

Eradication of chronic hepatitis C virus (HCV) infection and the development of hepatocellular carcinoma (HCC): a meta-analysis of observational studies

Rebecca L. Morgan, MPH¹; Brittney Baack, MPH²; Bryce D. Smith, PhD¹; Anthony Yartel, MPH³; Marc Pitasi, BS⁴; Yngve Falck-Ytter, MD⁵

¹Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, Georgia; ²Oak Ridge Institutes for Science and Education, Oak Ridge, Tennessee; ³Centers for Disease Control and Prevention Foundation, Atlanta, Georgia; ⁴Rollins School of Public Health, Emory University, Atlanta, Georgia; ⁵Case Western Reserve University, Case and VA Medical Center, Cleveland, Ohio

BACKGROUND

Rationale

- HCV is a leading cause of HCC, which occurs in approximately 15,000 persons annually in the United States.¹
- Antiviral therapy for HCV can result in eradication of the virus (i.e., absence of detectable HCV RNA) after treatment, known as sustained virologic response (SVR).²
- Persons who achieve an SVR have a lower risk of developing HCC and liver-related mortality.³
- Recent advances in HCV antiviral treatments, including the FDA approval of telaprevir and boceprevir, are making the achievement of SVR possible for the majority of patients undergoing therapy.⁴

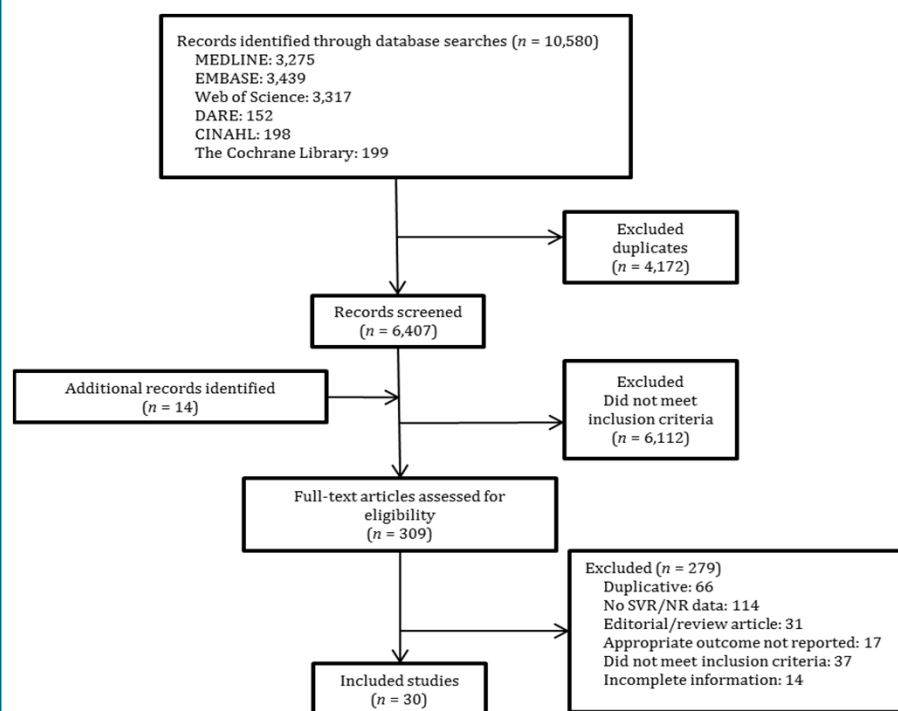
Purpose

- To determine the association between achievement of SVR and the development of HCC among HCV-infected persons.

METHODS

- A systematic review and meta-analysis, conducted using MEDLINE, EMBASE, CINAHL, the Cochrane Library, Sociological Abstracts, and DARE, examined the development of HCC among HCV-infected persons at all stages of fibrosis or with advanced liver disease (Metavir F3-F4 or Ishak 4-6) achieving SVR or not responding to treatment.
- English-language, observational studies targeting an adult population and with an average follow-up of at least two years were included.
- Two independent investigators reviewed and abstracted full articles.
- The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework was used to determine overall study quality.
- Pooled estimates (hazard ratios and incidence rates) were obtained through random-effects meta-analysis using the inverse-variance method.

Study Flow Chart

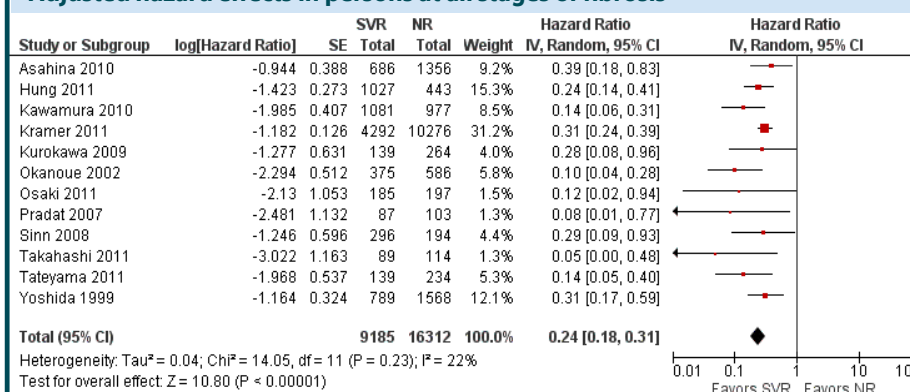


RESULTS

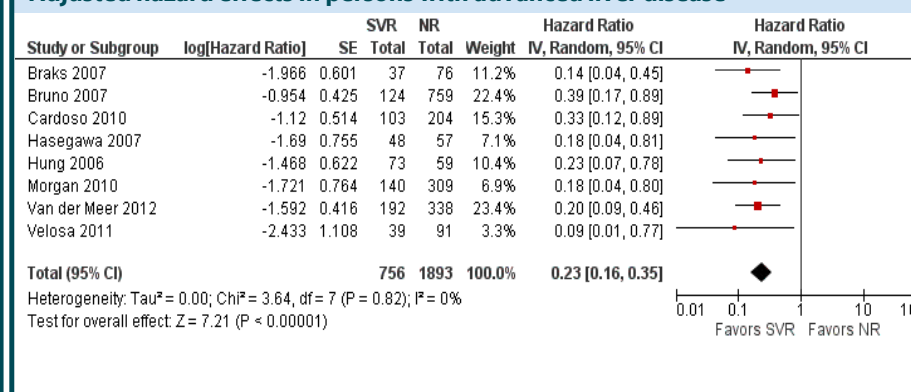
- Thirty observational studies met inclusion criteria, 18 of which provided adjusted effect estimates were used to calculate the pooled relative risk.
- Among HCV-infected persons with advanced liver disease, achievement of SVR significantly reduces the risk of HCC development by approximately 77% (HR=0.23 [95% CI, 0.16 to 0.35]; moderate quality evidence). Similarly, the relative risk reduction among HCV-infected persons at any stage of disease progression was estimated at 76% (HR=0.24 [95% CI, 0.18 to 0.31]; moderate quality evidence).

- Pooled annual incidence of HCC development among persons with advanced liver disease not responding to treatment was 3.3% (95% CI, 2.6% to 4.2%). By comparison, HCC developed at rate of 1.0% (95% CI, 0.7-1.5%) annually among persons with advanced fibrosis who achieved SVR.
- Judgments on study risk of bias were determined to not reduce confidence in the estimate of effect. The final quality of evidence was upgraded to Moderate based on reported large relative effect.

Adjusted hazard effects in persons at all stages of fibrosis



Adjusted hazard effects in persons with advanced liver disease



GRADE Evidence Profile	Outcome	Quality Assessment		Summary of Findings				
		Participants (Studies), n	Overall Quality of Evidence	Study Event Rates, n/N (%)		Relative Effect	Anticipated Absolute Effects	
				Failed or No Treatment	Viral Eradication		Risk with Failed or No Treatment	Absolute Effect with Viral Eradication (95% CI)
	HCC among Persons at all Fibrosis Stages	25,906 (12)	Moderate	990/16,312 (6.1)	145/9,185 (1.6)	Adjusted HR: 0.24 (0.18-0.31)	All Stages of Fibrosis, per year 17 HCC per 1000 (from 12 fewer to 15 fewer)	
	3.0-8.2 years follow-up						Advanced Liver Disease, per year 33 HCC per 1000 (from 18 fewer to 26 fewer)	

LIMITATIONS

- Excluded reports not written in English.
- Most studies were retrospective in nature; some publication bias possible.

CONCLUSIONS

- Achievement of SVR among persons infected with HCV at any fibrosis stage is associated with a significant relative risk reduction of developing HCC.
- Early treatment for HCV is essential in preventing the development of HCC.
- With the availability of newer and more effective therapies, SVR rates can be increased and HCC incidence rates can be reduced in the population of HCV-infected persons.

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For more information: **Rebecca L. Morgan**
 rmorgan2@cdc.gov
 +1(404) 639-6108

