitabine, FTC)	B
	Epivir (lamivudine, 3TC)	C
	Retrovir (zidovudine, AZT)	C
	Videx (didanosine, ddI)	B
	Viread (tenofovir, TDF)	B
	Zerit (stavudine, d4T)	C
	Ziagen (abacavir, ABC)	C
NNRTI	Intellence (etravirine, ETR)	B
	Sustiva (efavirenz, EFV)	D
	Viramune (nevirapine, NVP)	B
PI	Aptivus (tipranavir, TPV)	C
	Crixivan (indinavir, IDV)	C
	Fortovase HGC/Invirase SGC (saquinavir)	B/B
	Kaletra (lopinavir/ritonavir, LPV/r)	C
	Lexiva (fosamprenavir, f-APV)	C
	Norvir (ritonavir, RTV)	B
	Prezista (darunavir, DRV)	C
	Reyataz (atazanavir, ATV)	B
	Viracept (nelfinavir, NFV)	B
Other	Fuzeon (enfuvirtide, T-20)	B
	Selzentry (maraviroc)	B
	Isentress (raltegravir)	C

ART, mode of delivery and MTCT rates

Townsend, 2008[2]	MTCT rate (%)	n infected	Total
ART + elective caesarean section	0.7	17	2286
ART + planned vaginal delivery	0.7	4	559
ART + emergency caesarean section	1.7	15	877
Untreated elective caesarean section	5.8	3	52
Untreated planned vaginal delivery	25.0	2	8

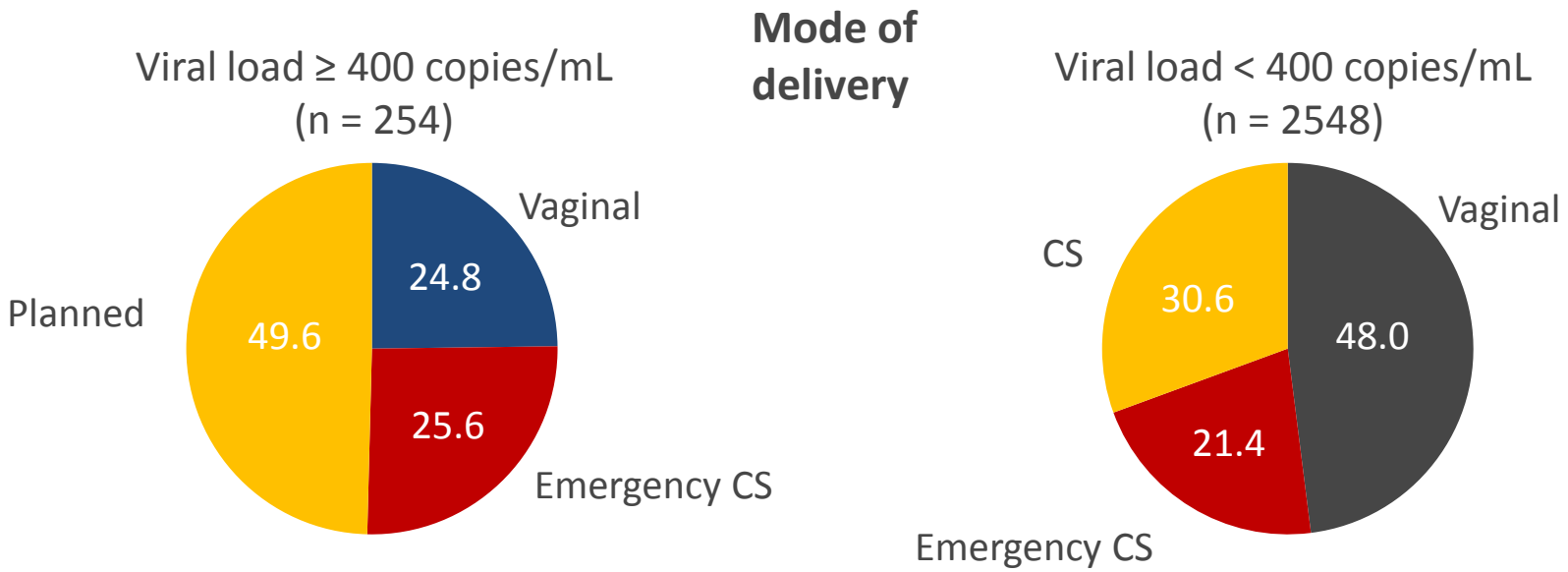
- Prematurity was a risk factor for MTCT[1]
- Early and sustained control of viral load is associated with a decreasing residual risk of MTCT[2]

ARVs used during pregnancy should be selected only if potential benefit justifies the potential risk[3]

1.Townsend, et al. AIDS 2008;22:973-81
2. Tubiana R, et al CID 2010;50:585–96
3. SmPCs. Available at http://www.ema.europa.eu Accessed March 2011

France: Mode of delivery in the French Perinatal Cohort

- Mode of delivery recorded for 2,802 pregnant women with HIV enrolled between 2005 and 2009 in the French Perinatal Cohort (EPF/ANRS CO1-11)

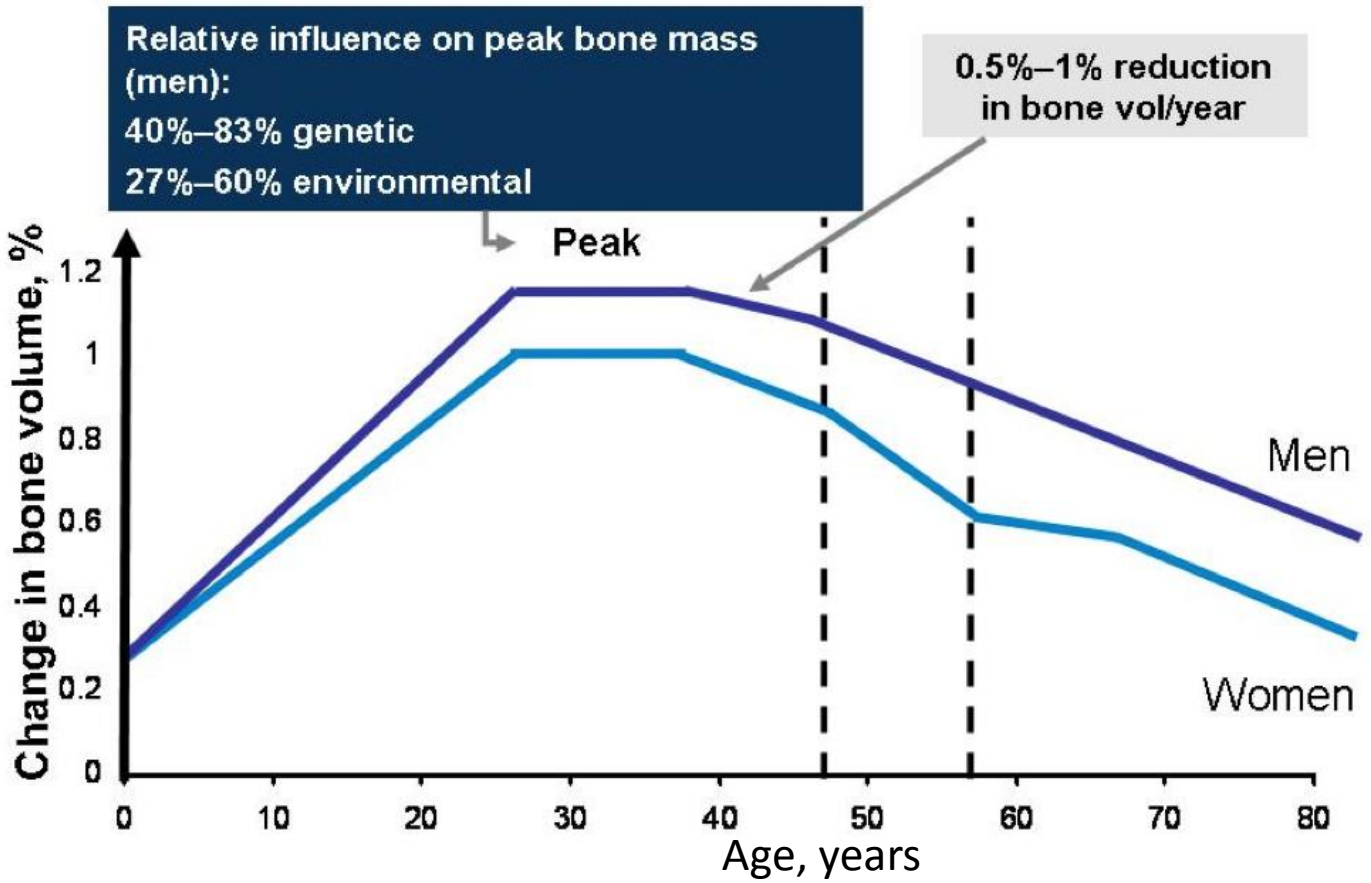


- Main indications of planned CS for viral load < 400 copies/mL was
  - 42% for a repeat CS
  - 18% for HIV exclusively

CS = caesarean section

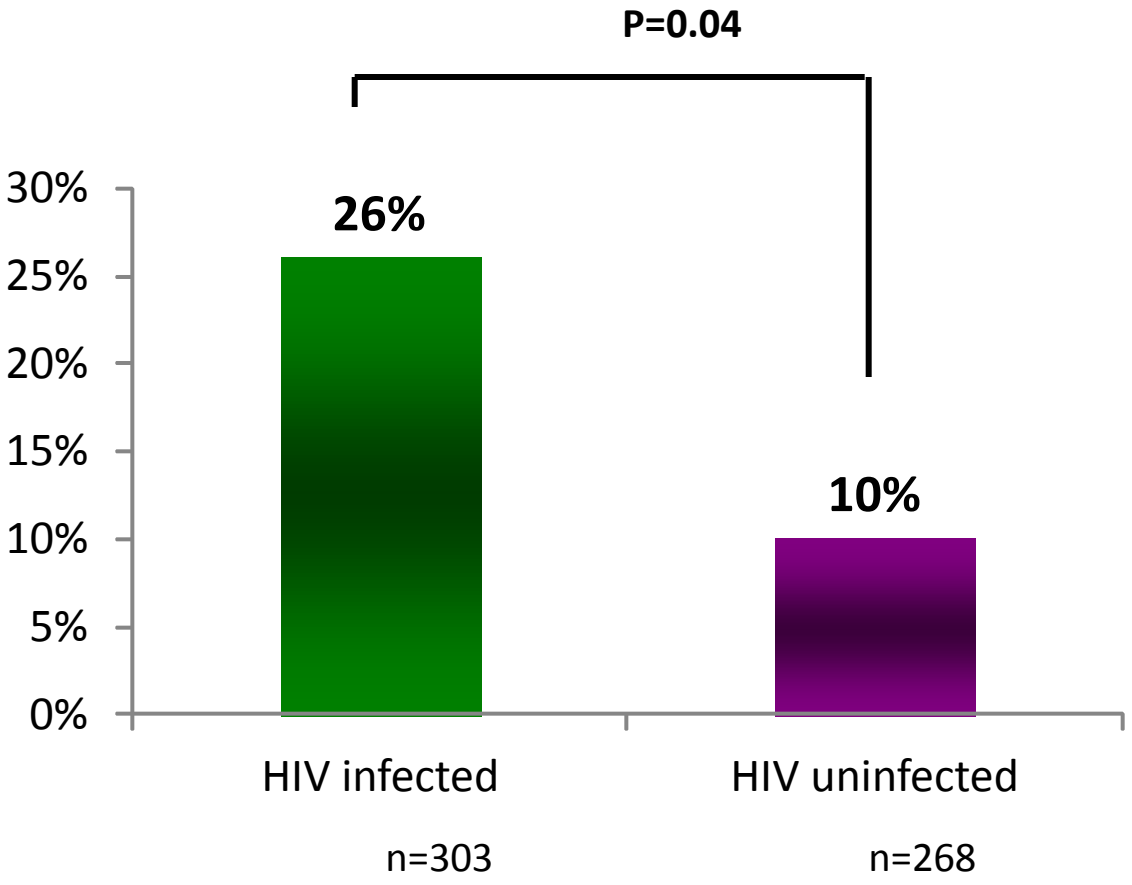
Jasseron et al. IAS 2011. Abstract CDC058.

BMD decreases with age



Orwoll ES, Klein RF, Endocr Rev, 1995: 16: 87-118

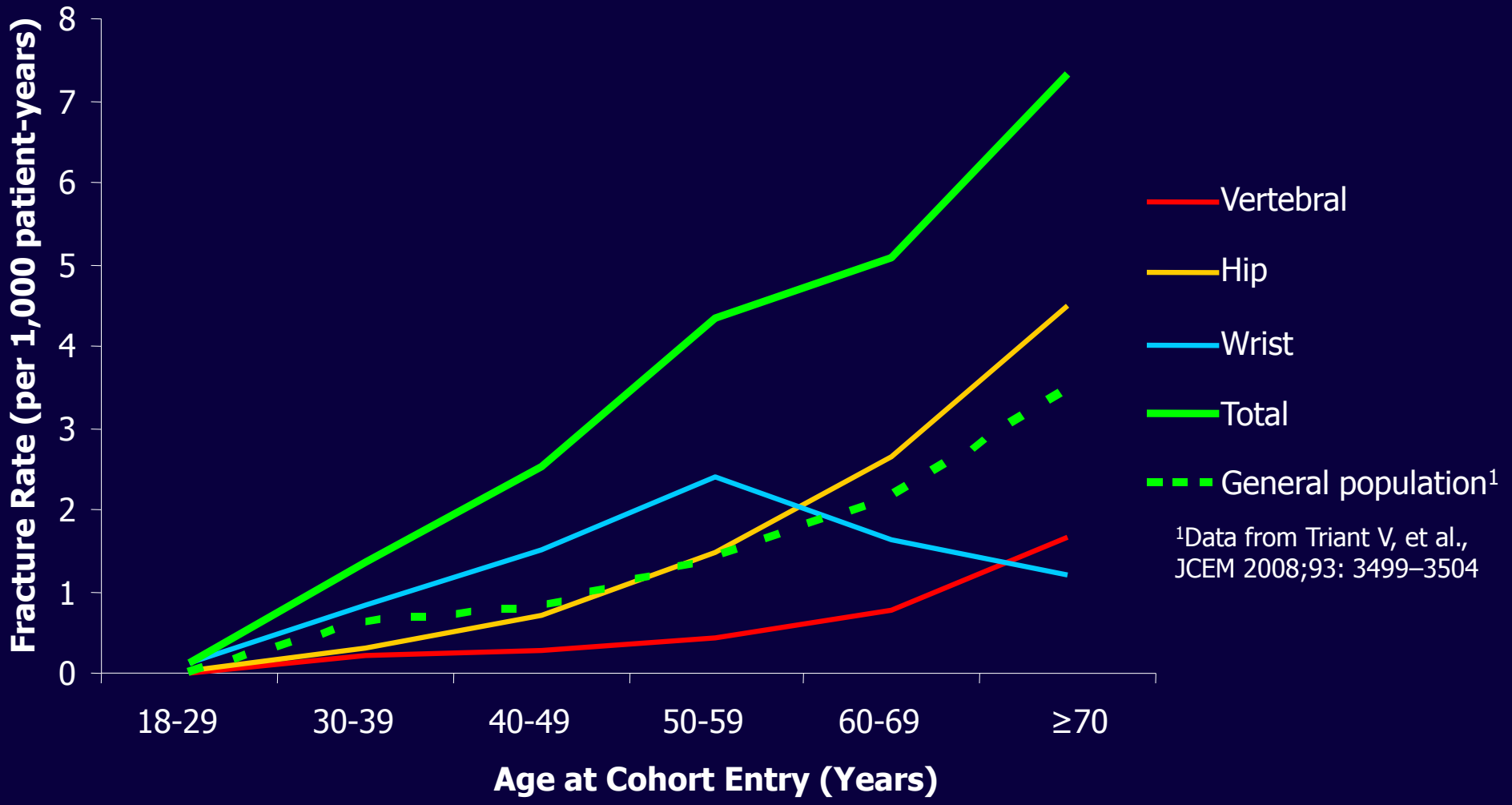
Menopause in HIV+ women
Early menopause *(< 40 aa)*



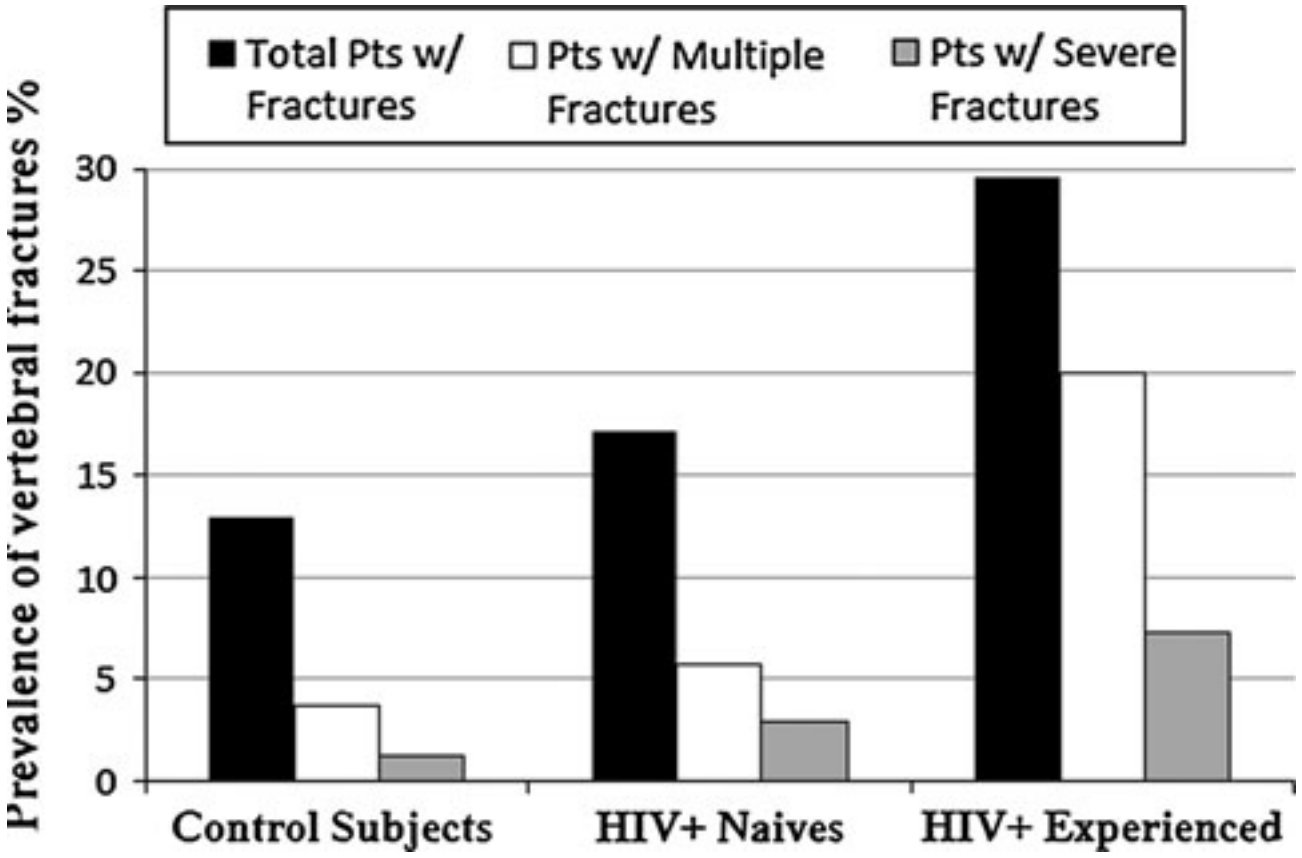
Women living with HIV were 73% more likely to experience early onset of menopause, compared with HIV-uninfected women (P=0.024) (46 *vs* 47)

Schoenbaum et al . Clin Infect Dis 2005.

Age-adjusted Rates of Osteoporotic Fractures (Entire Cohort)

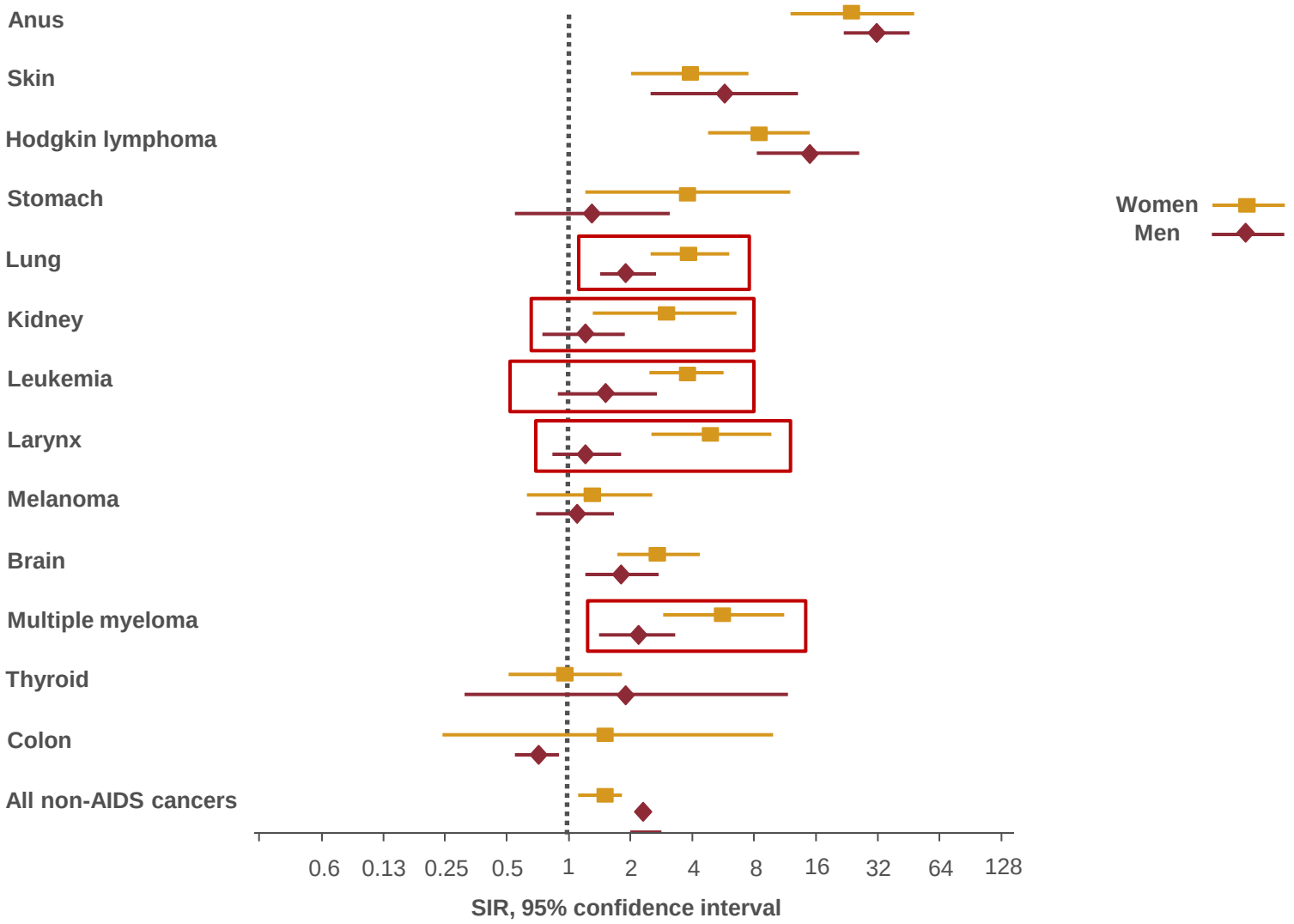


[1]Data from Triant V, et al., JCEM 2008;93: 3499–3504



Torti C et al. Endocrine. 2012;41:512-7

Meta-analysis of incidence of non-AIDS cancers in HIV+ patients by gender

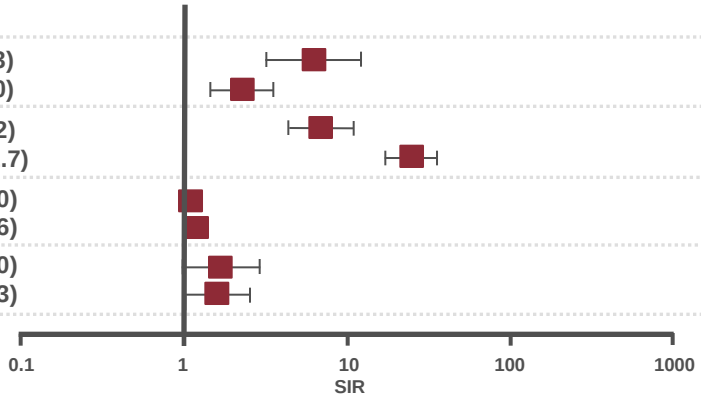


Shiels MS, et al. JAIDS 2009;52:611–22

Incidence of cancer in women with HIV

- Longer life expectancy of women with HIV on ART increases risk of developing both AIDS-defining and non-AIDS-defining cancers[1]
  - ≥7 fold increase in risk in Non-Hodgkin Lymphoma (NHL)[1-3]
  - ≥200 fold increase in risk Kaposi's Sarcoma (KS)[1]
  - ≥3 fold increase in risk cervical cancer[2]
- Standardised incidence ratios of cancers specific to women are shown below:

	Cohort	Meta-analysis SIR (95% CI)	Nº of studies	Observed Nº of cancers	Heterogeneity P value
HPV-related cancers					
Cervix uteri	HIV/AIDS	5.82 (2.98-11.3)	6	104	0.00
	Transplant	2.13 (1.37-3.30)	3	22	0.67
Vulva & vagina	HIV/AIDS	6.45 (4.07-10.2)	2	21	0.55
	Transplant	22.76 (15.8-32.7)	2	33	0.85
Breast	HIV/AIDS	1.03 (0.89-1.20)	2	194	0.60
	Transplant	1.15 (0.98-1.36)	5	156	0.66
Ovary	HIV/AIDS	1.63 (0.95-2.80)	5	30	0.34
	Transplant	1.55 (0.99-2.43)	3	23	0.61



1. Hessol N, et al. JAIDs 2004; 36:978–85
2. National Cancer Institute, HIV Infection and Cancer Risk 2010. Available at: http://www.cancer.gov/cancertopics/factsheet/Risk/hiv-infection. Accessed March 2011
3. Grulich AE, et al. Lancet 2007;370:59–67

Cancer screening – EACS

Problem	Patients	Procedure	Evidence of benefits	Screening interval	Additional Comments
Breast cancer	Women 50–70 yrs	Mammography	↓breast cancer mortality	1–3 years	
Cervical cancer	Sexually active women	Papanicolau test, HPV DNA test	↓cervical cancer mortality	1–3 years	Target age group should include at least the age range 30 to 59 years. Longer screening interval if prior screening tests repeatedly negative
Colorectal cancer	Persons 50–75 yrs	Fecal Occult Blood test	↓colorectal cancer mortality	1–3 years	Benefit is marginal

- **Regular screening and breast self-examination can reduce the risk of cancer**

EACS guidelines 2013. Available at http://www.europeanaidsclinicalsociety.org/guidelinespdf/EACS-EuroGuidelines_FullVersion.pdf . Accessed March 2011.

Cult Health Sex. 2014 Apr 16:1-17. [Epub ahead of print]

Can a woman refuse sex if her husband has a sexually transmitted infection? Attitudes toward safer-sex negotiation among married women in Bangladesh.

Jesmin SS1, Cready CM.

Author information

Abstract

In developing countries, HIV, sexually transmitted infections (STIs) and unintended pregnancy take an enormous toll on women's reproductive health, yet preventive programmes are lacking as married women's risks are frequently underestimated. We examined predictors of married Bangladeshi women's attitudes towards safer-sex negotiation using data on 15,178 currently married women aged 15-49 from the 2011 Bangladesh Demographic Health Survey. Approximately 92% of women believed that a wife's refusal to have sex with her husband is justified if he has an STI. Multilevel logistic regression analysis revealed that the likelihood of a woman holding this belief increased with her autonomy, as measured by the ability to go to a health centre/hospital without another adult, participation in household decision making and rejection of wife beating ($p < 0.001$). Other significant predictors were knowledge/awareness of STIs ($p < 0.05$), living in Dhaka division ($p < 0.001$) and younger age ($p < 0.01$). Our findings suggest that sexual health education programmes may be more effective if they include strategies to address social norms and cultural practices that limit women's autonomy in society.

Arch Sex Behav. 2014 Apr 12. [Epub ahead of print]

Adolescents' Beliefs About Forced Sex in KwaZulu-Natal, South Africa.

De Vries H1, Eggers SM, Jinabhai C, Meyer-Weitz A, Sathiparsad R, Taylor M.

Abstract

Gender-based violence has serious consequences for the psychological, physical, and sexual well-being of both men and women. Various gender roles, attitudes, and practices in South Africa create an environment that fosters submission and silence in females and hegemony and coercion in males. One of the expressions of this power inequity is a high prevalence of forced sex, which in its turn is associated with higher risk of HIV infection. This study therefore assessed potential gender differences in beliefs about forced sex and in prevalence of reported forced sex among high school students (N = 764) in KwaZulu-Natal. Results showed that significantly more boys were sexually active (26 %) than girls (12 %) and that boys experienced earlier sexual debut by over a year. Boys also held a more positive view about forced sex than girls since they associated it more often with signs of love, as an appropriate way to satisfy sexual urges, and as acceptable if the girl was financially dependent on the boy. The perception that peers and friends considered forced sex to be an effective way to punish a female partner was also more common among boys. On the other hand, boys were less knowledgeable about the health and legal consequences of forced sex, but no significant differences were found for other sociocognitive items, such as self-efficacy and behavioral intention items. Consequently, health education programs are needed to inform both boys and girls about the risks of forced sex, to convince boys and their friends about its inappropriateness and girls to empower themselves to avoid forced sex.

BRING BACK OUR GIRLS

Conclusions

- There are increasing numbers of women with HIV[1], many of whom are of child-bearing age
- Considerations for the management of women with HIV include:
  - Barriers to adherence[2,3]
  - Drug–drug interactions[4]
    - Potential interactions of oral contraceptives and ART must be considered
- Treatment guidelines do not differentiate between women and men, except those who are planning pregnancy or pregnant[5,6]
- More gender-specific clinical trials are needed, powered for both gender and regimen comparisons

1. WHO epidemiological factsheet. Available at http://www.who.int/hiv/pub/epidemiology/pubfacts/en/ Accessed March 2011
2. Turner BJ, et al. JGenInternMed 2003;18:248–57
3. Ammassari A, et al. Psychosomatics 2004;45:394–402
4. SmPCs. Available at http://www.ema.europa.eu. Accessed March 2011
5. EACS. Available at: http://www.europeanaidsclinicalsociety.org/guidelinespdf/EACS-EuroGuidelines_FullVersion.pdf. Accessed March 2011
6. Thompson MA, et al. JAMA 2010;304:321–33