

Table 2.6. Cohort studies of HCV and lymphoid malignancies

Reference, location, name of study	Cohort description	Detection method	No. of cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
<i>HIV-negative subjects</i> Ohsawa <i>et al.</i> (1999) Japan	2162 patients with HCV-related chronic hepatitis (1398 men, 834 women), admitted to 3 medical institutions in Osaka between 1957 and 1997; age range: 18–95 (median: 58) years; followed from date of diagnosis to 1997 (average follow-up: 5.7 years) Cancers occurring in cohort identified from Osaka Cancer Registry; standardized incidence ratio (SIR) calculated based on expected number of B-cell NHL cases using age- and calendar year-specific incidence rates from cancer registry	Anti-HCV: third-generation enzyme-linked immunosorbent assay (ELISA) HCV RNA: nested reverse transcription-polymerase chain reaction (RT-PCR)	[Obs:Exp] B-cell NHL, 4:1.90	2.1 (0.57–5.4)	Age and calendar year	[In meta-analysis by Dal Maso & Franceschi (2006)]

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Rabkin <i>et al.</i> (2002) USA, Child Health and Development Study	48420 gravida, male partners, and offspring from 20754 pregnancies, recruited from Kaiser Foundation Health Plan (California) between 1959 and 1966 95 cases of B-cell lymphoproliferative malignancies with stored sera (57 with B-cell NHL, 24 with multiple myeloma [MM], and 14 with Hodgkin disease [HD]), identified through 1996 by linkage with California Cancer Registry and California death registrations, mean age at diagnosis: 53.3 years; 95 controls selected from cohort subjects free of cancer diagnosis through 1996, individually matched to cases by race, sex, decade of birth, and smoking status	Anti-HCV: dually reactive in 2 different third-generation ELISAs, with confirmation by third-generation recombinant immunoblot assay (RIBA) HCV RNA: Amplicor RT-PCR assay	[Anti-HCV+ or HCV RNA+ / Anti-HCV- and HCV RNA-] B-cell NHL, 0/57 MM, 0/24 HD, 0/14	No HCV+ controls		[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)]

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Duberg <i>et al.</i> (2005) Sweden	27150 HCV-infected persons notified to Swedish Institute for Infectious Disease Control between 1990 and 2000 (19147 men, 8003 women); those with cancer diagnosis within 3 months of or preceding HCV notification excluded from analysis Cancers occurring in cohort through 2000 identified by linkage to Swedish Cancer Registry; SIRs calculated based on expected number of cases of NHL (ICD-7 200.1, 200.2, 200.3, 202.1, 202.2) chronic lymphocytic leukaemia (CLL) (ICD-7 204.1), and MM (ICD-7 203.0) using age-, sex-, and calendar-year-specific incidence rates from cancer registry	HCV notifications made in duplicate, one from clinician and one from laboratory having diagnosed infection – detection of anti-HCV by second- or third-generation ELISA, with confirmation by RIBA, widely used in Swedish laboratories; during late 1990s most HCV infections confirmed using detection of HCV RNA	[Obs:Exp] B-cell NHL, 20:10.06 CLL, 4:2.07 MM, 7:2.89	2.0 (1.2–3.1) 1.9 (0.53–4.95) 2.4 (0.97–5.0)	Age, sex, and calendar year	Excluding subjects with HIV infection, for B-cell NHL: SIR=1.6 (95% CI, 0.91–2.6) [In meta-analysis by Dal Maso & Franceschi (2006)]

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Amin <i>et al.</i> (2006) New South Wales	75834 HCV monoinfected (without HBV) persons notified to New South Wales Health Department's Notifiable Disease Database between 1991 and 2002 [study described in Table 2.3] SIRs calculated based on expected number of cases of NHL (ICD-10 C82-85,96), MM (ICD-10 C90), and HD (ICD-10 C81) using age-, sex-, and calendar-year-specific incidence rates derived from New South Wales population; NHL subtypes examined: follicular lymphoma (FL) (ICD-10 C82), diffuse NHL (ICD-10 C83), and T-cell NHL (ICD-10 C84)	Detection of anti-HCV or HCV RNA [assays used for testing NR]	[Anti-HCV+ or HCV RNA+] NHL, 33 FL, 6 Diffuse NHL, 19 T-cell NHL, 2 MM, 7 HD, 4	0.9 (0.6–1.2) 0.6 (0.3–1.4) 1.1 (0.7–1.7) 1.1 (0.3–4.2) 0.8 (0.4–1.7) 0.4 (0.2–1.1)	Age, sex, and calendar year	Investigators reported that SIR for diffuse NHL remained the same with exclusion of high HIV prevalence post codes.

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Ulcickas Yood <i>et al.</i> (2007) USA	Cohort of 3888 individuals with chronic HBV infection and comparison cohort of 205203 individuals without HBV infection (matched on health system, age, and sex), identified from patients 16 years of age and older in 2 health care delivery systems in Michigan and Northern California between 1995 through 2001, with no history of NHL or HIV; 114843 ([55%]) men; mean age: 39.9 (\pm 12.7) years; 1929 (0.9%) HCV seropositive 119 newly diagnosed cases of NHL occurred from 1995 through 2002 (median follow-up of cohorts: 3+ years), identified from tumour registries in each health system	HCV laboratory testing [assays used for testing NR]	<u>NHL</u> HCV Neg 116 Pos 3	1.0 2.4 (0.74–7.5)	Chronic HBV infection, sex, race and ethnicity, age, Charlson comorbidity score, median household income, and study site	

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<i>HIV-positive subjects</i> Waters <i>et al.</i> (2005) England	5823 HIV-positive patients at hospital in London, cohort followed since 1996 and seen at regular intervals for clinical assessment; anti-HCV testing introduced in 1998: 3642 (62%) tested with 362 anti-HCV seropositives 102 cases of NHL diagnosed over 34133 person-years of follow-up (average follow-up: [5.85] years); primary central nervous system lymphomas excluded	Anti-HCV: Abbot IMX system	<u>NHL</u> Anti-HCV Neg 56 Pos 7 Not tested 39	1.0 0.97 (0.44–2.1) 1.1 (0.71–1.6)	None	No information provided concerning age and gender of subjects, ascertainment of NHL cases, or implementation and timing of anti-HCV testing.

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Franceschi <i>et al.</i> (2006b) Switzerland, Swiss HIV Cohort Study	Nested case-control study conducted within ongoing cohort study, enrolling people infected with HIV since 1988 from 7 large hospitals in Switzerland, with follow-up every 6 months, information on cancer occurrence supplemented through linkage to 8 Swiss National Cantonal Cancer Registeries 298 cases of NHL with HCV serology and information on matching criteria occurred through 2004 (246 men, 52 women); 889 control subjects randomly selected from cohort with at least same follow-up length as case and with HCV serology (733 men, 156 women), matched 3-to-1 to case by centre of enrollment, gender, age (in 5-year groups), and CD4+ count	Anti-HCV: third-generation ELISA, with confirmation by RIBA	<u>NHL</u> Anti-HCV Neg 198 Pos 100	1.0 1.05 (0.63–1.75)	Centre, gender, age group, CD4+ count, HIV transmission category, and year of enrollment	