

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
<i>Africa</i> Cowgill <i>et al.</i> (2004) Egypt, 1999–2003	227 cases of B-cell NHL (137 men, 90 women), diagnosed (≤6 months prior to interview) at Egyptian National Cancer Institute in Cairo; mean age: 48.2 (±14.2) years; participation rate: 55%	227 hospital-based controls without cancer (137 men, 90 women), orthopaedic patients with fractures treated at Kasr El-Aini Faculty of Medicine Orthopaedic Hospital in Cairo; frequency matched to cases by sex, rural versus urban birthplace, and age (5-year categories); mean age: 47.7 (±13.7) years; participation rate: 76%	Anti-HCV: third-generation enzyme immunoassay(EIA) HCV-RNA: direct nested and conventional reverse transcriptase-polymerase chain reaction (RT-PCR)	Anti-HCV+ and HCV RNA+ / HCV RNA–	B-cell NHL, 94/126	2.9 (1.9–4.5)	Age, sex, birthplace, and current residence in Upper Egypt	[In meta-analysis by Dal Maso & Franceschi (2006)]
<i>Americas</i> Zuckerman <i>et al.</i> (1997) USA, 1994–1996	120 consecutive patients with B-cell NHL (63 men, 57 women), evaluated at outpatient haematology clinic of Los Angeles County-University of Southern California Medical Centre; anti-HIV- or HBsAg-positive patients excluded; age range: 23–84 (mean: 52) years; 78% Hispanic; histological type based on NCI Working Formulation classification 154 patients with other malignant haematological conditions also included as “control group”: 10 chronic lymphocytic leukaemia (CLL), 11 T-cell lymphoma, 45 Hodgkin disease (HD), 20 multiple myeloma (MM), 44 acute leukaemia, 23 chronic myelogenous leukaemia, and 1 hairy cell leukaemia	114 hospital-based controls without malignant haematological conditions (64 men, 50 women), unselected patients attending general medicine clinic at same centre as cases (with hypertension or ischaemic heart disease, diabetes mellitus, or primary hypothyroidism); anti-HIV- or HBsAg-positive patients excluded; age range: 20–79 (mean: 50) years; 72% Hispanic; participation rate NR	Anti-HCV: second-generation enzyme-linked immunosorbent assay (ELISA) HCV RNA: Amplicor RT-PCR assay	Anti-HCV+ or HCV RNA+ /Anti-HCV– and HCV RNA–	B-cell NHL, 26/94 [HD 2/43] [MM, 1/19]	[5.0 (2.0–12.6)] [0.84 (0.16–4.3)] [0.95 (0.11–8.3)]		[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)]

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Shariff <i>et al.</i> (1999) Canada, 1995–1997	88 patients with B-cell NHL (46 men, 42 women), newly referred to British Columbia Cancer Agency from 1996 to early 1997 on whom stored sample was available ([43%] of cases in database); patients with HIV excluded; age range: 23–86 (median: 61) years 37 patients with T-cell NHL (22 men, 15 women) also included as “control group”, newly referred to British Columbia Cancer Agency from 1995 through 1997 on whom stored sample was available (41% of cases in database); patients with HIV excluded; age range: 20–82 (median: 56) years	1085 health care workers presenting after a needle-stick injury, anti-HCV serology from records of Red Cross of British Columbia in 1992–1993; no demographic characteristics available for control group	HCV: anti-HCV by third-generation ELISA, with confirmation by EIA and recombinant immunoblot assay (RIBA); samples positive on all 3 assays further confirmed by Amplicor RT-PCR assay for HCV RNA	HCV +/-	B-cell NHL, 2/86 [T-cell NHL 0/37]	[2.3 (0.50–10.4)] ---		[In meta-analysis by Matsuo <i>et al.</i> (2004)]
Avilés <i>et al.</i> (2003) Mexico, 1997–1999	416 consecutive, previously untreated cases of B-cell NHL (256 men, 160 women); all Mexican-born, HIV-negative, and with no history of intravenous drug use or transfusion; age range: 29–83 (mean: 53.4) years Histological type based on WHO/REAL classification: 236 with diffuse large B-cell lymphoma (DLBCL), 97 with follicular lymphoma (FL), and 83 with marginal zone (MZ) lymphoma	832 healthy blood donors (712 men, 120 women), donating during same time period at central blood bank, matched to cases by sex and age (± 5 years); age range: 21–40 (mean: 29.8) years	Anti-HCV: third-generation ELISA and RIBA HCV RNA: RT-PCR	Anti-HCV+ and HCV RNA+ / Anti-HCV–	B-cell NHL, 2/414 DLBCL, 1/235 FL 1/96 MZ, 0/83	1.9, $p > 0.05$ [3.5 (0.22–56.75)] [8.65 (0.54–139.5)] ---	NR	[In meta-analysis by Matsuo <i>et al.</i> (2004)] NHL cases older and with lower proportion of men than blood donor controls. It is not clear whether the OR reported in the study is adjusted for any potential confounders; the crude OR is [4.0].

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Chindamo <i>et al.</i> (2002) Brazil, 1995–1998	109 cases of NHL (57 men, 52 women): 87 with B-cell NHL and 31 with T-cell NHL, patients in regular follow-up at Federal University of Rio de Janeiro Hospital, excluded if positive for HTLV-1 or HIV or if had previous treatment with interferon or ribavirin; age range: 13–84 (median: 50) years; participation rate NR Histological type based on WHO classification: 32 DLBCL, 11 lymphoplasmacytoid, 19 FL, 9 diffuse small cell, 4 mantle cell, 11 T-cell, 11 lymphoblastic 98 patients with histologically confirmed HD (n=67) or CLL (n=31) also included as “control group” (47 men, 51 women); time period and exclusion criteria same as for NHL cases; age range: 12–79 [median: 44] years	39371 blood donors in University Hospital from 1995 to 1998; gender distribution NR; median age: 40 years; 1.2% HCV prevalence reported	Anti-HCV: second- or third-generation ELISA, with confirmation by repeat third-generation ELISA HCV RNA: RT-PCR assay, determined for anti-HCV-negative NHL patients receiving chemotherapy 1 month before testing to exclude false-negatives	Anti-HCV +/-	All NHL, 10/99	[OR=10.7]		[In meta-analysis by Matsuo <i>et al.</i> (2004)] Number of HCV-positive blood donors NR.
					B-cell NHL, 8/79	[OR=8.3]		
					T-cell NHL, 2/20	[OR=8.2]		
					DLBCL, 3/29	[OR=8.5]		
					[HD, 1/66] [CLL, 1/30]	[OR=1.2] [OR=2.7]		

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Engels <i>et al.</i> (2004) USA, 1998–2000	813 incident cases of NHL (435 men, 378 women), sampled from cases aged 20–74 years in 4 areas of Surveillance, Epidemiology and End Results programme (Iowa, Detroit, Los Angeles, and Seattle); identified HIV-infected subjects excluded; mean age: 57 (±12.3) years; 1321 ([59%]) cases participated in study, of whom 61.5% had available blood sample Histological types based on WHO classification: 411 cases with low-grade B-cell NHL – 91 small lymphocytic lymphoma (SLL)/CLL, 20 lymphoplasmacytoid, 225 follicular, 26 MZ, 49 mucosa-associated lymphoid tissue (MALT) 275 cases with intermediate- or high-grade B-cell NHL – 37 mantle zone, 217 DLBCL, 13 DLBCL/immunoblastic variant, 8 Burkitt 50 cases with T-cell NHL (14 Mycosis fungoides, 36 other) and 77 cases with other/unknown NHL	684 population-based controls (371 men, 313 women), selected from general population in same 4 areas (stratified on residence, age, sex, and race to parallel distribution in cases), using random-digit dialling (controls aged 20–64 years) or from Medicare eligibility files (controls aged 65–74 years); identified HIV-infected subjects excluded; mean age: 58.2 (±12.4) years; 1057 ([52%]) controls participated in study, of whom 65% had available blood sample	HCV: anti-HCV by third-generation EIA, with confirmation by third-generation RIBA or second-generation Amplicor RT-PCR assay for HCV RNA	HCV +/-	All NHL, 32/781	1.8 (1.0–4.1)	Estimate for all NHL adjusted for sex, age, race, centre, and education Unadjusted estimates for NHL subtypes	[In meta-analysis by Dal Maso & Franceschi (2006)] MALT: OR=2.0 (95% CI, 0–7.2)
					Low-grade B-cell NHL, 18/393	2.2 (0.96–4.6)		
					SLL/CLL, 2/89	2.2 (0.96–4.6)		
					FL, 11/214	2.5 (1.0–5.8)		
					MZ, 2/24	4.0 (0–13.6)		
					Intermediate- and high-grade B-cell NHL, 8/267	1.4 (0.49–3.2)		
DLBCL 6/211								
[T-cell NHL, 2/48]	1.4 (0.39–3.3)							
	2.0 (0–6.5)							

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Morgensztern <i>et al.</i> (2004) USA, 2003–2004	90 consecutive patients with B-cell NHL (45 men, 45 women), evaluated at cancer centre and hospital in South Florida; mean age: 54.2 (\pm 14.2) years; 45% Hispanic; histological types based on WHO classification	96 hospital-based controls, consecutive patients with malignancies other than NHL [breast, head and neck, gastrointestinal, genitourinary, lung, other solid tumours] (31 men, 65 women); mean age: 56.2 (\pm 13.1) years; 63% Hispanic	HCV: anti-HCV by third-generation ELISA or RIBA, with confirmation by RT-PCR for HCV RNA	HCV +/-	B-cell NHL, 2/88	0.24 (0.03–1.6)	Gender and history of HCV risk factors [further adjustment for race did not affect OR]	
Morton <i>et al.</i> (2004) USA, 1995–2001	601 cases of NHL among female residents of Connecticut between ages of 21 and 84, identified using population-based Connecticut Tumor Registry, with no previous diagnosis of cancer and alive at time of interview; participation rate: 72%; 464 (77%) with sample for HCV testing Histological types based on WHO classification: 369 cases with B-cell NHL (44 CLL, 135 DLBCL, 103 follicular), 34 cases with T-cell NHL, and 61 cases with other type NHL	718 population-based controls, female residents of Connecticut between ages of 21 and 84, recruited using random-digit dialling for women under 65 years of age and from files of centres for Medicare and Medicaid Services for women over 65 years of age; frequency matched to cases by age (within 5-year groups); participation rate: 69% of women contacted through random-digit dialling, 47% of women from Medicare and Medicaid files; 534 (74%) with sample for HCV testing	HCV: anti-HCV by third-generation EIA, with confirmation by third generation RIBA or Amplicor RT-PCR assay for HCV RNA	HCV +/-	All NHL, 8/456 B-cell NHL, 7/362 CLL, 1/43 DLBCL, 2/133 FL, 4/103 T-cell NHL, 0/34	1.9 (0.5–7.3) 2.0 (0.6–8.2) 2.5 (0.1–22.7) 1.6 (0.1–9.8) 4.1 (0.8–19.4) ---	None [Inclusion of age, sex, education, body mass index, family history of cancer, history of alcohol consumption, and history of blood transfusion did not change estimated ORs by >10%.]	[In meta-analysis by Dal Maso & Franceschi (2006)]

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Spinelli <i>et al.</i> (2008) Canada, 2000–2004	795 cases of newly diagnosed NHL (463 men, 332 women), aged 20–79 from Greater Vancouver Regional District and Capital Regional District, enrolled from British Columbia Cancer Registry, without HIV infection and with information on HCV seropositivity; participation rate: 79% (HCV seropositivity determined for 96%) Histological types based on WHO classification: 717 cases with B-cell NHL (200 DLBCL, 212 FL, 92 MZ, and 195 other B-cell) and 78 cases with T-cell NHL	697 population controls (374 men, 323 women), selected from Client Registry of British Columbia Ministry of Health (subscribers to provincial health insurance plan), with information on HCV seropositivity; frequency matched to cases by sex, age (within 5-year age group), and residential location; participation rate: 46% (HCV seropositivity determined for 82%)	Anti-HCV: British Columbia CDC database (458 cases, 93 controls) – third generation ELISA, with third-generation chemiluminescence immunoassay; new testing (337 cases, 604 controls) – second-generation EIA, with confirmation by Inno-Lia	Anti-HCV +/-	All NHL, 19/776 B-cell NHL, 18/699 DLBCL, 12/200 FL, 0/212 MZ, 3/89 T-cell NHL, 1/77	2.6 (0.89–7.4) 2.9 (1.0–8.6) 7.3 (2.1–25.0) --- 6.1 (1.1–33.9) 0.37 (0.02–6.1)	Injection drug use [Inclusion of age, sex, region, ethnicity, education level, and history of tattooing, piercing, and blood transfusion did not change estimated ORs by >5%.]	Unadjusted OR for T-cell NHL: 1.8 (95%, 0.21–15.6)

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<p><i>Asia</i> Harakati <i>et al.</i> (2000) Saudi Arabia [study period NR]</p>	<p>56 patients with unequivocal diagnosis of B-cell NHL (40 men, 16 women), Saudi Arab nationals seen at King Fahad National Guard Hospital in Riyadh, no history of blood transfusion or liver disease; age range: 20–90 (median: 54) years; participation rate NR; histological type by Working Formulation classification</p> <p>41 patients with haematological malignancies other than B-cell NHL also included as “control group” (28 men, 13 women), randomly selected from same hospital with same exclusion criteria as NHL cases; age range: 16–77 (median: 46) years; participation rate NR</p>	<p>104 hospital-based controls, general medicine patients and healthy blood donors (68 men, 36 women), randomly selected from same hospital with same exclusion criteria as cases; age range: 20–88 (median: 54) years; participation rate NR</p>	<p>Anti-HCV: second-generation EIA, with confirmation by second-generation RIBA</p>	<p>Anti-HCV +/-</p>	<p>B-cell NHL, 12/44</p> <p>[Other haematological malignancies 2/39]</p>	<p>[9.2 (2.5–34.2)]</p> <p>[1.7 (0.28–10.7)]</p>		<p>[In meta-analysis by Matsuo <i>et al.</i> (2004)]</p>

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Mizorogi <i>et al.</i> (2000) Japan, 1993–1998	159 Japanese patients with newly diagnosed lymphoproliferative disorders (LPD) at Daisan Hospital in Tokyo: 121 with B-cell LPD (76 men, 55 women; age range: 27–92 [mean: 64] years) and 38 non-B-cell LPD (23 men, 15 women; age range: 19–84 [mean: 56] years) Histological type based on Working Formulation classification: B-cell LPD – 4 CLL, 17 MM, 100 B-cell NHL (65 men, 35 women; age range: 27–87 [mean: 63] years) Non-B-cell LPD – 5 adult T-cell leukaemia/ lymphoma, 8 HD, 25 non-B-cell NHL (16 men and 9 women; age range 24–83 [mean: 61] years)	516 hospital-based controls (322 men, 194 women), patients ≥30 years admitted to same hospital for first time between 1994 and 1995, excluded patients with liver diseases or LPD (134 with neoplasms and 385 with nonmalignant diseases); age range: 30–97 (mean age: 63) years; prevalence of HCV determined from discharge records	Anti-HCV: second-generation EIA	Anti-HCV +/-	Total B-cell LPD, 18/103 B-cell NHL, 17/83 Total non-B-cell LPD, 0/38	[2.5 (1.3–4.6)] [2.9 (1.55–5.4)] ---		[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)]
Kuniyoshi <i>et al.</i> (2001) Japan, 1990–1998	348 newly diagnosed cases of NHL (199 men, 149 women), admitted to 3 hospitals in Fukuoka; mean age: 60.3 (±14.1) years; participation rate NR; histological type based on Working Formulation classification	1513358 blood donors in Fukuoka from 1994 to 1999 (829117 men, 684241 women); HCV prevalence from Fukuoka Red Cross Centre; age range: 16–64 years	HCV: anti-HCV by third-generation ELISA, with confirmation by Amplicor RT-PCR assay for HCV RNA	HCV +/-	Male NHL cases, 17 (8.5%) Female NHL cases 3 (2.0%)	vs 0.72% HCV prevalence in male blood donors, p<0.0001 vs HCV prevalence in female blood donors, p=0.85	Age distribution	[In meta-analysis by Matsuo <i>et al.</i> (2004)] There are errors in Table 2 of the paper: 1) Lat two columns for female blood donors are the exact copy of the same data for male blood donors; 2) The total number of female blood donors should be changed from 829117 to 684241.

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Imai <i>et al.</i> (2002) Japan, 1994–2000	187 Japanese patients with NHL (101 men, 86 women): 156 with B-cell NHL (age range: 23–83 years) and 31 with T-cell lymphoma, residents of Osaka consecutively admitted to hospitals for initial treatment; histological type based on WHO classification	5-year birth cohort- and sex-specific anti-HCV prevalence data from 197600 first-time voluntary blood donors at Osaka Red Cross Blood Center in 1992; used to obtain expected number of anti-HCV-positive individuals	Anti-HCV: NHL cases – second- or third-generation ELISA; blood donors – second-generation passive haemagglutination assay	Anti-HCV+ O/E ratio	All NHL, 23:9.63 B-cell NHL, 21:8.07 T-cell NHL, 2:1.56	2.4 (1.4–3.4) 2.6 (1.5–3.7) 1.3 (0.00–3.1)	Birth cohort and sex	[In meta-analyses by Matsuo <i>et al.</i> (2004) and by dal Maso & Franceschi (2006)]
Kim <i>et al.</i> (2002) Korea, 1997–1998	222 newly diagnosed cases of NHL at Seoul National University Hospital (132 men, 90 women); age range: 14–85 (median: 52) years; participation rate NR; histological type based on Working Formulation classification	2 hospital-based control groups: (1) 439 patients with non-haematological malignancy (gastric cancer and sarcomas) (258 men, 181 women), diagnosed at same hospital during same time period as cases and (2) 444 visitors and patients without malignant diseases (264 men, 180 women), attending same hospital during same period as cases; matched to cases by age, sex, and date of admission; age range: 13–84 years; participation rate NR	Anti-HCV: second-generation ELISA	Anti-HCV +/-	NHL, 7/207	vs non-haematological malignancy control group: 2.0 (0.70–5.85) vs visitor/non-cancer patient control group: 1.2 (0.47–3.1)	None	[In meta-analysis by dal Maso & Franceschi (2006)]
Iwata <i>et al.</i> (2004) Japan, 1995–2001	145 consecutive cases of newly diagnosed malignant lymphoma (88 men, 58 women): 120 B-cell neoplasm, 16 T/NK-cell neoplasm, 7 Hodgkin lymphoma, and 2 unclassifiable, admitted to Toranomon Hospital in Tokyo; age range: 46–94 (median: 64) years	290 patients admitted to orthopaedics department (176 men, 114 women) and 284 patients admitted to otolaryngology department (175 men, 109 women), patients with history of malignancy excluded; matched to cases on age, sex, and year of visit; age range: 55–91 (median:62) years	Anti-HCV: from medical records –first- or second-generation EIA	Anti-HCV +/-	Lymphoma, 16/124	vs All controls: 2.45 (1.2–4.9) vs Orthopaedic controls: 3.7 (1.6–8.9) vs Otolaryngology controls: 1.95 (0.77–4.9)	Age, sex, year of visit, and HBsAg	[In meta-analysis by Matsuo <i>et al.</i> (2004)]

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Park <i>et al.</i> (2008) Korea, 1998-2001	235 patients with NHL diagnosed at Korea Cancer Center Hospital (139 men, 96 women); age range: 2-82 (mean 48.8) years; participation rate NR	235 patients with advanced gastric cancer diagnosed at the same hospital; matched to cases on age and sex; age range: 20-88 (mean 50.3) years; participation rate NR	Anti-HCV: second-generation ELISA	Anti-HCV +/-	NHL, 5	[0.71]		The case group included childhood NHL.
<i>Australia</i> Vajdic <i>et al.</i> (2006) New South Wales, 2000-2001	694 cases of newly diagnosed NHL (58% men), prospectively identified from population-based New South Wales Central Cancer Registry and high caseload clinicians, residents of New South Wales or Australian Capital Territory, excluded if had CLL, plasma cell myeloma, precursor B and T lymphoblastic leukaemia, lymphoid granulomatosis Grades 1 and 2, history of organ transplantation, or HIV infection; age range: 20-74 years; overall participation rate: 59% and consent rate: 86%; 597 (86%) provided blood sample, for HCV testing Histological type based on WHO classification: 95% with B-cell NHL; DLBCL and FL most common subtypes (33% each)	694 population-based controls, randomly selected from New South Wales and Australian Capital Territory electoral rolls; frequency matched to cases by age, sex, and residential area; overall participation rate: 41% and consent rate: 61%; 522 (75%) provided blood sample, for HCV testing	Anti-HCV: third-generation EIA, with confirmation by chemiluminescence immunoassay	Anti-HCV +/-	All NHL 3/682	1.3 (0.22-8.0)	Age, sex, geographic area, and ethnicity	[In meta-analysis by dal Maso & Franceschi (2006)] OR for B-cell NHL: 1.4 (95% CI, 0.23-8.6)

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<i>Europe</i> Ferri <i>et al.</i> (1994) Italy [study period NR]	50 consecutive patients with B-cell NHL (26 men, 24 women), Italian-born heterosexuals with no history of drug or alcohol abuse or interferon treatment; 48% undergoing chemotherapy; age range: 31–77 (mean: 63) years; histological type based on Working Formulation classification 30 Hodgkin lymphoma patients also included as “control group”; gender and age distributions NR	Group of 30 age-matched healthy subjects; gender and age distributions NR	Anti-HCV: second-generation ELISA and RIBA HCV RNA: nested RT-PCR	Anti-HCV+ or HCV RNA+ /Anti-HCV– and HCV RNA–	B-cell NHL, 17/33 [HD, 1/29]	No HCV+ healthy subjects		[In meta-analysis by Matsuo <i>et al.</i> (2004)] No information concerning source of case and control subjects.
Mazzaro <i>et al.</i> (1996) Italy [study period NR]	199 consecutive patients with NHL, referred to 3 haematological centres in northeast Italy; all Italian with stored serum samples collected at time of diagnosis; gender distribution NR; age range: 22–82 (mean: 64.5) years; participation rate NR; histological type based on Working Formulation classification 153 patients with other haematological malignancies (HD, CLL, myelodysplastic syndromes, plasma cell myeloma) also included as “control group”; gender distribution NR; age range: 18–85 (mean: 69) years; participation rate NR	6917 participants in population-based, Dionysos cohort study of residents of two towns in northeast Italy beginning in 1991; gender distribution NR; age range: 12–65 years; participation rate: 69%	Anti-HCV: second-generation EIA and RIBA	Anti-HCV +/-	NHL, 57/142 [Other haematological malignancy patients, 3.1%]	[13.55 (9.7–19.0)]		[In meta-analysis by Matsuo <i>et al.</i> (2004)]

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Musto <i>et al.</i> (1996) Italy [study period NR]	150 patients with B-cell NHL (66% >50 years old), 41 with CLL (93% >50 years old), and 90 with MM (88% >50 years old); gender distribution NR; participation rate NR	466 patients hospitalized for acute trauma (43% >50 years old); gender distribution NR; participation rate NR	Anti-HCV: third-generation assays	Anti-HCV +/-	B-cell NHL 40/110 CLL, 8/33 MM, 10/80	[6.4 (3.7–11.0)] [4.3 (1.8–10.2)] [2.2 (1.0–4.8)]		[In meta-analysis by Matsuo <i>et al.</i> (2004)] No information on source of case and control subjects.
Silvestri <i>et al.</i> (1996); Bellentani <i>et al.</i> (1994) Italy, 1993–1995	537 consecutive patients with lymphoproliferative disorders, seen at Division of Hematology of Udine University Hospital; all Italian-born, heterosexual, and with no history of drug abuse; gender and age distributions NR Histological types based on WHO classification: 311 cases with B-cell NHL – 92 CLL, 3 prolymphocytic leukaemia, 20 hairy cell leukaemia, 66 FL, 11 mantle cell, 10 MZ, 61 DLBCL, 2 Burkitt, and 2 precursor B-lymphoblastic leukaemia 57 cases with T-cell NHL, 68 cases with HD, 78 cases with MM, and 23 cases with acute lymphoblastic leukaemia (ALL)	6917 participants in population-based, Dionysos cohort study of residents of two towns in northeast Italy beginning in 1991; gender distribution NR; age range: 12–65 years, participation rate: 69%	Anti-HCV: second-generation EIA, with positive samples re-tested with same EIA and with second-generation RIBA	Anti-HCV +/-	B-cell NHL, 29/282 CLL, 4/88 FL, 5/61 DLBCL, 5/56 T-cell NHL, 2/55 HD, 0/68 MM, 3/75	[3.5 (2.3–5.2)] [1.5 (0.56–3.2)] [2.8 (1.1–7.0)] [3.0 (1.2–7.6)] [1.2 (0.30–5.1)] --- [1.35 (0.42–4.3)]		[In meta-analysis by Matsuo <i>et al.</i> (2004)] Investigators calculated prevalence ratios in paper.

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De Rosa <i>et al.</i> (1997) Italy, 1994–1995	315 patients with lymphoproliferative disorders (LPD) attending hospital of Federico II University Medical School (M/F ratio: 1.2), patients with previous history of cirrhosis or mixed cryoglobulinemia, drug abuse, or HIV infection excluded; age range (years): 15–88 (median: 62) for 263 B-cell LPD and 14–77 (median: 31) for 52 non-B-cell LPD; participation rate NR; [81%] of patients tested for anti-HCV during or after treatment Histological types based on Working Formulation classification: B-cell LPD – 91 B-cell NHL, 56 MM, 48 monoclonal gammopathy of uncertain significance, 13 Waldenstrom’s microglobulinaemia, and 7 hairy cell leukaemia Non-B-cell LPD – 43 HD and 9 T-cell NHL 93 outpatients >40 years old with metabolic disorders (diabetes, dyslipemia, vasculopathy) also included as “control group”; gender distribution NR; participation rates NR	1568 blood donors from same institution; gender distribution NR; 500 were >40 years old; participation rates NR	Anti-HCV: third-generation ELISA, with confirmation by third-generation RIBA HCV RNA: Amplicor RT-PCR assay	Anti-HCV+ or HCV RNA+ / Anti-HCV– and HCV RNA–	B-cell LPD, 59/204	[14.8 (9.3–23.6)]		[In meta-analysis by Matsuo <i>et al.</i> (2004)] 9 cases with T-NHL (0 with HCV).
					B-cell NHL, 21/70	[15.4 (8.4–28.2)]		
					MM, 9/47 CLL, 8/40	[9.8 (4.4–21.8)] [10.25 (4.4–23.8)]		
					Non-B-cell LPD, 1/51 HD, 1/42	[1.0 (0.13–7.5)] [1.2 (0.16–9.2)]		[Patients with metabolic disorders, 5/88]

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De Vita <i>et al.</i> (1998) Italy, 1994–1997	Incident HIV-negative NHL patients, newly diagnosed at Aviano Cancer Centre and Pordenonne General Hospital: 16 cases of NHL with liver or salivary gland involvement (9 men, 7 women; mean age: 62 years) and 68 concurrent cases of gastric and other NHL matched to cases of liver and salivary gland NHL on sex and age at diagnosis (± 5 years) (34 men, 34 women; median age: 61 years); histological type based on Working Formulation classification (NHL Pathological Classification Project, 1982)	73 hospital-based controls without lymphohaemopoietic neoplasms [described in Table 2.4]; group matched to liver and salivary gland NHL cases on sex and age (median age: 64 years)	Anti-HCV: second-generation ELISA, with confirmation by RIBA	Anti-HCV +/-	Liver/salivary gland NHL, 11/5 Gastric and other NHL, 9/59	51.5 (9.3–286) 4.3 (1.1–17.7)	Age, sex, and birthplace	
Paydas <i>et al.</i> (1999) Turkey [study period NR]	228 patients with lymphoproliferative disorders (LPD); gender distribution NR; age range: 15–85 (mean: 51) years; participation rate NR Disease types: 98 cases with NHL (mean age: 45 years), 38 with CLL (mean age: 57 years), 47 with MM (mean age: 60 years), 36 with HD (mean age: 45 years), and 9 with ALL	36266 blood donors living in southern Turkey; gender distribution NR; [$\sim 80\%$] ≤ 35 years old	Anti-HCV: third-generation ELISA	Anti-HCV +/-	All LPD, 26/202 NHL, 9/89 CLL, 4/34 MM, 5/42 HD, 7/29	[24.2 (15.7–37.3)] [19.0 (9.4–38.3)] [22.1 (7.8–62.9)] [22.4 (8.75–57.1)] [45.3 (19.6–105)]		[In meta-analysis by Matsuo <i>et al.</i> (2004)] No information on source of case and control subjects. The blood donors were much younger than the cases. The reported HCV prevalence in the donors increased with age; however, there were inconsistencies in the numbers given.

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Vallisa <i>et al.</i> (1999) Italy, 1990–1996	175 consecutive patients with untreated B-cell NHL (88 men, 87 women), patients with CLL, hairy cell leukaemia, and AIDS were excluded; mean age: ~63 years; participation rate NR Histological type based on WHO classification: 5 lymphocytic, 20 immunocytoma, 23 MZ, 12 mantle cell, 25 FL, 87 DLBCL, and 3 lymphoblastic	2 control groups without lymphoma: (1) 175 outpatients (metabolic disorders, other oncologic diseases, endocrinopathies, and hypertension) and (2) 175 hospital inpatients (cardiovascular, pulmonary, and cerebrovascular diseases and surgical patients); matched to cases by sex and age (± 2 years); participation rate NR	HCV: Anti-HCV by second-generation ELISA, with confirmation by second-generation RIBA or nested RT-PCR for HCV RNA	HCV +/-	All B-cell NHL, 65/110	vs Outpatient controls: [6.3 (3.4–11.6)]		[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)]
					MZ, 6/17	vs Inpatient controls: [5.5 (3.05–9.9)]		
					FL, 6/19	vs Outpatient controls: [3.8 (1.3–11.0)]		
					DLBCL, 32/55	vs Inpatient controls: [3.3 (1.1–9.4)]		
						vs Outpatient controls: [3.4 (1.2–9.7)]		
						vs Inpatient controls: [2.9 (1.0–8.3)]		
						vs Outpatient controls: [6.2 (3.1–12.3)]		
						vs Inpatient controls: [5.4 (2.8–10.5)]		

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Pioltelli <i>et al.</i> (2000) Italy, 1996–1997	300 newly diagnosed cases of B-cell NHL (145 men, 155 women), consecutive patients without previous solid neoplasm, other haematological malignancies, or autoimmune disorders at 11 institutions in Lombardy, patients with other B-cell neoplasms (CLL, acute leukaemia, MM, Waldenstrom’s macroglobulinaemia), T-cell and NK-cell neoplasms, and HD not included; all Italian born, HIV-negative, heterosexual, with no history of intravenous drug use or alcohol abuse, and no interferon treatment; age range: 17–92 (median: 63) years; histological type based on WHO classification	600 unselected patients (290 men, 310 women), recruited during routine visits at medicine, surgery, or traumatology departments at same hospital and time period as cases, without haematological malignancies, overt liver diseases, solid neoplasms, autoimmune diseases or treatment with corticosteroid or immunosuppressive agents; all Italian born, HIV-negative, heterosexual, with no history of intravenous drug use or alcohol abuse, and no interferon treatment; matched to cases by age and sex; age range: 18–92 (median: 64) years; participation rate NR	Anti-HCV: third-generation ELISA and RIBA tests	Anti-HCV +/-	B-cell NHL, 48/252	2.0 (0.70–27.1)	NR	[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)] It is not clear how the OR and 95% CI were obtained or whether a matched OR was estimated. The crude OR is calculated as: [2.05 (95% 1.3–3.1)].
Zucca <i>et al.</i> (2000) Switzerland, 1990–1995	180 consecutively diagnosed patients with B-cell NHL (101 men, 79 women), with serum sample obtained at time of diagnosis at Istituto Oncologico della Svizzera Italiana, no history of prior active liver disease or mixed cryoglobulinaemia and all HIV-negative; age range: 16–87 (median: 61) years Histological type based on WHO classification: 31 SLL and lymphoplasmocytoid/immunocytoma, 13 MZ, 46 FL, 24 mantle cell, 58 DLBCL (including high-grade MALT), and 8 other high-grade lymphoma	5424 new blood donors from same area, tested between 1992 and 1997; HCV prevalence from Swiss Red Cross Transfusional Medicine Service for Canton Ticino registry data; sex and age distributions NR; 0.9% HCV prevalence reported	Anti-HCV: micro-EIA, with confirmation by immunoblot	Anti-HCV +/-	All B-cell NHL, 17/163 FL, 3/43 DLBCL, 8/50	[OR=11.5], p<0.001 [OR=7.7] [OR=17.6]		[In meta-analysis by Matsuo <i>et al.</i> (2004)] No information on anti-HCV assays used for blood donors. Number of HCV-positive blood donors NR.

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Hausfater <i>et al.</i> (2001) France, 1998	813 consecutive patients admitted to Haematology Department of La Pitié-Salpêtrière University Hospital in Paris during 4-month period (437 men, 376 women), enrolled from outpatients and inpatients requiring blood sample analysis; age range: 12–93 (mean: 53) years 394 cases with LPD: 164 B-cell NHL, 107 CLL, 34 HD, 54 MM, 12 Waldenstrom's macroglobulinaemia, 17 ALL, and 6 hairy cell leukaemia	694 hospital-based controls patients (203 men, 491 women), patients admitted to Internal Medicine Department of same hospital and during same time period as cases, excluded if known prior chronic HCV infection and/or LPD; age range: 11–91 (mean: 50) years	Anti-HCV: third-generation ELISA	Anti-HCV +/-	All LPD, 11/383	[6.6 (1.8–23.9)]		[In meta-analysis by Matsuo <i>et al.</i> (2004)]
					B-cell NHL, 3/161	[4.3 (0.86–21.5)]		
					CLL, 2/105	[4.4 (0.72–26.6)]		
					HD, 1/33	[7.0 (0.71–68.9)]		
				MM, 1/53	[4.3 (0.44–42.5)]			
Montella <i>et al.</i> (2001b); Montella <i>et al.</i> (2001a) Italy, 1997–1999	205 incident patients with lymphoma in hospital-based case-control study [described in Table 2.4]; participation rate NR Histological type based on WHO classification: 101 cases with B-cell NHL (56 men, 45 women; age range: 13–85 [median: 59] years); 41 with MM (22 men, 19 women; age range: 43–82 [median: 65] years); 63 with HD (44 men, 19 women; age range: 15–71 [median: 44] years)	226 patients with no history of malignant tumour [described in Table 2.4]	HCV: anti-HCV by third-generation ELISA, with confirmation by Amplicor RT-PCR assay for HCV RNA	HCV +/-	B-cell NHL, 25/76	3.7 (1.9–7.4)	Age and sex	[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)]
					MM, 13/28	4.5 (1.9–10.7)		
					HD, 6/57	1.9 (0.6–6.3)		

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Kaya <i>et al.</i> (2002) Turkey [study period NR]	70 patients with NHL (42 men, 28 women), not previously treated with corticosteroids or immunosuppressive drugs and no history of blood transfusions, alcohol abuse, drug abuse, homosexuality, hepatic disease, autoimmune disease, or any other malignant disease; age range: 17–74 (mean: 45.9) years; participation rate NR; histological type based on Working Formulation classification	70 healthy age- and sex-matched subjects (39 men, 31 women); age range: 16–79 (mean: 45.4) years; participation rate NR	Anti-HCV: third-generation micro-EIA	Anti-HCV +/-	NHL, 1/69	1.0 (0.61–16.4)	None	[In meta-analysis by Matsuo <i>et al.</i> (2004)] Source of control and case subjects NR.

Table 2.7. Case–control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Mele <i>et al.</i> (2003); Bianco <i>et al.</i> (2004) Italy, 1998–2001	Newly diagnosed HIV-negative cases of lymphoproliferative and myeloproliferative diseases, patients ≥15 years old consecutively admitted to haematology wards of 10 hospitals in different cities throughout Italy Histological type based on WHO classification: 400 cases with B-cell NHL (246 men, 154 women) – 205 DLBCL, 10 Burkitt, 15 mantle cell, 18 SLL, 13 lymphoplasmacytic, 79 FL, 25 MALT, 15 MZ, and 20 unspecified (Mele <i>et al.</i> , 2003) 30 cases with T-cell NHL (26 men, 4 women), 157 with HD (100 men, 57 women), 100 with CLL (67 men, 33 women), 107 with MM (53 men, 54 women) (Bianco <i>et al.</i> , 2004)	396 hospital-based controls (205 men, 191 women), patients ≥15 years old with newly diagnosed diseases unrelated to HCV, admitted to other departments in same hospitals as cases; participation rate NR	Anti-HCV: third-generation EIA, with confirmation by third-generation RIBA HCV RNA: Amplicor RT-PCR assay	Anti-HCV+ or HCV RNA+ / Anti-HCV– and HCV RNA–	B-cell NHL, 70/330	3.1 (1.8–5.2)	Age, sex, level of education, and place of birth	[In meta-analyses by Matsuo <i>et al.</i> (2004) and by Dal Maso & Franceschi (2006)]
					DLBCL, 39/166	[4.0 (2.3–6.9)]		
					FL, 11/68	[2.75 (1.3–5.9)]		
					T-cell NHL, 4/26	2.2 (0.6–6.7)		
					HD, 5/152	1.2 (0.6–3.3)		
CLL, 9/191	1.3 (0.56–2.9)							
MM, 5/102	0.6 (0.23–1.8)							
Yenice <i>et al.</i> (2003) Turkey [study period NR]	134 patients admitted to Haematology and Oncology Clinic of SSK Okmeydani Training Hospital: 84 with B-cell NHL (48 men, 36 women; age range: 36–71 years) and 50 with Hodgkin lymphoma (20 men, 30 women; age range: 23–69 years); participation rate NR	100 health blood donors (40 men, 60 women), no previous history of surgery, blood transfusion, or viral hepatitis; age range: 17–64 years; participation rate NR	Anti-HCV: third-generation ELISA	Anti-HCV +/-	B-cell NHL, 6/78 HD, 1/49	[7.6 (0.90–64.6)] [2.0 (0.12–33.0)]		

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
de Sanjose <i>et al.</i> (2004) Spain, 1998-2002	529 newly diagnosed cases of lymphoid malignancy (290 men, 239 women), consecutive patients at 4 medical centres (1 in Barcelona, 2 in Tarragona, 1 in Madrid); mean age: 62 years; participation rate: 76%; 505 HIV-negative, non-transplant recipient cases included in analysis Histological types based on WHO classification: 467 cases with B-cell lymphoma – 80 DLBCL, 74 plasma cell myeloma, 114 CLL, 39 FL, 24 MZ, 25 splenic marginal zone, 21 lymphoplasmacytic, 5 low-grade NOS, 5 lymphoma NOS, 55 Hodgkin lymphoma, and 25 other B-cell 38 cases with T-cell lymphoma	600 hospitalized patients (311 men, 289 women), synchronically identified and matched to cases by age (± 5 years), sex, and study centre; participation rate: 92%; 599 HIV-negative, non-transplant recipient controls included in analysis	Anti-HCV: third-generation ELISA HCV RNA: second-generation Amplicor RT-PCR assay	Anti-HCV+ or HCV RNA+ / Anti-HCV- and HCV RNA-	All lymphoma, 30/475	1.6 (0.89–2.8)	Age, sex, and centre of diagnosis	[In meta-analysis by Dal Maso & Franceschi (2006)]
					B-cell lymphoma, 28/439	1.6 (0.89–2.8)		
					DLBCL, 6/74			
					CLL, 7/107			
					FL, 1/38	2.3 (0.87–6.0)		
					MZ, 2/22	1.5 (0.59–3.7)		
					HD, 3/52	0.87 (0.11–6.85)		
T-cell lymphoma, 2/36	3.1 (0.65–14.4)							
						1.9 (0.51–7.1)		
						1.5 (0.33–6.7)		
Sève <i>et al.</i> (2004) France, 1997–1998	212 incident cases of B-cell NHL (122 men, 190 women), HIV-negative patients in lymphoma database of Department of Haematology at Lyon-Sud Hospital; age range: 21–90 (median: 59.5) years; participation rate NR Histological types based on WHO classification: 5 lymphoplasmacytoid, 31 FL, 109 DLBCL, 21 mantle cell, 17 MALT, 16 MZ, 7 SLL, and 6 Burkitt	974 hospital-based controls (451 men and 523 women), HIV-negative patients in database of transfusion patients at same hospital during same time period as cases, patients transfused in haematology department and patients with lymphoma excluded; age range: 18–101 (median: 67) years; participation rate NR	Anti-HCV: second-generation ELISA, with confirmation by second-generation RIBA	Anti-HCV +/-	All B-cell NHL, 6/206 FL, 0/31 DLBCL, 2/107	1.3 (0.51–3.4) --- 1.4 (0.41–4.9)	Age and sex	[In meta-analysis by Dal Maso & Franceschi (2006)] MALT lymphoma: OR=9.9 (95% CI, 2.6–37.7)

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Talamini <i>et al.</i> (2004); dal Maso <i>et al.</i> (2004); Talamini <i>et al.</i> (2005) Italy, 1999–2002	225 cases of incident NHL (120 men, 105 women), patients between 18 and 84 years at 2 national cancer institutes and 3 hospitals in province of Pordenone and in Naples, all HIV-negative; median age: 59 years; participation rate: [97%] Histological type based on WHO classification: 78 cases with low-grade B-cell NHL – 18 SLL/CLL, 10 lymphoplasmacytic, 36 FL, 4 MZ, 10 MALT 129 cases with intermediate- and high-grade B-cell NHL – 2 mantle cell, 93 DLBCL, 19 DLBCL/ immunoblastic, and 10 Burkitt 16 cases with T-cell NHL and 7 with unknown NHL 62 incident cases of Hodgkin lymphoma (33 men, 29 women); median age: 30 years [dal Maso <i>et al.</i> (2004)]	504 hospital-based controls (341 men, 163 women), patients between 18 and 84 years admitted to same hospitals as cases, for acute conditions – exclusions: malignant diseases, conditions related to alcohol and tobacco consumption, hepatitis, chronic disease that might have changed lifestyle habits, and haematological, allergic, and autoimmune diseases; median age: 63 years; participation rate: [92%]	Anti-HCV: third-generation microparticle EIA, with confirmation by Inno-LIA HCV RNA: second-generation Amplicor RT-PCR assay, determined for anti-HCV-negative NHL cases to exclude false-negatives	Anti-HCV+ or HCV RNA+ / Anti-HCV– and HCV RNA–	All NHL, 44/181 Low-grade B-cell NHL, 16/62 FL, 0/36 Intermediate- and high-grade B-cell NHL, 24/100 DLBCL, 19/74 HD, 1/61	2.6 (1.6–4.3) 3.2 (1.6–6.3) --- 2.4 (1.3–4.3) [2.6 (1.45–4.7)] 0.9 (0.1–7.2)	Sex, age, centre, education, and place of birth Sex, age, centre, and education	[In meta-analysis by Dal Maso & Franceschi (2006)]

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Sonmez <i>et al.</i> (2007) Turkey, 2002–2005	109 patients with biopsy-confirmed lymphoma (45 men, 64 women): 71 with DLBCL and 38 with SLL, admitted to Black Sea Technical University Hospital; excluded if transfused or had major surgery, tooth extraction, or parenteral treatment in last 6 months; mean age: 58.1 (±16) years; participation rate NR; histological type based on WHO classification	551 hospital-based controls (228 men, 323 women), patients from same hospital as cases, selected from orthopaedics, general surgery, urology, ophthalmology, and otorhinolaryngology; mean age: 58.3 (±16) years	HCV: anti-HCV by third-generation ELISA, with confirmation by PCR assay for HCV RNA	HCV +/-	All lymphoma, 3/106 DLBCL, 2/69 SLL, 1/37	0.53 (0.13–1.9) [0.54 (0.13–2.3)] [0.50 (0.07–3.8)]	None	

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
Schöllkopf <i>et al</i> (2008) Denmark, Sweden, 1999–2002	3673 patients with newly diagnosed malignant lymphoma, enrolled in nationwide case-control study (Scandinavian Lymphoma Etiology study) of entire Danish and Swedish populations aged 18–74 years; required to speak Danish or Swedish and to have no history of organ transplantation, HIV infection, or prior haematopoietic malignancy; participation rate: 81% for NHL cases and 91% for Hodgkin lymphoma cases; 85% of participating cases provided blood sample; analysis included 2819 participants who donated blood and were of at least second-generation Danish/Swedish origin: 2353 cases with NHL (1423 men, 930 women; median age: 61 years) and 466 with Hodgkin lymphoma (252 men, 214 women; median age: 36 years) Histological type based on WHO classification: 2193 cases with B-cell NHL (596 DLBCL, 577 CLL, 454 FL, 123 mantle cell, 87 MZ, 94 lymphoplasmacytic) and 160 cases with T-cell NHL	3187 population controls, randomly sampled from entire Danish and Swedish populations using computerized population registries; frequency matched to cases within each country by sex and age (in 10-year intervals); required to speak Danish or Swedish and to have no history of organ transplantation, HIV infection, or prior haematopoietic malignancy; participation; 71%; 65% of participating controls provided blood sample; analysis included 1856 (1013 men, 843 women) participants who donated blood and were of at least second-generation Danish/Swedish origin	Anti-HCV: third-generation ELISA, with confirmation by third-generation RIBA	Anti-HCV +/-	All NHL, 20/2333	2.2 (0.9–5.3)	Age, sex, country of residence, and education level	
					B-cell NHL, 20/2173	2.4 (1.0–5.8)		
					DLBCL, 5/591			
					CLL, 6/571			
					FL, 4/450	2.4 (0.8–7.8)		
					MZ, 0/87			
T-cell NHL, 0/160	2.7 (0.9–8.4)							
HD, 0/466	2.7 (0.8–10.0)							

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
<i>Pooled Analyses</i>								
Nieters <i>et al.</i> (2006) EPILYMPH, Europe, 1998–2004	1807 HIV-negative cases of lymphoid malignancies (1011 men, 796 women), consecutively enrolled in multicentre case-control study, analysis restricted to cases in 5 countries (Germany, Italy, Spain, Ireland, and France) with available serum sample, cases excluded if organ-transplant recipient; [63%] ≥55 years old; participation rates: 82%-93% Histological type based on WHO classification: 1465 cases with B-cell lymphoma – 392 DLBCL, 210 FL, 342 CLL, 221 MM, 41 lymphoplasmacytoid 35 splenic MZ, 77 other MZ, 60 B-cell NOS 101 cases with T-cell lymphoma and 239 with Hodgkin lymphoma	1788 HIV-negative controls (957 men, 831 women), randomly drawn from population registries in Germany and Italy and from same hospitals as cases for remaining studies, in hospital-based studies controls excluded if main reason for hospitalization was cancer, organ transplantation, or systemic infection; frequency matched to cases by age (±5 years), sex, and study centre; [60%] ≥55 years old; participation rates: 44–66% for population controls and 60–96% for hospital controls	Anti-HCV: third generation ELISA HCV RNA: Amplicor RT-PCR assay	Anti-HCV+ or HCV RNA+ / Anti-HCV– and HCV RNA–	B-cell lymphoma, 48/1417 DLBCL, 18/374 FL, 2/208 CLL, 10/332 Splenic MZ, 1/34 Other MZ, 3/74 MM, 7/214 T-cell lymphoma, 2/99 HD, 3/236	1.5 (0.95–2.2) 2.2 (1.2–3.9) 0.50 (0.12–2.1) 1.2 (0.56–2.4) 0.83 (0.11–6.35) 1.8 (0.52–5.9) 1.4 (0.61–3.2) 0.88 (0.21–3.7) 0.97 (0.27–3.5)	Country, age, and sex	

Table 2.7. Case-control studies of HCV and lymphoid malignancies

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
de Sanjose <i>et al.</i> (2008) International Lymphoma Epidemiology Consortium, 1988–2004	4784 HIV-negative cases of NHL (2443 men, 2341 women), enrolled in 7 case-control studies involving 17 centres in USA, Canada, Australia, Italy, Spain, France, Germany, Ireland, and Czech Republic, cases excluded if organ-transplant recipient; 66% ≥55 years old; participation rates: 72–97% Histological type based on WHO classification: 40 Burkitt, 1494 DLBCL, 144 lymphoplasmacytoid, 383 MZ, 608 CLL/SLL, 244 other B-cell lymphoma, 206 other T-cell lymphoma, 248 NHL NOS, 1181 FL, 117 Mycosis fungoides/Sezary syndrome, 119 mantle cell	6269 HIV-negative controls (3333 men, 2936 women), from population-based sources for 11 centres and hospital-based for 6 centres, controls excluded if organ-transplant recipient; except in 1 study in Italy, frequency matched to cases by age, sex, and study site (1 study in USA also matched by race); 61% ≥55 years old; participation rates: 44–66% for population controls and 60–96% for hospital controls	Anti-HCV: third-generation ELISAs	Anti-HCV +/-	All NHL 172/4612	1.8 (1.4–2.25)	Age, sex, race, and study centre	Results from 5 studies already published: Engels <i>et al.</i> (2004), Morton <i>et al.</i> (2004), Nieters <i>et al.</i> (2006), Talamini <i>et al.</i> (2004), Vajdic <i>et al.</i> (2006)
					DLBCL, 76/1418	2.2 (1.7–3.0)		
					MZ, 17/366	2.5 (1.4–4.2)		
					CLL/S LL, 22/586	1.5 (0.92–2.4)		
					FL, 23/1158	1.0 (0.18–3.1)		
Other T-cell lymphoma, 6/200	1.4 (0.60–3.3)							