

## Self-Evaluation Problems

### Class 6

### Answer Key

Below find results from an article (Carre, N, et al, *International Journal of Epidemiology* 27:897-903,1998) on the incidence of clinical AIDS after CD4<sup>+</sup> cell count falls below 200/ $\mu$ L (CD4 threshold) in different exposure groups. The CD4 threshold is predictive of clinical AIDS; the purpose of this study was to determine if other biological and clinical parameters at CD4 threshold are also predictive of clinical AIDS. The main biological and clinical parameters include: age at threshold, CD4 cell slope, p24 positive antigenaemia, thrush, seborrheic dermatitis, oral hairy leukoplakia, zoster and other conditions. The exposure groups include homosexual men, heterosexual men and women, hemophiliacs and injecting drug users.

**Table 2** Crude and adjusted relative risks of progression to AIDS after the CD4 cell threshold of 200/ $\mu$ L (n = 333)

Covariate:	Crude RR	(95% CI)	Adjusted RR	(95% CI)
<b>Exposure group</b>				
Haemophiliacs	1.00		1.00	
Injecting drug users	1.61	(0.73–3.53)	1.21	(0.53–2.74)
Homosexual men	2.52	(1.37–4.62)	1.77	(0.92–3.40)
Heterosexual men	1.87	(0.85–4.11)	1.36	(0.59–3.15)
Heterosexual women	1.09	(0.53–2.21)	1.07	(0.52–2.19)
<b>Age at CD4 threshold<sup>a</sup></b>	1.11	(0.95–1.30)	1.19	(1.00–1.42)
<b>CD4 cell slope<sup>b</sup></b>				
>(–) 9.7 cells/months	1.00		1.00	
≤(–) 9.7 cells/months	2.14	(1.53–3.00)	2.27	(1.59–3.23)
<b>p24 antigenaemia<sup>b</sup></b>				
Negative	1.00		1.00	
Positive	1.89	(1.36–2.61)	1.82	(1.28–2.60)
<b>Thrush<sup>b</sup></b>				
Absent	1.00		1.00	
Present	1.41	(0.97–2.04)	1.58	(1.03–2.41)
<b>Seborrheic dermatitis<sup>b</sup></b>				
Absent	1.00		1.00	
Present	1.24	(0.89–1.74)	1.12	(0.79–1.60)
<b>Oral hairy leukoplakia<sup>b</sup></b>				
Absent	1.00		1.00	
Present	0.97	(0.58–1.63)	0.89	(0.50–1.58)
<b>Zoster<sup>b</sup></b>				
Absent	1.00		1.00	
Present	1.22	(0.74–1.99)	0.90	(0.54–1.50)
<b>Other conditions<sup>b,c</sup></b>				
Absent	1.00		1.00	
Present	0.89	(0.57–1.40)	0.99	(0.61–1.58)

<sup>a</sup> Per 10-year increase.

<sup>b</sup> During the 24 months prior to the CD4 cell threshold of 200/ $\mu$ L.

<sup>c</sup> Fever and/or weight loss and/or diarrhoea and/or night sweating.

- 1) What is the 95% confidence interval for the relative risk (e.g. **hazard ratio**) of clinical AIDS after CD4 threshold comparing patients with and without thrush?

**The 95% confidence interval for the hazard ratio (relative risk) of clinical AIDS after CD4 threshold comparing patients with and without thrush is 0.97 to 2.04.**

- 2) What is the 95% confidence interval for the relative risk of clinical AIDS after CD4 threshold comparing patients with and without thrush, but now controlling for other biological and clinical parameters? Compare your answer to your answer from problem 1. Why are they the same or different?

**The 95% confidence interval for the hazard ratio (relative risk) of clinical AIDS after CD4 threshold comparing patients with and without thrush, controlling for other biological and clinical parameters, is 1.03 to 2.41.**

**These two confidence intervals are different from each other because the interval in problem 1 does not adjust for the biological and clinical parameters (possible confounders) as in problem 2.**

- 3) Calculate the estimated relative risk of clinical AIDS after CD4 threshold comparing homosexual and heterosexual men, adjusting for other biological and clinical parameters.

**Adjusted RR (Homosexual Men versus Haemophiliacs) = 1.77**

**Adjusted RR (Heterosexual Men versus Haemophiliacs) = 1.36**

**These adjusted HRs (RRs) are estimates obtained from a Cox model, so based on these we can obtain the estimated  $\beta$ 's that correspond to Homosexual and Heterosexual Men.**

**Estimated  $\beta_{\text{Homosexual}} = \log(1.77) = 0.57$**

**Estimated  $\beta_{\text{Heterosexual}} = \log(1.36) = 0.31$**

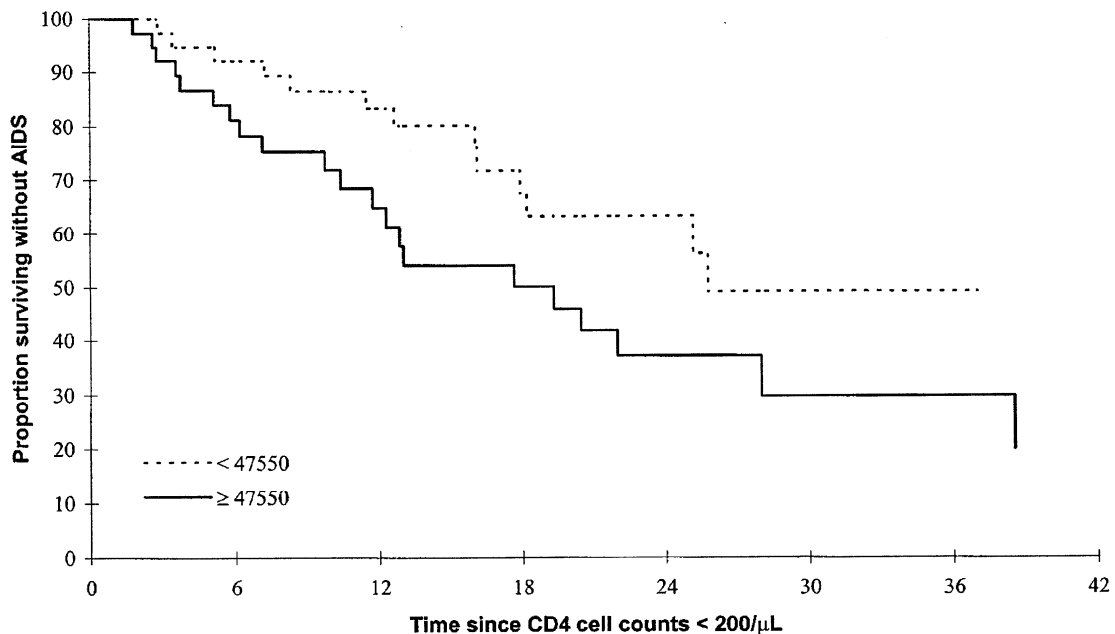
**Now to compare the risk of clinical AIDS for the homosexual and heterosexual men, we simply look at the difference in these two log relative risks.**

**Estimated Log RR comparing homosexual to heterosexual men :**

$$0.57 - 0.31 = 0.26$$

**So, the Estimated HR comparing homosexual to heterosexual men :  $e^{0.26} = 1.30$**

Of the 333 patients in the study, 77 patients had measurements of HIV RNA level at the CD4 threshold. Below find the Kaplan Meier estimates of the survival function for those patients with HIV RNA level less than 47,550 copies/ml compared to those with greater than or equal to 47,550 copies/ml.



**Figure 1** AIDS-free survival curves once the CD4 cell count has fallen below 200/ $\mu$ L according to the median serum HIV-1 RNA level (47 550 copies/ml) at the CD4 cell count threshold ( $n = 77$ )

- 4) Summarize the main finding of Figure 1 with regard to the effect of HIV RNA level on the incidence of clinical AIDS. Use quantitative information to make your points.

**Based on the two survival curves presented in Figure 1, we conclude that there is evidence in the data to suggest that those patients with HIV RNA level < 47550 copies/ml at the CD4 threshold have a higher survival than those patients with HIV RNA level  $\geq$  47550 copies/ml. At approximately 26 days from CD4 threshold for patients with HIV RNA level < 47550 copies/ml, 50% of the patients have no clinical AIDS; while the median survival for those patients with HIV RNA level  $\geq$  47550 copies/ml is estimated to be approximately 18 days.**

**In order to determine if this difference in the survival estimates is statistically significant, a log rank test could be used. This test was presented in the paper with a corresponding p-value = 0.06. Therefore, using a significance level of 0.05, the two survival curve estimates are not statistically significantly different from each other. The author could also have included confidence intervals for the two survival estimates to provide a visual display of the variability associated with the survival estimates for the two groups.**