

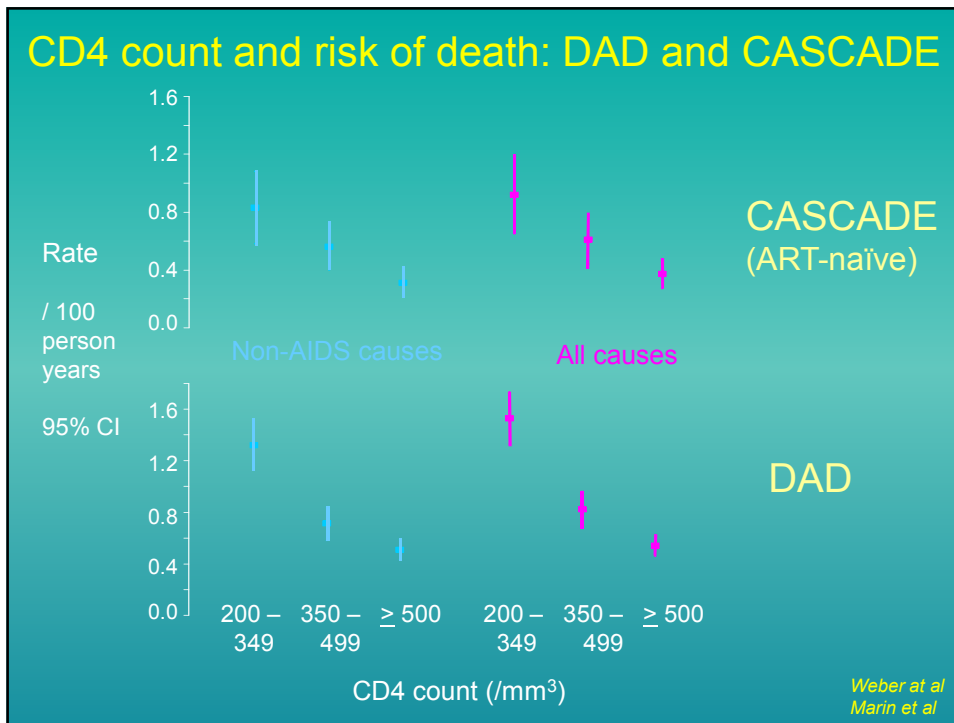
CROI 2008

- Epidemiology
- Prevention
- Transmission
- Testing

Epidemiology

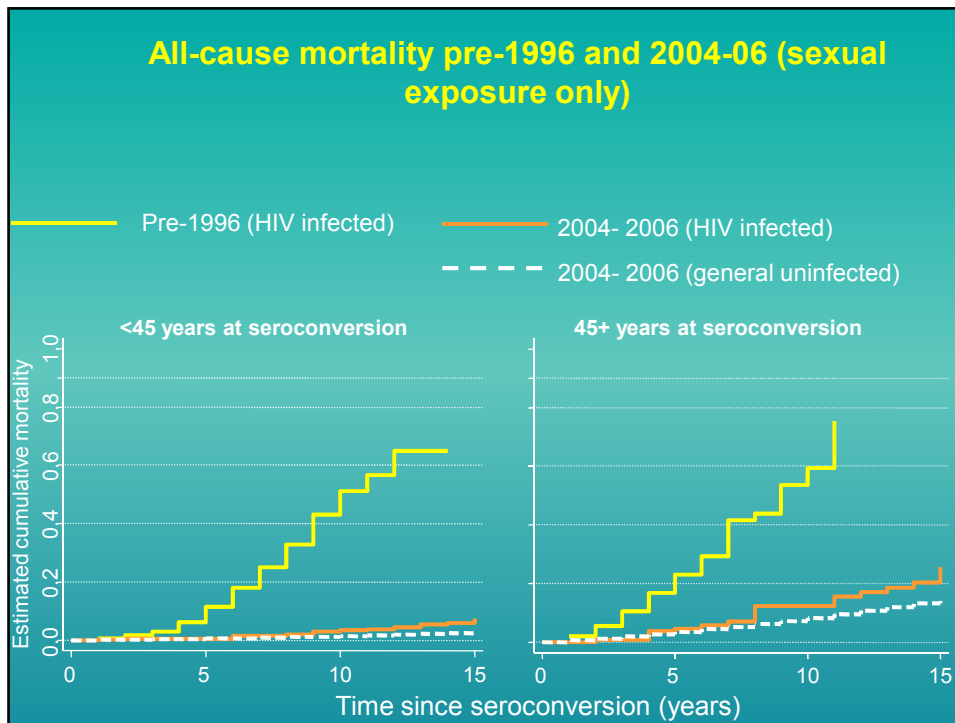
Is HIV associated with excess mortality in patients with high CD4 counts compared to the general population ?

- A Phillips Plenary: Morbidity and Mortality (4th Feb)
Might HIV increase serious non-AIDS conditions and non-AIDS death?
- Porter abs 14: Changes over time in the risk of death following HIV seroconversion compared with mortality in the general population (CASCADE collaboration).
- Lodwick abs 141: Age/sex-specific death rates in ART naïve patients with CD4 count above 350/mm³ compared with the general population.



Changes over time in the risk of death following HIV seroconversion compared with mortality in the general population (CASCADE collaboration). **Abs 14**

Calendar period	Person-years of follow-up	Observed deaths (n=2475)	Expected deaths (n=226)	Excess deaths	Mortality rate/ 1000 PY	Excess mortality rate/ 1000 PY
Pre-1996	30 228	1290	54.3	1235.7	42.7	40.9
198-99	16 136	220	32.2	187.8	13.6	11.6
2002-03	16 679	180	39.5	140.5	10.8	8.4
2004-06	13 695	117	35.1	81.9	8.5	6.0



Age/sex-specific death rates in ART naïve patients with CD4 count above 350/mm³ compared with the general population.

Deaths

- 24 cohorts; 47,474 pts; 113,643 yrs with CD4 >350
 - Compared to national death rates calculated standardised mortality ratios (SMR)
 - 487 deaths
- Overall death rate 4.9 per 1000 pyrs

HIV related	79	16.2%
Non-HIV related	235	48.3%
Unknown	173	35.5%

Lodwick et al: Results – SMRs

	Observed deaths	Expected deaths	SMR	95% CI
MSM	117	97.08	1.21	1.00-1.44
Heterosexual	82	24.63	3.33	2.65-4.13
IDU	227	22.22	10.21	8.93-11.63

Lodwick et al: Results - Predictors of death

	Rate Ratio*	95% CI	p-value
CD4 count (100/mm ³ higher)	0.95	0.90-0.99	0.0185
Risk group			
MSM	1.00		
Heterosexual	1.95	1.43-2.66	<0.0001
IDU	5.92	4.74-7.40	<0.0001
Other / not known	2.12	1.37-3.27	0.0007
Female gender	0.74	0.59-0.93	0.0093
Age group			
20-30	1.00		
30-40	1.35	1.07-1.71	0.0119
40-50	1.85	1.41-2.43	<0.0001
50-60	3.06	2.11-4.44	<0.0001
60-	6.10	3.74-9.96	<0.0001

* mutually adjusted

Summary

- Excess mortality has declined significantly over time
- Excess mortality associated with risk group, (largely IDU), and older age.
- In MSM, younger age, and early infection excess mortality is marginal.
- However national mortality rates do not take account of risk behaviour or sexuality

Prevention / Transmission

- Does male circumcision protect against HIV transmission ?
- Does HSV suppressive therapy with acyclovir protect against HIV acquisition ?
- What is the impact of an ART rollout programme on incidence of HIV transmission in sub-saharan Africa ?
- Does surveillance data on MTC transmission provide evidence to support current management guidelines in the UK ?

Circumcision in HIV+ men

- Rakai RCT in HIV+ men (CD4>350) (n=1015).
- Immediate vs.deferred (at 24 months) circumcision.
- Outcome: HIV incidence in wives, STIs in men and wives
- Participants provided with information on HIV prevention, wound care, free condoms, abstinence from sex post operatively.
- Analysis: restricted to 165 discordant couples

Wawer et al Abs 33Lb CROI 2008

Circumcision in HIV+ve Men

- non-significant *increase* in HIV incidence in wives seen (14.4% vs 9.1%, p= 0.42), highest in first 6 months
- Due to too-early resumption of sex? Incidence in wives of men resuming sex > 5 days prior to certified wound healing 28.8% (5/18) v others 9.5% (6/63)
- Rates of condom use and STIs comparable in female spouses in both arms
- HIV+ men will want circumcision, as lack will be seen as = HIV+, so healing guidelines need emphasis

Wawer et al Abs 33Lb CROI 2008

Acyclovir for HSV-2 prophylaxis

- HPTN 039: large RCT of 400mg acyclovir BiD for high-risk HIV-women (Africa) and MSM (N & S America). N= 3172
- **Rationale:** to stop HIV **acquisition**. Epidemiological studies show HSV-2+ \Rightarrow \uparrow HIV sero-conversion (RR = 1.7-3.1)
- **Result:** 16% *more* sero-conversions on ACY vs placebo (non-significant: p=0.39); 3.9 v 3.3 /100pys

37% reduction in genital ulcers, but less than seen in other studies (typically 80%)

Celum et al Abs 32 CROI 2008

Impact of ART on HIV Transmission: Uganda

- 926 ART naïve patients (75% women) enrolled in an ART programme
- Follow up 36 months, condoms provided
- By 3 years number reporting recent sex increased 50% in men and 62% in women
- 'Risky sex' 9% in men and 5.6% in women at baseline; declined to year 2 but at baseline year 3
- 92% reduction in estimated risk of HIV transmission: 45.7 to 4.2 /1000 pys
- 1 seroconversion occurred in sero-discordant couples in year 1, none in year 2 and 3

Bunnell et al Abs 29 CROI 2008

MTC Transmission: UK and Ireland

Very Low Risk of MCT in UK and Ireland in Women who Achieve Viral Suppression (2000-2006).

National Study of HIV in Pregnancy & Childhood (NSHPC)

- National surveillance scheme for paediatric and obstetric HIV in the UK and Ireland.
- Children followed up to establish infection status: Uninfected = negative PCR after one month of age, or negative antibody test after 18 months of age

Abs 653 CROI 2008

	MTCT rate	95% CI	n infected	total
Overall	1.2	(0.9 - 1.5)	61	5151
2000 - 2002	1.6	(1.0 - 2.4)	23	1456
2003 - 2006	1.0	(0.7 - 1.4)	38	3695
At least 14 days of ART	0.8	(0.6 - 1.1)	40	4864
ART and mode of delivery				
HAART + elective CS	0.7	(0.4 - 1.2)	17	2337
HAART + planned vaginal	0.7	(0.2 - 1.8)	4	565
HAART + emergency CS	1.7	(1.0 - 2.8)	15	877
ZDV mono + elective CS	0.0	(0.0 - 0.8)	0	467
HAART				
HAART from conception	0.1	(0.0 - 0.6)	1	928
HAART + VL<50 copies/ml	0.1	(0.0 - 0.4)	3	2117

Transmission rates were lower in 2003-2006 than in 2000-2002 ($p=0.069$).

In women on HAART there was no difference in MTCT rates between VD and LSCS ($p=1.00$).

3/2117 infants infected despite maternal HAART and viral load <50 copies/ml. 2/3 had positive PCR tests at 72 hours suggesting *in utero* transmission

Infection status was available for 86.8% (5151/5930) of infants; 1.2% were infected.

Rates were particularly low in women who had at least 14 days of ART, were on HAART when they became pregnant, or had viral loads < 50 copies/ml

Conclusions

- No difference in MTCT rates
 - HAART with elective caesarean section,
 - HAART with planned vaginal delivery, and
 - ZDV monotherapy with elective caesarean section.
- 3 transmissions with viral load <50 copies/ml, two probably occurred *in utero*.

Abs 563 CROI 2008

Summary

- Circumcision in HIV +ve men did not protect against HIV transmission
- HSV suppressive therapy not associated with decreased risk of HIV acquisition
- ART associated with decreased risk of HIV transmission in discordant couples in sub-Saharan Africa
- Low incidence of MTC transmission in the UK
- Near patient testing and opt out testing strategy in emergency departments resulted in marginal increase in new HIV diagnoses compared to targeted testing.