

Table 2.1. Cohort Studies of HCV and Hepatocellular Carcinoma

Reference, location, name of study	Cohort description	Detection method	No. of cases/deaths	Relative risk (95% CI)	Adjustment for potential confounders	Comments
<i>Americas</i> Guiltinan <i>et al.</i> (2008) USA	Retrospective cohort of 10259 anti-HCV-positive allogeneic blood donors (6627 men, 3632 women) and 10259 anti-HCV-negative donors (6627 men, 3632 women) matched to HCV+ donors on year of donation, sex, year of birth, and zip code; identified from 17 blood centres in southern USA between 1991 and 2002; excluded if lifetime history of drug use or clinical hepatitis, HIV-positive, or missing data on sex, year of birth, or zip code; 75% aged 30–49 years. 17 Liver cancer deaths through 2003 (average follow-up: 7.7 years), identified using the US National Death Index death certificate data with cause of death based on ICD-9 and -10 codes	Anti-HCV: repeatedly reactive to second-generation EIA, with confirmation by second-generation RIBA	Anti-HCV Neg 1 Pos 16	1.0 16.6 (2.2–125.5)	Matched on sex, age, and zip code (as proxy for race/ethnicity and socioeconomic status)	

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<i>Asia</i> Chang <i>et al.</i> (1994); Taiwan, China	9775 men (aged 30–85 years), participants in community-based cancer screening project in 6 townships, enrolled between 1984 and 1986 and followed to 1992 (years of follow-up: 0.5–6.0 years) 55 cases of primary liver cancer (ICD-9 code 155) identified through annual interviews and linkage with the national death certification system (ICD-9 code 155); 38 cases had available frozen serum sample; 4 controls per case matched on age (± 1 year), residence, and date of recruitment	Anti-HCV: duplicate testing with second-generation EIA; repeatedly reactive samples considered positive	Anti-HCV Neg 33 Pos 5	1.0 88.2 (5.2–1509)	Age, residence, date of recruitment, HBsAg, vegetable consumption, and chronic liver disease history	More than 95% of primary liver cancer deaths assumed to be HCC. The results from a shorter follow-up through March 1990 were published in Yu & Chen (1993).
Yuan <i>et al.</i> (1995) China, Shanghai Cohort Study	18244 men (aged 45–64 years) residing in 4 areas of Shanghai, enrolled between 1986 and 1989 and followed to 1993 76 incident cases of HCC identified through routine review of Shanghai Cancer Registry records and death certificates and annual recontact; 10 or 5 controls per case matched on age (± 1 year), time of sample collection (± 1 month), and neighbourhood of residence (n=409)	Anti-HCV: second-generation enzyme-linked immunosorbent assay (ELISA)	Anti-HCV Neg 75 Pos 1	1.0 5.0 (0.3–79.9)	Age, time of sample collection, and neighbourhood of residence	

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Boschi-Pinto <i>et al.</i> (2000) Japan, Miyazaki Cohort Study	965 residents of Village A in Miyazaki Prefecture (389 men, 576 women), enrolled in prospective, community-based cohort study of residents who attended government-sponsored health examinations offered annually to residents ≥ 40 years of age (56% ≥ 54 years old at baseline), followed from 1984 to 1994 with 96% follow-up rate; 222 anti-HCV-positives, 743 anti-HCV-negatives 8 deaths due to liver cancer, based on monitoring of mortality by local public health nurses	Anti-HCV: second-generation particle agglutination assay, with confirmation by second-generation RIBA	Anti-HCV Neg 2 Pos 6	1.0 8.2 (1.6–41.6)	Age, sex, smoking, drinking, and human T lymphotropic virus type I	Liver cancer deaths were not confirmed by medical records.

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Mori <i>et al.</i> (2000) Japan	3052 residents of Town K on Kyushu Island (974 men, 2078 women), enrolled in prospective, community-based cohort study of residents who attended government-sponsored mass screening programme for liver disease offered annually to residents ≥ 30 years of age (mean age at enrollment: 58.1 (± 13.5) years), followed from 1992 to 1997 (mean follow-up: 4.6 years) with 97% follow-up rate; most subjects examined annually at liver disease screenings using conventional liver function test, subjects with abnormal results advised to attend clinic or hospital; 380 with high titre anti-HCV, 275 with low titre anti-HCV, 2397 without anti-HCV 22 newly diagnosed cases of HCC (14 men, 8 women), based on review of subjects' medical charts or from linkage with Saga Prefectural Cancer Registry	Anti-HCV: second-generation passive haemagglutination assay	Anti-HCV Neg 3 Low titre+ 1 High titre+ 18	1.0 3.4 (0.35–33.5) 40.4 (11.7–139.2)	Age and sex	

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Sharp <i>et al.</i> (2003) Japan, Radiation Effects Research Foundation Life Span Study	7647 members of cohort of Japanese survivors of 1945 atomic bombings who were residents of Hiroshima or Nagasaki and still alive in 1950–1952, autopsied in 1954–1988 with archival tissue samples and clinical records 238 confirmed HCC cases (169 men, 69 women, aged 20–90 years at death), based on review of medical material; 894 controls who died of disease other than liver cancer, matched to potential cases on sex (633 men, 261 women), city of residence at time of bombings, radiation exposure, age at death, year of death; HCV status determined for 62.7 % (149) of cases and 61.7% of controls (552)	HCV RNA: reverse transcription-polymerase chain (RT-PCR) reaction of RNA extracted from liver tissue	HCV RNA Neg 82 Pos 67	1.0 5.9 (2.7–13.4)	Radiation exposure, year of death, age at death, city, sex, HBV infection, and cirrhosis	
Wang <i>et al.</i> (2003) Taiwan, China	11837 men (aged 30–64 years), participants in community-based cancer screening project in 7 townships in main Taiwan Island and Penghu Islets, enrolled between 1990 and 1992 and followed to 2000 (mean follow-up: 7.8 years); 549 anti-HCV-positives, 11288 anti-HCV-negatives 115 newly diagnosed cases of HCC identified between 1991 and 2000, through linkage to National Cancer Registry and National Death Certification System	Anti-HCV: second-generation EIA	Anti-HCV Neg 100 Pos 15	1.0 2.45 (1.4–4.2)	Age at recruitment, residence, and HBsAg	Two other studies from the same 7 townships were published elsewhere: Sun <i>et al.</i> (2003); Sun <i>et al.</i> (1996)

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<i>Australia</i> Amin <i>et al.</i> (2006) New South Wales	75834 HCV monoinfected (without HBV) persons notified to New South Wales Health Department's Notifiable Diseases Database between 1990 and 2002 (47903 men, 27931 women); median age at viral hepatitis notification: 34 years; 10% of cohort estimated to be co-infected with HIV Incident HCC cases (ICD-10 code C22.0) occurring in cohort through 2000 identified by linkage to New South Wales Cancer Registry; standardized incidence ratio obtained from expected number of cases calculated using age-, sex-, and calendar year-specific incidence rates derived from New South Wales population; cancers prior to, or within 1 year subsequent from notification excluded	HCV status: detection of anti-HCV or HCV RNA [assays used for testing NA]	<u>Obs:Exp</u> HCC 143:6.4	22.5 (19.1–26.5)	Age, sex, and calendar year	