Published in final edited form as:

J Hepatol. 2016 February ; 64(2): 517–518. doi:10.1016/j.jhep.2015.10.028.

Response to comment on "Increased incidence of cancer and cancer-related mortality among persons with chronic hepatitis C infection, 2006–2010"

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Keywords

HCV; hepatitis C virus; cancer; incidence; mortality; CHeCS

We thank Dr. Shiels and co-authors for reading and commenting on our study.1,2

To summarize, we compared the age-adjusted incidence and mortality of 12,126 persons with chronic hepatitis C virus (HCV) infection in the Chronic Hepatitis Cohort Study (CHeCS) to Surveillance, Epidemiology and End Results Program (SEER) cancer registry data and to death certificate information from the Multiple Causes of Death (MCOD) database. We found that the incidence and mortality of many non-liver cancers were significantly higher in persons with HCV infection than in the comparison groups who approximate the US population.

We also found that the mean age of cancer diagnosis and cancer-related death was younger for persons with HCV infection in the CHeCS. These latter analyses were not age-adjusted and the subject of the comments of Shiels et al. With regard to the younger age at cancer diagnosis among HCV-infected CHeCS patients, our Methods indicate we used the SEER13 database with exclusion of one of the 13 registries, the Alaska Natives registry. We did this to create a better comparison group for CHeCS: this "SEER12" more closely approximates the population of the other 49 states. In contrast, Shiels et al. compared our underlying population to SEER13. When we attempted to reproduce their analyses, but by comparing age of cancer diagnosis in CHeCS to SEER12, we found that the software developed to analyze data from SEER, called 'SEER*STAT,' (Surveillance Research Program, National Cancer Institute SEER*Stat software (seer.cancer.gov/seerstat) version 8.2.1) appears to lack the required functionality.

Specifically, age data can only be extracted from SEER13. There is no function to exclude a SEER registry (i.e. Alaska Natives) and then pull age data. We think this may be why Shiels et al. came to a different conclusion.

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Conflict of interests: None.

Shiels et al. indicated a particular concern with the ≥64 year age group, the age group with the highest cancer incidence, and noted a smaller proportion of persons aged ≥64 in CHeCS (10%) versus SEER13 (19%). Using U.S. Census data corresponding to each SEER12 registry (i.e., SEER 13 excluding Alaska Natives) and for the US overall, by age group, we found the percentage of persons 64 years or older for SEER was 11.8% and for the entire U.S. population was 14.6%. We think that given the large numbers of patients involved, these close percentages may represent a statistically significant difference between CHeCS and either SEER or the US population.

In considering the younger age of death among HCV-infected CHeCS cancer patients, it is helpful to remember that CHeCS patients have full ascertainment of their HCV infection, and analyses data from CHeCS and the MCOD show they die at a younger age compared with decedents without HCV infection.3,4 MCOD data –i.e., death certificates–only record 19% of patients who actually have HCV infection at the time of death.3 In sum, HCV-infected patients who develop cancer may indeed die at a younger age because of the contribution of both HCV infection and cancer to their morbidity and mortality.

As a practical matter, we think that cancer screening-related guidelines should be based on all available data including ours. Given our age-adjusted findings of increased cancer-related incidence and mortality among persons with chronic HCV infection, we think that both general clinicians and specialists should be aware of these elevated risks and take preventive action, such as facilitating tobacco and alcohol cessation and curing HCV with recommended antiviral therapy.

Sincerely yours,

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Abbreviations

HCV	hepatitis C virus
CHeCS	Chronic Hepatitis Cohort Study (CHeCS)
SEER	Surveillance, Epidemiology and End Results Program
MCOD	Multiple Causes of Death (registry of death certificates)
SEER13	thirteen SEER cancer registries including: Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah, Los Angeles and San Jose-Monterey, Rural Georgia and the Alaska Native Tumor Registry
SEER12	all registries in SEER13, excluding the Alaska Native Tumor Registry

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