My first article for the HCV Advocate appeared 20 years ago. Hepatitis C virus infection (HCV) wasn’t curable yet. HCV is now easily curable and one would think the problem is solved, but it isn’t. Numerous obstacles stand in the way of eliminating this disease. A large percentage of the population is still undiagnosed because of inadequate HCV screening. Access to health care is uneven, particularly for those who need it the most.

Never would I have imagined that one of the obstacles to care would come from a vocal few in the HCV community. They believe that the cure for HCV is dangerous, even deadly. This small faction is certain in their beliefs and vocal in their opinions. I believe their intentions are good in that they don’t want others to be harmed by HCV treatment.

Do they have a case? Rather than dismiss their concerns, I went on a fact-finding mission. Could HCV medications be riskier than reported and advertised?
I began by reviewing the data. Most of the research shows that HCV treatment using direct-acting antivirals (DAAs) are: 1) safe, and 2) improve quality and quantity of life. However, what if you don’t trust the Food and Drug Administration (FDA), pharmaceutical companies, or the mainstream medical establishment? What if you or someone you know became sick or died during or after using HCV DAAs? What if your experience doesn’t match what you are being told?

This is the crux of the problem. Experience can look like fact. If a loved one got liver cancer and died a year after finishing HCV treatment, it’s natural to wonder if treatment caused this.

Recent Data
As I mentioned, the data support the safety and benefits of HCV treatment. In one large study, there was a 71 percent drop in risk of hepatocellular carcinoma (liver cancer or HCC) after a successful treatment outcome (sustained virologic response or SVR). Many other studies had similar outcomes. For brevity’s sake, I’ll just mention a recent one.

In a recent paper by Lisa Backus and colleagues, data were collected from 103,346 HCV patients with genotypes 1, 2 and 3. Those with cirrhosis, liver cancer, HIV or history of liver transplantation were excluded. The data were from the Department of Veterans Affairs, collected 2013-2017. Of the 40,664 patients treated with interferon-free DAA regimens, 39,374 (96.8%) had SVRs. There were 62,682 untreated patients.

Findings: First, the mortality rate for patients who did not have an SVR was more than two and a half times that of patients who did. Second, the mortality rate for untreated patients was nearly three and a half times that of SVR patients. (Direct-Acting Antiviral Sustained Virologic Response: Impact on Mortality in Patients without Advanced Liver Disease; accepted January 29, 2018 Hepatology)

Suppose though that you already have cirrhosis. This is where the benefits of HCV treatment begin to narrow. Most studies show that cirrhotic patients who have an SVR have a reduced incidence of HCC. What we do know is:

• Advanced liver disease is the biggest risk for HCC development.
• HCC risk decreases if you have an SVR even if you have cirrhosis.
• This risk exists whether you were treated with peginterferon, DAAs, or not at all.
• HCC risk increases with age and levels of a liver cancer marker, alpha-fetoprotein (AFP).

It’s important to note that liver cancer deaths have nearly doubled since the 1990’s. HCV isn’t the only factor for this rise in HCC. Hepatitis B, fatty liver, obesity, inactivity, alcohol and other lifestyle factors contribute to cancer risk.
What If You Don’t Trust the Data?

I examined global data. Information from regulatory agencies outside of the U.S. looks similar to the FDA’s info. However, if you don’t trust regulatory agencies, there is a source that is above reproach. Meet James Freeman, MD, the Australian physician who defied authority by prescribing generic hepatitis C medicines to patients who could not otherwise get treatment. With over 3000 patients and no links to big pharma or government regulatory agencies, I asked Freeman if he had concerns about the safety of DAAs.

Freeman responded, “To me, the remarkable thing about these medications is actually how safe they are, not how dangerous they are.” He acknowledges that there have been both significant side effects and deaths but the rates are very low. Freeman points out that initially, the United States rationed treatment. This means that the sickest patients were the first to be treated; older patients who were already at risk for serious complications and death. In fact, they did better than one might expect.

Freeman does caution that no drug is 100 percent safe. However, DAAs are safer than hepatitis C infection. “Hepatitis C is a very unpleasant disease that amputates 10 years of life from the average patient. Most of that death rate is not liver failure or HCC; it’s cardiovascular, diabetes, lymphoma, and renal cell carcinoma, and more, all of which occur at higher rates in hep C patients.”

Freeman stated emphatically that if he had concerns about the safety of hepatitis C medicines, he would sound the alarm.

So Why Do Some Patients Think That DAAs are Dangerous?
The answer to this is complicated. Here are a few explanations:

Most of us aren’t skilled at understanding data. Some of the most vocal opponents who question the safety of DAAs have pointed to information they obtained from the FDA Adverse Event Reporting System (FAERS). If you don’t know how to interpret that information, it can be overwhelming. There are tens of thousands of adverse events. Honestly, it looks like DAAs are dangerous. However, they aren’t.

Dr. Freeman helped me out on this one by organizing the data so I could see it more clearly. Looking at

“To me, the remarkable thing about these medications is actually how safe they are, not how dangerous they are.”

— James Freeman, MD

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reports collected from 2014 to 2017, there were 782 deaths (with an estimate of a million people treated). This sounds huge, but given the seriousness of the patients’ medical conditions, you’d expect it to be ten times that. In other words, 782 deaths sounds horrible (and is, especially if you know are among the counted), but the fact that the number is so low affirms the safety of DAAs.

Note: The FAERS reports are raw, and without supporting information, some of the reports are useless or misleading. For instance, hepatitis C was reported as a side effect of DAAs. Clearly, the reporter made a mistake.

Our brains are wired to connect dots, even when they shouldn’t be connected. A friend with cancer told me that there is a lot of cancer in our county. She wondered if this was due to a factor unique to our community. In fact, the cancer rate where I live is no different from anywhere else. A more likely explanation is that because my friend talks openly about her cancer, others talk to her about their cancer. She sees cancer all around her.

So, if you post to Facebook that your loved one died from liver cancer after having undergone HCV treatment, you may be hearing from people with similar experiences. You may draw false conclusions about this.

Here is another way that hepatitis C treatment may be incorrectly implicated: adverse events that happen long after the medicines have been eliminated from the body are not a reason for a recent symptom. Also, if more than one person experiences the same adverse event, we may draw false conclusions. This is why science designs studies to minimize bias. Our experiences are subjective, and not useful indicators of truth.

We latch on to studies that support our claims. Initially, a couple of studies reported an increase of HCC following DAA treatment. These studies were small and had flaws. Larger studies show us otherwise. However, if you feel strongly in your belief, it can be hard to let go of research that supports your claim. We see what we want to see.

We care about each other. It’s painful when loved ones are hurt or die. We want to know why; we may blame others for these injuries. We feel helpless and want to protect others from suffering the same misery. We turn to social media, warning others about the dangers of DAAs. There we get affirmation for our beliefs because we meet people who had similar experiences. This affirmation feels like proof, but it isn’t. That’s because…
We confuse experience with evidence. Personal experience creates our beliefs. If we are convinced that DAAs caused a medication side effect or cancer, there is little reason to believe otherwise. We think we have evidence, when in fact we have anecdotes. Anaïs Nin summed it up when she wrote, “We don’t see things as they are; we see things as we are.”

The Danger
People may be frightened away from hepatitis C treatment if they think it is dangerous. However, untreated hepatitis C increases the risk for heart disease, stroke, liver and kidney cancer, lymphoma, Parkinson’s, and diabetes. False allegations about DAAs could lead to huge consequences.

This has already happened. People died because they didn’t want to undergo interferon-based hepatitis C treatment. I understand that choice, knowing how difficult interferon-base treatment was. However, we are in a new era. DAAs are effective, with minimal side effects. The benefits far exceed the risks.

What We Can Do
I am guessing that this article won’t change any minds. I have been publicly attacked for my views and will likely incur a few more barbs. Advocates I hold in high regard have also been targeted. We are accused of being in “pharma’s pocket.” This is particularly amusing since anyone who knows me knows that I am a thorn in the side of pharma.

However, there are ways we can act. I think the lesson here is that we aren’t educating people sufficiently. Health care providers and advocates need to increase awareness about the risks associated with advanced liver disease. We need to spread the following:

“Get treated for hepatitis C, and the earlier the better. However, if you have or nearly have cirrhosis, you are still at risk for liver cancer, even if your hep C is cured. DAAs may help but are not a guarantee against HCC. Liver cancer kills quickly. If you already have cirrhosis, be sure you are being followed by a specialist. Get the prescribed diagnostic tests, go to your appointments faithfully, and do everything you can to live a healthy lifestyle. If you don’t have cirrhosis but your liver disease is advanced, you too need to be closely monitored for HCC.”

If you are brave, try to correct misinformation with good data. However, know that you may be attacked. Never, ever attack anyone else. After you have said your piece, don’t engage any longer. If you are on the side of science, you have a powerful ally.

Lucinda Porter, RN, is a long-time contributor to the HCV Advocate and author of “Free from Hepatitis C” and “Hepatitis C One Step at a Time.” She blogs at www.LucindaPorterRN.com and HepMag.com


Study Aims and Results
The study was undertaken to understand the improved outcomes (defined as the lower risk of death) among treated patients compared to untreated patients. The treated patients received HCV direct-acting antiviral (DAA) medications.

The Veterans Affairs conducted the study. The patient population was comprised of 103,346 veterans with HCV genotypes 1, 2 and 3. Various HCV direct-acting antiviral (DAA) medications (interferon-free) were used to treat 40,664 Veterans. The overall cure rate in the treated group was 96.8%.

The groups (non-treated group vs. treated group) were compared for overall survival. The authors reported that there was a 69% reduction in all-cause deaths compared to the untreated patients.

Conclusions
DAA treatment and cure of hepatitis C in early stage HCV disease (without cirrhosis) dramatically decreased disease progression and death.

Editorial Comments
This study is the largest yet conducted with DAA HCV medications to show the benefit of being cured. In the analyses, the reduction in deaths is further proof of the effectiveness of DAA therapy.

The study confirms that DAA therapy reduces deaths and should settle the question of whether we should treat everyone with hepatitis C. That answer should be a resounding YES!

“This study is the largest yet conducted with DAA HCV medications to show the benefit of being cured.”
Study Aims and Results
The study was undertaken to understand the relationship between substance abuse and hepatitis C (HCV) in children by analyzing geographic and inpatient hospitalization data from 2006 to 2012.

During the study period (2006 to 2012) the number of hospitalizations of children with HCV increased by 37%. The mean age was 17.6 years old. Children (teenagers) aged 19-20 years old represented 68% of the total number of the HCV cases diagnosed. The children represented a 54% increase of HCV diagnoses of the years sampled.

The highest rates of HCV diagnoses were in whites, lower income populations, and occurred in the Northeast and Southern regions of the U.S.

The prevalence of substance use in children with HCV increased from 25% in 2006 to 41% in 2012.

The authors acknowledged that their study does not give an accurate estimate of the number of children with hepatitis C since children typically have few or no symptoms of HCV. But it does give an estimate of children with inpatient hospitalization due to substance abuse.

Conclusions
During the study period, there was a dramatic increase in hospitalizations of children with HCV related to substance use. The study pinpointed that the largest group of children with HCV and substance abuse are teenagers living in the Northeast and Southern areas of the United States.

Editorial Comments
These findings are not surprising. The second epidemic of HCV has mainly gone unchecked in the Northeast and the South, mostly in Appalachia. We have yet to address the newest epidemic of HCV on a large scale. Until we do, our most vulnerable population, children, will needlessly suffer.
Study Aims and Results
This study was conducted to identify the most cost-effective model to diagnose the highest number of people with hepatitis C. Three different one-time simulations were tested and compared to the current ‘baby boomer’ testing model—one-time testing for all persons born 1945-1965:

1. People ≥ 40 years old
2. People ≥ 30 years old
3. People ≥18 years old

All of the simulations included testing people who are at high risk for acquiring hepatitis C. The outcomes of the study included quality-adjusted life expectancy, costs, and cost-effectiveness.

The results of the study predicted that testing everyone ≥18 years old for HCV resulted in 256,000 additional hepatitis C positive results. The cost-effective model was cost-effective, increased cure rates, reduced deaths and improved overall quality of life in persons with hepatitis C.

Conclusions
Testing everyone 18 years old and older (in addition to risk-based testing) for hepatitis C is predicted to identify more than a quarter of a million more people with hepatitis C in addition to other benefits listed above.

Editorial Comments
‘Baby Boomer’ testing has had limited success. It makes sense to expand testing the number of people to identify, treat and cure a potential quarter of a million Americans. We now have medications that can cure almost 100% of people treated with minimal side effects. It may be time to start the process to initiate a one-time test for all Americans. It could be offered as an opt-out test as it is with HIV

“We now have medications that can cure almost 100% of people treated with minimal side effects.”
Article: Glecaprevir/Pibrentasvir for Hepatitis C Virus Genotype 3 Patients with Cirrhosis and/or Prior Treatment Experience: A Partially Randomized Phase 3 Clinical Trial—D. Wyles, et. al.


Study Aims and Results
A study of Mavyret (glecaprevir/pibrentasvir co-formulated into one pill) taken once-a-day was conducted to find out the cure rates of hepatitis C (HCV) genotype 3 treatment-naïve and treatment-experienced patients with and without cirrhosis. There were 131 patients enrolled in the study. These were patients without serious HCV disease progression. The treatment length, prior treatment information, liver disease status, and cure rates are listed below:

<table>
<thead>
<tr>
<th>Treatment Duration</th>
<th>Patient Population</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 weeks TE without cirrhosis</td>
<td>91% (20 of 22 pts)</td>
<td></td>
</tr>
<tr>
<td>16 weeks TE without cirrhosis</td>
<td>95% (21 of 22 pts)</td>
<td></td>
</tr>
<tr>
<td>12 weeks TN with cirrhosis</td>
<td>98% (39 of 40 pts)</td>
<td></td>
</tr>
<tr>
<td>16 weeks TE with cirrhosis</td>
<td>96% (45 of 47 pts)</td>
<td></td>
</tr>
</tbody>
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* TE = treatment experience; TN = treatment naïve
There were no serious side effects or treatment discontinuations.

Conclusions
The combination of glecaprevir—an HCV protease inhibitor—plus pibrentasvir—an NS5A inhibitor—produced up to 98% cure rates. Of note, people who did not achieve a cure in this trial (6 people) were invited to enroll in www.clinicaltrials.gov #NCT02939989. The study includes HCV DAA’s Mavyret plus sofosbuvir.

Editorial Comments
This study has three of the most difficult disease characteristics to treat—HCV genotype 3, treatment experienced and cirrhosis. You will note that the difference in cure rates between the 12 and 16-week treatment-experienced groups without cirrhosis was minimal. The current study proved that the vast majority of patients treated with Mavyret could overcome these difficult treatment obstacles. It will be interesting to find out if the addition of sofosbuvir—an HCV polymerase inhibitor—a different HCV viral protein can cure the remaining six patients. I know this study is a scientific endeavor, but I wonder if just adding ribavirin would be as effective (and cheaper) alternative than adding another expensive drug. Perhaps the study participants were offered ribavirin in the new study protocol.

Alan Franciscus is the Executive Director of the Hepatitis C Support Project and the Editor-in-Chief of the HCV Advocate Website.
WHAT’S UP!

This month we are featuring the following new and updated information:

Check out our new video that chronicles a patient and her medical team from hepatitis C treatment to cure and beyond.¹

PATIENT VIDEO

A Basic Guide to Hepatitis B
Read this informative guide to learn all about hepatitis B.²

Harm Reduction Fact Sheets
We have reviewed and updated all of our harm reduction fact sheets.³

HR FACT SHEETS

Harm Reduction Glossary
Check them out along with our Harm Reduction Glossary.⁴

HR GLOSSARY

Don’t forget to check out the PackHealth – a free resource to help patients navigate their HCV treatment journey from applying for treatment to cure!

Do you have hepatitis C? Get support. Get answers.

Enroll online: packhealth.com/hcv

As easy as 1-2-3!
1. Enter your contact info
2. Use promo code: HCV2017
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8am-5pm | Monday-Friday

ªhttp://hcvadvocate.org/hepatitis-c-video/
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ªhttps://packhealth.com/hcv/

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