Hepatitis C: How to win the war

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Against the backdrop of the sobering reality that hepatitis C kills more people than any other infectious disease in the United States – killing more people, in fact, than HIV and 59 other reportable infectious diseases *combined* – the urgent need to address this public health crisis should be a matter of the highest priority for healthcare providers.(1) The hepatitis C virus (HCV) is known as a "silent killer" because it can take years for a chronic HCV infection to slowly and silently do enough damage to your liver to make you feel sick. And yet, for reasons that are still being sorted out, the important job of screening baby boomer risk group patients for hepatitis C does not appear to be a top priority for the majority of healthcare providers in the United States.

Since HCV is the most common blood-borne infection in America, I was shocked to discover how little my doctor knew about it, but he did order a hepatitis C test for me when I asked him to do so. After being diagnosed with a chronic hepatitis C infection, I was treated successfully. I am now HCV free, and I believe every HCV-infected person deserves to have that same outcome.

Along with the series of facts presented in this article, I couldn't resist the temptation to include statements of personal opinion because hepatitis C attacked my liver, and I took it personally. But enough about me. HCV is a potentially lethal virus that has attacked millions of people, a large percentage of whom are unaware of their infection. This is not a skirmish. This is war.

Winning a war against a disease requires a multifaceted strategic approach. Most of the work associated with the therapeutic element of the strategic plan for winning the war against HCV has already been done. The days of arduous therapies lasting 24 to 48 weeks with only a ~50% rate of success and horrific side effects are finally over. We now have a number of once-daily, well tolerated direct-acting antiviral (DAA) medicines approved for use in the U. S. that can cure hepatitis C in over 90% of all cases with a course of treatment that lasts only 8 to 12 weeks.

The recent FDA approval of AbbVie's Mavyret™ (three pills once a day) treatment for HCV has triggered any number of news stories about the beginning of a new "price war" between and among AbbVie, Gilead and Merck. Gilead has dominated the HCV therapeutic market ever since their first DAA, Sovaldi®, was approved by the FDA in December, 2013. AbbVie's first DAA therapy, Viekira Pak®, was approved a year later, but Gilead's second DAA product, Harvoni®, had already taken the market by storm during the fourth quarter of 2014 as the first ever single-pill treatment for HCV. Merck jumped in with their own one-pill-a-day treatment for hepatitis C, Zepatier®, during the first quarter of 2016, and with AbbVie's latest addition to the lineup of DAAs, biotech business reporters are all abuzz about the HCV market share tug of war.

The war that we should all be focusing on, however, is the war against the disease itself. With that in mind, since it would be impossible to win this war without the antiviral medicines that the pharmaceutical manufacturers are producing, the underlying dynamics of the HCV market must be taken into account as we craft our larger strategy for victory in the war against hepatitis C.

When the incoming tide of prescriptions that were being written for DAAs began to show signs of ebbing during the fourth quarter of 2015, it was widely assumed in business and financial circles that Gilead had squeezed most of the juice out of the HCV market, that DAA drug prices would start trending downward, and that the size of the market would be gradually shrinking from that point forward. Prices did decline as expected, and shortsighted investors have lost

interest in the once hot HCV market, but the number of patients currently being treated and the average cost per treatment are not the only factors to consider when evaluating the size and the future potential of a therapeutic market. One of the most important factors to consider in any therapeutic market analysis is the projected number of patients who *will be* treated over time.

In this case, though, the pharmaceutical market analysts don't seem to be accounting for the potential impact of the approximately 2 million HCV-infected people in the U.S. who have not yet been diagnosed. I wonder how many of those market analysts remember what Pfizer did when the analysts of 20 years ago were calling Lipitor® a latecomer with no future because the cholesterol-lowering drug market was saturated and limited by the existing number of patients with hyperlipidemia. Keenly aware of the fact that there were still millions of Americans with hyperlipidemia who had not yet been diagnosed, Pfizer launched a *Know Your Numbers* campaign to educate consumers about the importance of routine cholesterol testing, even for people who are considered to be in good health with no obvious risk factors for cardiovascular disease. Meanwhile, Pfizer and Warner Lambert sales managers were shipping cholesterol test kits to sales reps who were giving the kits to physicians with free samples of Lipitor® and copies of an impressive chart showing the cholesterol-lowering performance of Lipitor® compared to other statins. The subsequent increase in cholesterol testing gave rise to a corresponding increase in the number of newly diagnosed hyperlipidemia patients. Thousands of providers prescribed Lipitor® for those newly diagnosed patients in addition to switching millions of existing hyperlipidemia patients from other statins to Lipitor®. During the years following the successful launch of Lipitor® in 1997, the overall effectiveness of cholesterol management in the U.S. improved, Lipitor® became the best-selling medicine of all time, and Pfizer proved that therapeutic market analysts are missing a critically important piece of the market analysis puzzle when they fail to see the potential for the undiagnosed population to get tested and turn a bleak outlook into a remarkable success story.

The DAA drug makers have so far chosen not to follow the Pfizer model by giving away free test kits, presumably because hepatitis C testing does not have the widespread conceptual support among healthcare providers that cholesterol testing had 20 years ago. This lack of conceptual support is as perplexing as it is frustrating because the Centers for Disease Control and Prevention (CDC) and the U.S. Preventive Services Task Force (USPSTF) have both recommended that all baby boomers receive a one-time screening test for HCV.(2)

One out of every 30 boomers has a chronic hepatitis C infection, and most of them don't know it. Boomers are six times more likely to have a chronic HCV infection than the general population of adults in America, and yet thousands of healthcare providers, most of whom are well aware of the CDC and USPSTF screening recommendations, are failing to follow the recommendations to screen boomers for HCV. This is true even in New York where a law that I lobbied for (as a citizen lobbyist) requires providers to offer HCV testing to all boomer patients during any episode of non-emergent care, and there is no evidence to indicate that giving providers free test kits would motivate the non-screening providers to suddenly start screening.

In addition to the baby boomer risk group that is defined by birth year (1945-1965), people of any age who are most at risk for HCV infection are those who inject drugs and those who are HIV positive. Approximately 25% of HIV-positive patients are coinfected with HCV. Healthcare providers who specialize in treating and monitoring HIV-positive patients are doing a good job of identifying HIV/HCV coinfections, and providers who specialize in treating patients with substance abuse disorders are routinely ordering HCV tests for those with a history of injecting.

In fact, all of these diagnostic efforts have uncovered a new epidemic. People who are being treated for opioid use disorder are now being diagnosed with chronic HCV at an alarming rate.

The general association of hepatitis C with injection drug use has given rise to a social stigma surrounding the disease. A large percentage of boomers who never used illicit injectable drugs are under the mistaken impression that there is no need for them to get tested for hepatitis C, and those who do have a history of injectable drug use tend to shy away from getting tested because of the stigma associated with testing positive. Well guess what, boomers, a landmark study that was published in *The Lancet: Infectious Diseases* has shot down the "shooting up" theory of why ~80% of all hepatitis C infections in the U.S. are found in the baby boomer population. Most of us were infected decades ago, not by illicit drug use but by medical professionals who used unsterilized syringes to administer vaccines and other injectables when we were kids.(3)

With so many boomers having been infected by healthcare providers who failed to properly sterilize syringes, why are so many of today's providers now adding insult to injury by failing to screen their boomer patients for hepatitis C? The excuse offered by many providers is that patients who've donated blood at some point during the past 25 years don't need to be tested because donated blood has been routinely screened for HCV since 1992. If no blood donor ever missed or misplaced a blood center screening notification, and if donating blood somehow protected you from ever being infected with HCV, then that might be a valid excuse for not testing. But people often miss positive screening notices from blood centers, and a transmissible exposure to HCV-infected blood can of course occur at any time. So much for that excuse.

Then there are the providers who see no point in testing patients with no symptoms of liver disease because so many health insurers are refusing to cover HCV treatment for patients whose liver damage is "not severe." This shockingly misguided view of hepatitis C screening and the "you're not sick enough" excuse for denying insurance coverage are leaving patients caught in the middle with no one to hold the providers accountable for their poor judgment, and only a few devoted litigators to hold the insurers accountable for refusing to cover insured patients.

Since most symptoms of chronic hepatitis C don't appear until liver damage is so advanced that the liver begins to fail, and since the reported degree of liver damage is determined by laboratory analysis of biopsy specimens collected during a largely hit-or-miss tissue sampling procedure, the "no symptoms, no test" posture is dead wrong, and insurers know very well that they're playing a dangerous game of chance by allowing such a critically important insurance decision to be based on a hit-or-miss procedure.

There is no excuse for failing to screen baby boomers for the most epidemiologically deadly infection in America, and refusing DAA treatment coverage for any properly insured patient with a confirmed diagnosis of chronic hepatitis C is unconscionable. Health insurance decision makers who refuse to authorize DAA treatment for chronically infected patients with "not severe" liver damage are clearly acting in bad faith and obviously working against those of us who are trying to win the war against this public health crisis.

The obstructive tactics used by health insurers and the continual downplaying of disease progression risk have so thoroughly distorted public and provider perceptions of the hepatitis C epidemic that millions of people are now under the false impression that hepatitis C is not a formidable public health threat. The great paradox here is that when analysts began to see the HCV market in the U.S. as a rapidly diminishing segment of the pharmaceutical industry after about 500,000 Americans had been treated with DAAs during 2014, 2015 and early 2016, at

least that many people had been denied access to treatment, and upwards of 2 million additional HCV-infected people in the United States were unaware of their infection.

The vast majority of those people still don't know they're infected. Getting those ~2 million people tested is much more than a business opportunity for the pharmaceutical manufacturers. It's a moral obligation for healthcare providers. For the sake of every person with a diagnosed-but-untreated or not-yet-diagnosed hepatitis C infection, we simply must find a way to get the untreated patients treated and to diagnose as many of those hidden infections as possible by closing the large gap between screening potential and screening performance.

Most of the efforts to educate healthcare providers about the recommendations to screen all boomers for HCV have failed to make a significant impact. By the end of 2015, more than three years after the CDC recommendation was announced and widely reported by the news media, a dismally low percentage (13.8%) of baby boomers in the U.S. had been tested for hepatitis C.(4) The CDC's *Know More Hepatitis* campaign, launched in 2012 with a budget too small for prime time, has given public health officials something to talk (to each other) about at conferences, but the actual impact of the campaign has been disappointing to say the least.

It has now been more than five years since the CDC screening recommendation was published. Gilead's *Get Tested* campaign, launched in October, 2016, sparked a transitory increase in the bimonthly rate at which boomers were getting tested, but the baseline rate was so low at the start of the campaign that we're still only up to about 23% of all boomers who have been tested for HCV, and that includes the hundreds of thousands who have already been diagnosed and treated.

It is also worth noting that the recently reported increase in the number of insurance approvals for HCV treatment does not mean that there has been an equal increase in the number of newly diagnosed patients. Many of the newly treated patients were previously diagnosed and had been waiting for insurance approval for a long time. (There will always be an inverse correlation between price and approvals. As the cost of a therapy goes down, the number of insurance approvals goes up.)

The news of these delayed insurance approvals has given no great comfort to those who are still waiting to be approved for treatment. In spite of the fact that DAA drug prices have declined dramatically during the past two years, many thousands of hepatitis C patients are still being told that they're not sick enough to require treatment. These patients are, in fact, being used by insurers as pawns in a price erosion/liver erosion waiting game.

The "we don't have enough money" story that is being spun by public and private health insurers is disingenuous at best, and at worst, a blatant misrepresentation of the facts. Before the new era of HCV therapy began in December, 2013, insurers routinely paid anywhere from $51,500 to $78,200 per course of treatment for a "triple therapy" (interferon, ribavirin and boceprevir) that only worked for about half of the patients who suffered through it. Compare that to the pricing of well tolerated DAA regimens that cure over 90% of HCV patients at an average cost to insurers that has been under $51,000 in the U.S. for the past two years. And with Mavyret™ in the cost averaging calculation, the average per-regimen cost to insurers is about to drop below $20,000.

Insurers must now face the fact that after establishing a precedent by covering the old triple therapy, refusing coverage for a much lower cost, much better tolerated and far more effective treatment for HCV is indefensible. Moreover, the systemwide healthcare costs associated with all of the liver failures and cancers that will develop if hepatitis C patients are not treated will greatly exceed the cost of treating all patients with a chronic HCV infection, especially at today's prices.

In a declining price environment, an increase in the number of new treatment starts is to be expected, but simply treating those who have already been diagnosed will not allow us to claim victory in the war against this disease. In order to win this war, we need to organize and launch a dynamic mass media campaign to shake things up and tell ~60 million boomers why it's so important for them to get tested.

The campaign that those of us in the HCV activist community are working on is being designed to evolve into something much greater than an education campaign. The campaign's radio and TV/video messaging with 1-800-GET-TESTED® as the direct response gateway will give rise to a movement with so much energy behind it that insurers and pharmacy benefit managers will be subjected to tremendous pressure to approve treatment for all chronically infected hepatitis C patients regardless of symptoms or liver biopsy results.

Insurers take heed, boomers still have what it takes to form a movement with the same level of passion we had during the 60s and 70s. The time has come to stop waiting for healthcare providers to take the lead. We need to fire up the boomers and their family members with a barrage of media messages and an interactive direct response mechanism (1-800-GET-TESTED®) that will allow us to communicate with respondents and answer questions in real time.

Investing $100 million in this campaign would make a significant impact. Even if only 20% of the ~60 million boomers who need to get tested do so during the first year of the campaign, approximately 350,000 people who didn't know they had a chronic hepatitis C infection will become aware of their HCV-positive status. Knowledge is power. The movement to secure insurance approval for all chronic hepatitis C patients becomes exponentially stronger as more and more people become aware of their HCV status.

If we simply allow the disease to run its course for the "not sick enough" and those who don't know they're infected, our healthcare system will eventually have to cope with hundreds of thousands of patients with cirrhosis and liver failure, many of whom will be needing liver transplants or treatments for liver cancer if they even survive long enough to have that choice. In order to avoid such terribly unnecessary outcomes and the extremely high healthcare costs associated with those outcomes, we must launch this outreach campaign as soon as possible.

Pharmaceutical manufacturers have a long history of sponsoring campaigns of this nature, but since drug money always seems to come with the potential for conflicts of interest, our program model calls for at least one non-conflicted organization to serve as a gatekeeper, specifically, an overseer to ensure that the administrative functions of the campaign are conducted in accordance with the highest standards of ethical conduct. In the final analysis, our primary mission is to launch and manage a 100% patient-centered campaign that will ultimately save many thousands of livers and lives.

We have the ability, the tools, and yes, even the money, to win the war against hepatitis C. The only thing we've been lacking, until now, is the unwavering determination to do so, and that unwavering determination will be coming soon to a video viewing device near you.

(1) https://www.cdc.gov/media/releases/2016/p0504-hepc-mortality.html

(2) https://www.cdc.gov/nchhstp/newsroom/2012/hcv-testing-recs-pressrelease.html
https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/hepatitis-c-screening

(3) http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(16)00124-9/fulltext

(4) http://www.ajpmonline.org/article/S0749-3797(17)30092-2/fulltext