

**Table 2.46. Case-control and cohort studies of Hepatocellular carcinoma – studies after year 2000**

| Reference, study location and period   | Organ site (ICD code)             | Characteristics of cases   | Characteristics of controls   | Exposure assessment                                    | Exposure categories  | Relative risk (95%CI)*   | Adjustment for potential confounders  | Comments  |
|--|-----------------------------------|--|---|--|--|--|---|---|
| Franceschi <i>et al</i> , (2006)<br>Northern Italy (Pordenone) and Naples, 1999–2002<br>Hospital-based | HCC, 78% histologically confirmed | All new cases admitted to selected hospitals (N=229, out of 261 eligible). | Patients admitted to same hospitals with acute conditions, excluding tobacco or alcohol-related diseases and hepatitis; frequency matched by area, calendar period, gender, and age to cases (N=431 out of 467 eligible subjects) | Face to face interview with standardized questionnaire | Never smoker<br>Former smoker<br>Current smoker<br><br><b>Intensity (Current smokers only)</b><br>Never smoker<br>1-14<br>≥15<br>p for trend         | 1.0<br>0.82 (0.45–1.50)<br>1.14 (0.61–2.15)<br><br>1.0<br>1.15 (0.55–2.42)<br>1.13 (0.52–2.45)<br>0.87 | Age, gender, center, education  | Interaction with HBsAg <sup>+</sup> and/or anti-HCV <sup>+</sup> :<br>OR for never/former smokers 23.4 (13.5-40.6 and for current smokers 44.3 (19.7-99.3). OR for current smokers versus never/former smokers for in those HBsAg- and/or anti-HCV-1.02 (0.53-1.97)   |
| Hassan <i>et al</i> , (2008)<br>MD Anderson Cancer Centre, Houston USA, 2000–2006<br>Hospital-based    | HCC histologically confirmed      | All new case admitted to MD Anderson (N=319, out of 390 eligible subjects) | Healthy nonblood relatives of the cases, excluding liver, GI, lung or UADT cancers (N=1061, 82% of eligible subjects). No matching.   | Face to face interview with standardized questionnaire | <b>Intensity (cigs/days)</b><br><b>Men</b><br>Never smoker<br>≤20<br>20+<br>p for trend<br><b>Women</b><br>Never smoker<br>≤20<br>20+<br>p for trend | 1.0<br>1.9 (1.2–3.3)<br>1.7 (1.0–3.2)<br>-<br><br>1.0<br>1.0 (0.5–1.9)<br>0.8 (0.2–3.1)<br>-           | Age, ethnicity, marital status, residence, HCV, HBV, diabetes, alcohol consumption, family history of cancer, education | Potential residual confounding (all covariates have a statistically significant association with case-control status<br><br>The effect of quitting smoking in men is not credible<br><br>The effect of HCV infection was enhanced in men by smoking. OR HCV+ smoking – 28.9 (7.3-114.2) versus HCV+ smoking + 136.3 (43.2-429.6) while smoking did not effect of HBV infection. |

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|---|------------------------------|---|--|--|---|---|---|--|
| Hassan <i>et al.</i> , (2008) (Contd)   | HCC histologically confirmed | All new case admitted to MD Anderson (N=319, out of 390 eligible subjects)  | Healthy non-blood relatives of the cases, excluding liver, GI, lung or UADT cancers (N=1061, 82% of eligible subjects). No matching. | Face to face interview with standardized questionnaire                       | <b>Duration (years)</b><br><i>Men</i><br>Never smokers<br>≤20<br>>20<br>p for trend<br><i>Women</i><br>Never smokers<br>≤20<br>>20<br>p for trend<br><br><b>Years since cessation</b><br><i>Men</i><br>≤10<br>>10<br><i>Women</i><br>≤10<br>>10<br>(never smokers ref category) | 1.0<br>1.6 (0.9–2.9)<br>2.1 (1.2–3.6)<br>-<br><br>1.0<br>0.4 (0.2–1.2)<br>1.5 (0.7–2.9)<br><br>2.4 (1.2–4.9)<br>1.7 (0.9–2.8)<br>1.1 (0.4–2.9)<br>0.8 (0.4–1.8) | Age, ethnicity, marital status, residence, HCV, HBV, diabetes, alcohol consumption, family history of cancer, education | Potential residual confounding (all covariates have a statistically significant association with case-control status)<br><br>The effect of quitting smoking in men is not credible<br><br>The effect of HCV infection was enhanced in men by smoking. OR HCV+ smoking – 28.9(7.3-114.2) versus HCV+ smoking + 136.3(43.2-429.6) while smoking did not effect of HBV infection. |
| Ohishi <i>et al.</i> , (2008)<br><br>Hiroshima and Nagasaki cohort (nested case-control), Japan<br>Population-based | HCC                          | Cohort established in 1958, 20000 atomic bomb survivors plus persons not present in the cities at time of bombing. Incident HCC cases identified through Cancer Registry (N=359, 224 with serum samples)<br>Controls randomly selected among those matching the cases for age, gender, city, time and method of serum storage (N=644).<br>Counter matching on radiation exposure. |  | Self-administered standardized questionnaire (administered in 1965 and 1978) | Never smoker<br>Former smoker<br>Current smoker   | 1.0<br>1.12 (0.25–5.07)<br>2.03 (0.82–4.98))  | Age, gender, city, time and method of serum storage. Counter matching on radiation exposure                             |  |