How to approach the expected wave of “cured” chronic Hepatitis C applicants

The substantial net benefit of combining improved antiviral treatment and surveillance measures, including non-invasive testing such as Fibroscan and FibroSure/FibroTest, is creating a changed focus for underwriting Hepatitis C.

An overview of Hepatitis C
The pathophysiology of Hepatitis C is met by a full cascade of liver inflammation and fibrosis. If the virus is not eliminated, the inevitable consequences include progressive fibrosis with its risk for development invariably towards stage 4 cirrhosis with fulminant liver failure and decompensation (esophageal varices, ascites, spontaneous bacterial peritonitis and hepatic encephalopathy), and hepatocellular carcinoma (HCC). The possibility of treatment with a resultant cure was unlikely. Traditionally, the underwriting process has reflected and incorporated these well-known consequences. Individuals with proven higher stages of fibrosis were typically provided substandard offers or declined coverage.

Detecting Hepatitis C in an application
Insurers rely on traditional requirements, such as paramedical laboratory tests, to detect Hepatitis C. Underwriters look for abnormal liver function tests (LFTs) and serology which includes anti-Hepatitis C antibody and HCV RNA. The presence of reactive antibodies for Hepatitis C (anti-HCV antibody) merely confirms exposure to virus, however, it does not in and of itself confirm chronic active Hepatitis C. To confirm whether the virus cleared spontaneously by one’s own immune system or continues to persist would require testing for the presence of the antigen (HCV RNA).

At least half adults exposed to the Hepatitis C virus will not spontaneously clear the virus. At best, spontaneous viral clearance is estimated to be 14–50% with most recent studies reporting 46%. Thus, more than half of those exposed will develop chronic active disease. Currently, there is no vaccine to prevent Hepatitis C, as there is for Hepatitis B.

Underwriting Hepatitis C
Historically, insurers have proved cautious when underwriting Hepatitis C given its known progressive consequences. Underwriters usually approach these cases cautiously – including assessments of current liver function tests (LFTs), liver ultrasounds to rule out the possibility of liver tumors and Alpha-Fetoprotein (AFP) levels to reduce the probability of an occult hepatocellular carcinoma (HCC). To do this, they rely on liver biopsy reports which indicate an individual’s stage of fibrosis. Higher stages correlate with more severe fibrosis, with stage 4 indicating cirrhosis. Higher stages also correlate with increased risks of HCC –

Despite the increase in cases, Hepatitis C is essentially being cured and liver fibrosis reversing – an outcome unfathomable just a few years ago.

Key Facts
177 m Global prevalence of Hepatitis C exposure
55% of those infected develop chronic active Hepatitis C
99% of individuals treated with the novel Direct Acting Antiviral drugs can expect SVR (sustained virologic response) and might be deemed cured from an underwriting perspective
making underwriting severe cases even more challenging. Any lack of information in the records, often prompts the actions of postponement or decline. And if liver ultrasounds and AFP are favorable, ratings would be based upon age (to correlate with duration and likelihood of progressive fibrosis) and current LFTs, resulting in a substandard rating at best.

Applicants treated with antivirals undergo similar evaluations by underwriters. Unfortunately, medical studies show that antiviral treatments did not result in sustained virologic responses (SVR). SVR is defined as undetectable RNA level 12 weeks following completion of treatment. A study found that SVR with peginterferon and ribavirin was attainable in approximately one-third of patients. Those who failed to achieve SVR had a higher risk of developing liver related complications (HR 4.73) and liver related death (HR 3.71) within 3.5 years. Liver transplantation has been deemed the inevitable management for those that progress to cirrhosis. Consequentially, applicants with Hepatitis C and failed treatment have proved to be a challenging risk for insurers to cover.

Introduction of non-invasive diagnostic tests
Liver biopsy has been the gold standard for diagnosing and determining the progression of liver fibrosis since the 1920s. However, it was never without significant complications. It is expensive and requires a short stay in hospital due to associated pain, bleeding and pneumothorax risk. The results are based on an extremely small piece of liver, leading to significant variability in interpretations by different pathologists. For some community pathologists, this resulted in up to 25% of liver biopsies over staged and 73% understaged.

The ability to determine the presence and extent of fibrosis, by means other than liver biopsy, has been broadened by non-invasive tests.

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Methodology</th>
<th>Benefits</th>
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<tr>
<td>Fibroscan</td>
<td>Ultrasound-based technique</td>
<td>Non-invasive, provides accurate fibrosis stage for known etiology of liver disease, provides degree of steatosis</td>
<td>Cannot diagnose etiology of liver disease</td>
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<td></td>
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<td>Cut offs differ for various etiologies of liver disease</td>
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<tr>
<td>FibroTest/FibroSure</td>
<td>Blood test using 6 analytes</td>
<td>Non-invasive, provides accurate fibrosis stage no matter the etiology of liver disease</td>
<td>Cannot diagnose etiology of liver disease</td>
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<tr>
<td>Liver Biopsy</td>
<td>Tissue extraction</td>
<td>Can provide diagnosis for liver disease</td>
<td>Understages degree of fibrosis</td>
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<td></td>
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<td></td>
<td>Complications due to invasive procedure</td>
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Fibroscan, FibroTest and FibroSure have enabled the industry to not only underwrite Hepatitis C, but to do so with improved risk stratification.

Medical advances mean better outcomes
Diagnostic tests are just one piece of the puzzle. Medical therapy plays a massive role – if not the most critical role – in driving Hepatitis C outcomes. For instance, direct acting antivirals have completely replaced those antiquated drugs with proven SVRs of 99%. The treatments are safe, well tolerated, require usually only 1 pill a day to be taken for 12–24 weeks depending on genotype. There may be some more resistant genotypes that do require additional medications. However, they too reach SVRs close to 100%.

As a result, we can now assume that an individual treated with one of the direct acting antivirals (DAAs) is cured of Hepatitis C. And not only cured but proven to have regression in their pre-treatment liver fibrosis staging. Importantly, recent medical evidence shows this phenomenon holds true not just for mild cases, but for patients with advanced fibrosis and even cirrhosis. Further, there is evidence to suggest this regression can begin as early as 2 weeks into treatment.

Underwriting Impact – How might our decisions change?
Until recently, an individual with Hepatitis C, untreated and at stage 3 fibrosis would be a decline for most underwriting manuals in the market. Today, that same individual who receives treatments and reaches SVR with DAAs can expect to see regression of their fibrosis as their liver begins to regenerate.

By using non-invasive testing, we can determine current liver fibrosis staging accurately and follow that regression on an individual basis. This enables us to provide better rates for those with minimal to no fibrosis status. Applicants who previously received substandard offers or declines can now be reconsidered and possibly receive standard ratings. As the price of treatment continues to drop and becomes more accessible, we can expect more cures of Hepatitis C applicants with reason to reconsider an improved rating. This, alongside changes in screening practices, is creating new opportunities for applicants and insurers alike. Life Guide will reflect advancements in non-invasive testing as part of our August 2020 release.
Resources


2. https://jamanetwork.com/journals/jama/fullarticle/2762186


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