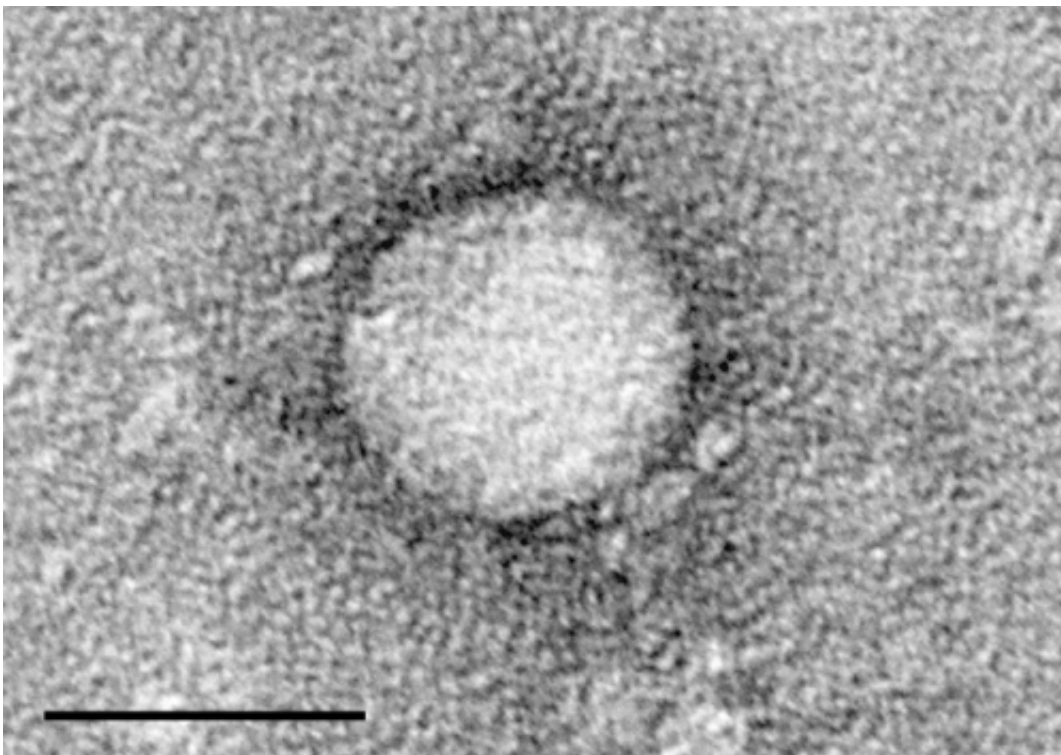


Direct-acting antivirals reduce risk of premature mortality and liver cancer for people with chronic hepatitis C

February 12 2019



Electron micrographs of hepatitis C virus purified from cell culture. Scale bar is 50 nanometers. Credit: Center for the Study of Hepatitis C, The Rockefeller University.

The first prospective, longitudinal study investigating treatment of chronic hepatitis C with direct-acting antivirals finds that the treatment

is associated with reduced risk of mortality and liver cancer, according to a study published in *The Lancet*. The research is the first to demonstrate the clinical effectiveness of direct-acting antivirals on the disease and suggests that they should be considered for all patients with chronic hepatitis C infection.

For ethical reasons a trial with a control arm is not possible and researchers approached this by setting up an observational study of around 10,000 patients. At follow up, about three-quarters had been treated with direct-action antivirals and a quarter were untreated. The incidence of death and hepatocellular carcinoma—the most common form of [liver cancer](#)—were significantly decreased in patients who were treated. Their risk of decompensated cirrhosis was not reduced by the [treatment](#).

Around the world, an estimated 71 million people are chronically infected with the hepatitis C virus (HCV). The infection causes complications such as cirrhosis, [liver disease](#), hepatocellular carcinoma, and many people die as a result. Over the last 15 years, these complications have tripled and models predict they will peak between 2030 and 2035. The World Health Organization (WHO) has set targets for the elimination of hepatitis C, and a reduction of related complications. Recently, a modelling study published in *The Lancet* found that major progress towards these targets by 2030 is possible, but will require vast improvements in screening, prevention, and treatment.

Previous work has shown there is a reduction of risk for complications and mortality in patients who are treated with interferon or direct-acting antivirals, but few studies have compared treated and untreated patients. The aim of direct-acting [antiviral drugs](#) is to achieve a sustained virological response, meaning that the virus is undetectable in the blood of the patients. A [recent Cochrane Review found](#) no evidence for or against the treatment having a long-term effect on death and disease, so

this large study is timely, and may help doctors and patients with treatment plans.

In this study, 10,166 patients were recruited from 32 centres in France. At a median of 33 months, 9,895 patients had available follow up information and were included in the analysis, with 7,344 treated with direct-acting antivirals and 2,551 untreated. During follow-up, 218 patients died (129 treated, 89 untreated), 258 reported hepatocellular carcinoma (187 treated, 71 untreated), and 106 had decompensated cirrhosis (74 treated, 32 untreated).

Overall, the study finds that direct-acting antiviral treatment is associated with reduced risk for global mortality and hepatocellular cancer, but not decompensation of cirrhosis. The researchers initially found an increase in risk associated with treatment with direct-acting antiviral treatment, but once they had adjusted for variables such as age, sex, body-mass index, severity of liver disease, geographical origin, infection route and other factors, they found a reduced risk.

Patients who were treated were 52% less likely to die prematurely than people who were not treated (the estimated adjusted risk of death at one year in untreated patients in the cohort is 84 deaths per 10,000 patients, and in those who were treated was 40 per 10,000), and 33% less likely to present with hepatocellular carcinoma (the estimated adjusted risk of developing [hepatocellular carcinoma](#) within a year in untreated patients in the cohort was 129 cases per 10,000 patients, and 86 per 10,000 in people who were treated).

In a subgroup of 3,045 patients with cirrhosis at baseline, the same association was found for mortality and hepatocellular cancer, provided the patients achieved an undetectable level of HCV in their blood. The researchers believe this is because the treatment induces a sustained virological response, allowing the liver to regenerate which decreases

risk.

Professor Fabrice Carrat of the Sorbonne Université, France, said: "Taking a large cohort like this provides the opportunity to evaluate the effect of direct-acting antiviral therapy on the long-term outcomes of patients with hepatitis C. We saw a reduction of risk for complications related to the disease, and to mortality, and believe this treatment should be considered for all patients with chronic hepatitis C infection."

In the study, only a few patients underwent liver biopsy to confirm cirrhosis, with platelet levels or prothrombin time—a blood test—used to classify whether a patient had cirrhosis or not. A validation study using other non-invasive markers of fibrosis suggested that their methods correctly classified cirrhosis in the patients.

Patients who received more than one course of direct-acting antivirals were considered to have had continuous exposure, even where there may have been a lag time or if the first course may not have been associated with sustained virological response. This should have underestimated the response to the drugs rather than overestimated them so does not affect the result.

The study excluded patients with a history of decompensated cirrhosis and liver transplantation and these are the patients who would be at highest risk for complications. The potential benefits of treatment in this group could be underestimated because of their exclusion, as trial data shows improvements in liver function in patients with decompensated [cirrhosis](#) who achieved a sustained virological response.

Writing in a linked Comment, Dr. Raymond T Chung, Director of the Liver Center at Massachusetts General Hospital, USA, says: "The study by Carrat and colleagues offers substantive evidence that cure of HCV delivered by all-oral direct-acting antiviral regimens is associated with

clinical benefits. These findings firmly counter those of a Cochrane review of direct-acting antiviral treatment trials that could neither confirm nor reject if direct-acting antivirals had an effect on long-term HCV-related morbidity and mortality. They also provide the best evidence to date to support guidance documents that recommend direct-acting antiviral treatment for all [patients](#) with chronic HCV infection. Finally, they provide credence to the achievability of the goals set out by WHO, not only to eliminate HCV but also to substantially reduce its complications."

More information: Fabrice Carrat et al, Clinical outcomes in patients with chronic hepatitis C after direct-acting antiviral treatment: a prospective cohort study, *The Lancet* (2019). [DOI: 10.1016/S0140-6736\(18\)32111-1](#)

Provided by Lancet

Citation: Direct-acting antivirals reduce risk of premature mortality and liver cancer for people with chronic hepatitis C (2019, February 12) retrieved 24 April 2024 from <https://medicalxpress.com/news/2019-02-direct-acting-antivirals-premature-mortality-liver.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--