Table 2.2 - Cohort studies of KSHV and Kaposi Sarcoma

Reference, location, name of study	Cohort description	Detection method	No. of cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Whitby et al. (1995), UK	Nested case-control study of 11 AIDS-KS patients and 132 HIV infected MSM without KS	KSHV DNA detected in PBMC by PCR	6/18 cases were KSHV positive, compared to 5/132 controls	12.7 (2.9-58.4)	None	Blood collection was a median of 30 months prior to diagnosis
Moore et al. (1996), USA	Nested case-control study of 21 AIDS-KS patients and 23 HIV infected MSM without KS	KSHV DNA detection in PBMC by PCR	11/21 cases were KSHV positive compared to 2/23 controls	11.6 (1.8-93.6)	None	Blood collection was up to 21 months prior to diagnosis
Gao et al. (1996), USA	Nested case-control study of 40 AIDS-KS patients and 40 HIV infected MSM without KS This study is also included in the "case-control" tables	Serology: latent nuclear antigen	21/40 cases were KSHV seropositive prior to diagnosis. At diagnosis 32/40 cases were seropositive. 7/40 controls were seropositive at time of pseudo diagnosis	*5.2 (1.7-16.6)* *Probably underestimated* At diagnosis: 18.9 (5.4-69.8)	Matched for CD4 count at time of diagnosis	Blood was collected 6-75 months prior to diagnosis among cases only; in controls, assessment of KSHV status was made at time of pseudo diagnosis only – OR is likely to be underestimated therefore
Parravicini et al. (1997), Italy	Nested case-control study among organ transplant recipients (one heart transplant and the rest were renal tranplants)	Positive to one or more of 4 assays against lytic and latent antigens	10/11 cases KSHV seropositive prior to transplantation compared to 2/17 controls	75 (4.7-3500)	None	Samples from pre-transplant period; KS developed at least 2 years post-transplantation

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Renwick et al. (1998), Netherlands	Cohort of 1459 MSM and 1167 drug users	Serology: latent and lytic nuclear antigen	62/71 cases were seropositive prior to diagnosis	3.2 (1.9-5.3) among those KSHV seropositive at enrollment 5.0 (2.9-8.6) among those who seroconverted after enrollment	Adjustment for CD4 count made no material difference to results	It is unclear how many of those without KS were KSHV seropositive; among 600 HIV-infected MSM the prevalence was 49% overall and 62% among the 193 who developed AIDS (including those with KS)
Melbye et al. (1998), Denmark	Nested case-control study of 10 AIDS-cases and 31 AIDS patients with other conditions	Serology: latent nuclear antigen	8/10 cases were KSHV seropositive prior to diagnosis; it is unclear how many controls were KSHV seropositive	Cannot estimate	N/A	Nested within a cohort of 259 homosexual men, 8.9% of whom were HIV infected at enrollment and followed for 15 years; 41 developed AIDS (10 had KS)
Regamey et al. (1998), USA	220 renal transplant recipients followed for two years post transplant. Tested for antibodies against KSHV on day of transplant and at 1 year	Serology: latent and lytic antigens	2/2 cases were KSHV positive 1 year since transplantation compared to 37/218 controls	Not estimated No 0 1.0 Yes 2 ∞ [2.5–∞]	N/A	KS developed between 12 and 26 months post transplant and occurred among the 25 people who seroconverted between the day of transplant and 1 year post transplant
Chatlynne et al. (1998), USA	Sera from a hospital series of HIV infected people were available for 31 people who subsequently developed KS	Serology: whole virus assay	26/31 cases were KSHV seropositive prior to diagnosis	Not estimated	N/A	Comparison was made with various other groups (with lower seroprevalence); this study is also included in the case-control table

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Francès et al. (1999), France	166 renal transplant recipients tested for KSHV antibodies before transplantation and followed for 30 months or more	Serology: latent antigens	4/4 cases KSHV seropositive prior to transplantation compared to 12/162 controls	P<0.0001	N/A	3 cases were of African origin and the other worked in the French Overseas Department
Rabkin et al. (1999), Canada	Nested case-control study of 3 transplant recipients with KS and 6 controls, tested for KSHV pre-transplant	Serology: latent antigens and whole-virus assay	1/3 cases KSHV seropositive compared to 1/6 controls	2.5 (0-195)	N/A	Controls were matched to cases for ethnicity and type of allograft
Grulich et al. (1999), Australia	115 MSM with AIDS (but not KS initially	Serology: latent and lytic antigen	30/37 cases KSHV seropositive to either assay, compared to 22/51 controls	4.4 (1.9-10.2); positive to either assay. Latent assay: 2.1 (1.1-4.1); lytic assay: 4.3 (2.0-9.2)	None	Time from blood sample to diagnosis: 3-5 years
O'Brien et al. (1999), USA	Cohort of 134 HIV seropositive MSM	Serology: latent nuclear antigen	24/32 cases were KSHV seropositive prior to diagnosis compared to 51/103 of those without KS	3.6 (1.7-9.5)	Adjusted for CD4 count and HIV viral load	Median time from blood collection to diagnosis: 13 months; range 4-27 months

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Rezza et al. (1999), Italy	Cohort of 366 HIV seropositive people from various exposure categories	Serology: latent nuclear antigen	20/21 cases were KSHV seropositive prior to diagnosis compared to 120/345 of those without KS	Overall: 29.6 (3.9-224.3) Low titer vs. neg: 24.8 (3.2-192.6) High titer vs. neg: 51.8 (6.1-441.3)	Adjusted for age at seroconversion	Median time from blood collection to diagnosis: 6 years; range 0.4-10.7 years. Risk of KS increased with increasing anti-KSHV antibody titer
Jacobson et al. (2000), USA	A study of 251 MSM who were all co-infected with HIV and KSHV; the whole cohort comprised 400 HIV infected people and included 149 people who were not KSHV seropositive. No data on the occurrence of KS in these 149 were provided	Serology: lytic antigens	182 were KSHV seropositive before seroconverting to HIV (34 developed KS) and 69 became KSHV seropositive after HIV infection (8 developed KS)	Compared to those who were KSHV infected before HIV infection, those who seroconverted to KSHV after HIV had 2.6 (1.1-6.1) times the risk of KS	Adjusted for CD4 count	Data on the risk of KS in KSHV positive compared to negative people were not provided. The number of KS cases in KSHV negative people was not shown
Francès et al. (2000), France	400 renal transplant recipients recruited prior to transplant	Serology: latent antigens	9/9 cases were KSHV seropositive, compared to 23/391 controls	P<0.0001	None	Minimum follow-up: 2 years. Note: there may be overlap between this study and the 1999 Frances study above

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Quinlivan et al. (2001), Switzerland	Nested case-control study within the Swiss HIV cohort; 28 cases of KS and 28 matched controls	3 serological assays: Latent nuclear antigen (N-IFA), latent membrane antigen (M-IFA) and lytic antigen	N-IFA: 17/28 cases KSHV seropositive compared to 9/28 controls M-IFA: 20/28 and 17/28 Lytic: 4/28 and 4/28	N-IFA: 3.0 (1.0-11.1) M-IFA: 1.7 (0.5-6.7) Lytic: 0.9 (0.2-6.8)	Controls matched to cases for observation time, CD4 count, sex, age and HIV risk group	Median time between blood sample and diagnosis 4.7 years (range 3-7 years).
Cattani et al. (2001), Italy	175 transplant recipients, tested for KSHV pre-transplant and followed up to 10 years	Serology: latent and lytic antigens	6/7 cases KSHV seropositve compared to 20/168 controls	34.4 (4.3-274.0)	N/A	One other person seroconverted after transplantation and developed KS
Emond et al. (2002), France	150 heart transplant patients, tested for KSHV pre-transplant	Serology: latent antigens	1/1 case KSHV seropositive compared to 3/149 controls	-	N/A	The patient with KS developed it 7 months post transplant. One person seroconverted after transplantation.
Engels et al. (2003), USA	Nested case-control study in a cohort of 132 MSN; 29 KS cases and 57 controls, matched for KSHV serostatus, CD4 count and time between sampling and diagnosis/pseudodiagnosis (average of 1 year)	All participants were seropositive using a lytic assay. Viral load was assessed by measuring KSHV DNA in PBMC	7/29 KSHV seropositive cases had detectable viral load at least 1 year prior to diagnosis, compared to 2/57 KSHV seropositive controls	11.7 (1.8-76.0)	Adjusted for KSHV antibody titre, CD4 count and HIV viral load	All participants were KSHV seropositive. Exposure measure was presence of HHV8 DNA in PBMC

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Reference, location, name of study	Cohort description	Detection method	No. of cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
Marcelin et al. (2004), France	99 liver transplant patients tested for KSHV pre-transplant and at 6 months post transplant	Serology: latent and lytic antigens	3 patients had antibodies against latent and lytic antigens pre-transplant. None developed KS after >2years follow-up. 4 patients infected from the donor, but only had antibodies against lytic (not latent) antigens at 6 months post-transplant – of those, 2 subsequently developed KS	-	N/A	Both patients with KS were diagnosed at autopsy with disseminated disease and had evidence of KSHV DNA in PBMC prior to diagnosis. No other patients in the cohort developed KS

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Newton et al. (2006), UK	Case-control study nested within 3 UK clinical trials of treatment for HIV. Include 189 cases of KS with blood taken >6months prior to diagnosis. 189 controls matched for period of follow-up prior to diagnosis, trial, age, sex, ethnicity, HIV transmission group, treatment.	Serology: latent and lytic antigens	Latent: 72/189 cases and 23/189 controls Lytic: 61/187 cases and 36/187 controls (insufficient sera for 2 case/control pairs)	Latent: 4.4 (2-3-8.3) By Titer: Neg: 1.0 Min: 3.5 (1.4-8.7) Med: 4.1 (1.7-10.2) Max: 8.7 (1.9-40.4) (ptrend<0.001) Lytic: 2.0 (1.2-3.4) By titer Neg: 1.0 Min: 1.2 (0.5-3.1) Med: 2.8 (1.3-6.3) Max: 1.4 (0.6-3.2) (ptrend=0.02)	Adjustment for CD4 count	Cohorts comprised mainly MSM. Time between sampling and diagnosis/pseudo-diagnosis>900 days Risk of KS increased with increasing titer of antibodies against both latent (p<0.001) and lytic (p=0.02) antibodies
García-Astudillo & Leyva-Cobián (2006), Spain	1019 organ transplant recipients; 231 liver transplant patients and 788 kidney transplant patients.	Serology: lytic and latent antibodies	9/9 cases KSHV seropositive compared to 4/1010 controls	- P<0.001	N/A	Time between sampling and diagnosis of KS between 2 - >21 months

Note: criteria for inclusion in this table are simply that testing for KSHV occurred in samples that were collected prior to diagnosis of KS, rather than at (or after) the time of diagnosis. Some studies are included here and in the case-control table.