



# HEPATITIS C

## A **CRISIS** IN THE AFRICAN AMERICAN COMMUNITY

### Findings and Recommendations

A PEER-REVIEWED CONSENSUS PAPER | OCTOBER 2013



National  
Medical  
Association

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# THE NATIONAL MEDICAL ASSOCIATION'S HEPATITIS C TASK FORCE

The Hepatitis C Task Force was formed by the NMA in 2011 to formally address and create an action plan around the crisis of Hepatitis C in the African American Community. One of the Task Force's initial recommendations was to convene a Consensus Panel. Many of the members of the Task Force serve as experts on the Consensus Panel. Their assistance is invaluable to the ongoing work of the NMA in combating Hepatitis C.

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# EXECUTIVE SUMMARY

## STATEMENT OF THE PROBLEM

In 1998, the Centers for Disease Control and Prevention turned the public health community's attention to the impending threat of hepatitis C (HCV) and the urgent need to engage in HCV risk-based screening as a first step in protecting the nation from its risks.<sup>1</sup> With the 2000 publication of the Institute of Medicine's *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*,<sup>2</sup> the public health community acknowledged the emergence of yet another infectious disease that was leading to disability and early mortality among Americans. In May 2011, with the release of the Department of Health and Human Resources report, *Combating the Silent Epidemic of Viral Hepatitis: Action Plan for the Prevention and Control of Hepatitis B and C*,<sup>3</sup> the nation formally declared war against a virus whose asymptomatic status exponentially increases the potentiality for severe morbidity and early mortality. More recently, the June 2013<sup>4</sup> release of the U.S. Preventive Service Task Force's *Screening for Hepatitis C Virus Infection in Adults: Recommendation Statement* endorsed the CDC's recommendation that persons born between 1945 and 1965 be provided one time HCV cohort-based screening. As a result, a new tool was added to the arsenal of practices that can be used to address this disease.

Despite such measures, more efforts are needed. A number of trends support this conclusion. First, the sheer magnitude of persons infected by this disease suggests that more resources must be directed towards its remediation. The Centers for Disease Control and Prevention,<sup>5</sup> citing data from the most statistically robust study to date of HCV (Armstrong et al., 2006)<sup>6</sup>, estimates that 3.2 million of the estimated 4,060,000 persons ever infected with HCV are chronically infected. As a point of comparison, this same CDC division estimates that 1,148,200 persons aged 13 and older are living with HIV infection.<sup>7</sup> Moreover, while it is estimated that 207,600 or 18.1% of persons infected with HIV are unaware of their infection, an estimated 75% of HCV infected persons do not know of their infection.<sup>8</sup> Thus, as with HIV, the implementation of strategies to contain and reduce the incidence and prevalence of this disease must be continual.

Viral hepatitis is not, however, an ethnically-neutral infection. HCV has a disparate morbidity and mortality impact among certain ethnic groups. In 2010, there were 32,587 newly reported cases of hepatitis C.<sup>9</sup> Approximately 17,408 persons did not report race/ethnicity. Of the 15,179 persons who did report race/ethnicity, 3209 or 21.1% were African American—a group that is only 14% of the American population. Recently released data estimates reveal that there were 32,474 reported cases of HCV in 2011.<sup>10</sup> While 54.2% of these cases

failed to report race/ethnicity, 14,871 of these cases did so. Approximately 2,681 of the cases that did report race were African American. Thus, African Americans were 18.1% of the new cases that reported race.<sup>11</sup>

This same CDC dataset also revealed that in 2008, the death rate per 100,000 from HCV was 4.37 for Caucasians and 7.82 for African Americans.<sup>12</sup> Thus, African Americans died from HCV 78.9% more often than did Caucasians.<sup>13</sup> This disparity represented an improvement from 2004 when the death rates for African Americans and Caucasians were 6.51 and 3.46 respectively indicating that African Americans died from HCV 88.2% more often than Caucasians. In 2011, however, reported HCV death rates dropped to 4.0 per 100,000 Caucasians and 7.72 per 100,000 African Americans. However, African Americans died from HCV 91.6% more often in 2011 than in 2010.<sup>14</sup> Thus, the limited data available suggest that the disparity in HCV death rates may have increased. In addition, African Americans are also less responsive to the pharmacologic agents currently used in the treatment of this infection. Yet, despite such findings, the growing movement to address this disease has remained much too silent regarding African Americans and HCV disparities.

Cognizant of a growing body of research which reveals that the complexities inherent in HCV and African Americans require elucidation and explication, the National Medical Association (NMA) decided to take action and, establishing the National Hepatitis C Project in 2011. One of the many tasks assumed by this initiative was an HCV in African Americans Consensus Panel Paper. From May 4–6, 2013, NMA convened a Consensus Panel of the nation's leading experts on African Americans and hepatitis C. This Consensus Panel Paper is the result of this discussion and dialogue.

## METHODS

A group consisting of physician/researchers, federal government representatives, policy analysts, health education experts, community advocates, and private sector representatives addressed several key questions utilizing the consensus panel format.

1. What is the prevalence and incidence of hepatitis C in the African American community?
2. What are some of the unique risk factors associated with hepatitis C in the African American community?
3. How can disparities in HCV screening and diagnosis, treatment and treatment outcomes be decreased?
4. Will these disparities persist as new therapies emerge?

5. What strategies can be adopted to support reductions in identified HCV disparities?
6. How can unique issues of African Americans be integrated more fully into the growing consciousness of the public health community regarding the current and prospective HCV “crisis”?

## FINDINGS AND RECOMMENDATIONS

Through a review of literature, the personal research of the presenters, and the opinions of the Consensus Panel members, a number of findings resulted.

### African Americans and HCV Prevalence and Incidence

The Consensus Panel found that the two primary sources of data on the magnitude of HCV in the US - the National Health and Nutrition Examination Survey (NHANES), 1986–94 and 1999–2002—may underestimate the prevalence of HCV among African Americans. First, no data from the National Health and Nutrition Examination Survey (NHANES) on racial/ethnic prevalence rates and HCV have been analyzed and reported since 2006. Second, because this survey captures data on only the non-institutionalized population, it bypasses homeless populations and the incarcerated, with disproportionate numbers of African Americans and other subpopulations at higher risk for HCV.

In contrast, HCV incidence data are calculated based upon reported cases from the Centers for Disease Prevention and Control, Viral Hepatitis Surveillance System. However, more than 50% of the cases reported fail to capture race/ethnicity.

The Consensus Panel therefore identified an urgent need to improve data collection and analysis for the estimation of HCV prevalence and incidence rates. Additionally, recommendations were made regarding changes in the NHANES dataset. The Consensus Panel also identified strategies that can be used to effect changes in CDC’s National Notifiable Disease Surveillance System relative to HCV.

### Unique Risk Factors Associated with HCV and African Americans

Often viewed as a highly stigmatized disease that results from personal behavioral choices, the Consensus Panel found that many of the risk factors associated with HCV’s prevalence and incidence are socially determined. The “Social Determinants of Health” framework is based upon the premise that while personal behaviors such as diet, medication adherence, and other areas of choice behavior impact health outcomes, environmental, economic, and political variables have strong

*indirect* impacts upon health-related individual choices (Koh, Oppenheimer, and Massin-Short, 2010)<sup>15</sup>. For example, one factor that corresponds to the higher rate of HCV among persons born between 1945 and 1965 is a high rate of illicit drug use, in general, and injection drug use specifically. Indeed, the rate of past month illicit drug use among persons age 50 to 59 grew from 2.7 percent in 2002 to 6.3 percent in 2011 as the baby boom cohort group aged. However, illicit drug use was initialized in this group as the socio-cultural “revolution” of the 1960s and 1970s occurred. Similarly, approximately 10% of African Americans use illicit drugs relative to 8.7% of Caucasians (SAMSHA, 2012).<sup>16</sup> Thus, African Americans are at greater risk of HCV.

Injection drug users comprise a preponderance of people with HCV infections. However, Lelutiu-Weinberger et al (2009)<sup>17</sup>, in a meta-analysis of data from 29 prevalence and 11 incidence studies, discovered that the presence of HCV infection may be higher among both African American and Latino injection drug users than among Caucasian injection drug users. Because this possible trend differs geographically, additional research is needed to definitively determine whether the risk factors for HCV among injection drug users differ by race/ethnicity.

Using data from the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Department of Labor, the Consensus Panel found that illicit drug use is higher among those with fewer years of education and higher rates of unemployment. African Americans are disproportionately represented in both of these categories. Other risk factors for HCV may also differ by race/ethnicity.

### Disparities in HCV Screening, Diagnosis and Treatment

#### HCV Screening

Multiple studies have found that 50–75% of people with an HCV infection are unaware of their status. Thus, independent of race/ethnicity, there is an urgent need for physicians to revise their screening processes. In particular, there is a need for accessible screening for African Americans and other persons born between 1945 and 1965. The CDC recommends the use of both risk-based and cohort-based screening. The U.S. Preventive Services Task Force (USPSTF) recently endorsed CDC’s recommendation of one-time cohort screening to reach the 2 million or so cases of HCV in persons born between 1945–1965. Risk-based screening will detect the presence of HCV in other groups. However, the Consensus Panel also recommended that physicians closely adhere to CDC’s recommendation to screen all HIV positive persons for HCV. The Panel also suggested that all persons who test positive for HCV be screened for an HIV co-infection.

The Panel recommended mandatory screening for inmates in jails and prisons. As is known, Weinbaum, Lyerla, and Margolis (2003) from the Centers for Disease Control and

Prevention found that approximately 12% to 35% of all U.S. inmates may have a chronic HCV infection. Of particular interest, CDC suggested that as many as 29% to 43% of all persons who were HCV positive at the time of the study may have been inmates at one time.

Finally, the Panel recommends the broader use of rapid testing to expand screenings among underserved populations. The use of rapid testing improves, greatly, the probability that positive results are received. It simplifies the overall screening effort. Studies have shown that greater than 90% of test results are delivered to patients with rapid testing in contrast with less than 50% of patients who return to discover their status with lab-based testing.

One study also found that African Americans are less likely to be screened for HCV in the presence of *known* risk factors, and less likely to be referred to a sub-specialist for consideration of treatment. Thus, systemic variables may continue to be operative in creating HCV disparities among African Americans. There is a need to increase the knowledge of both patients and providers about the traditional risk factors that are associated with the HCV infection.

## HCV Treatment Eligibility

Significant differences exist in the degree of treatment eligibility between African Americans and Caucasians. The IDEAL study found that 40.2% of African Americans failed the eligibility screening compared with 28% of non-African Americans. Differentials also exist between the two ethnic groups in terms of the percent of those who are HCV-infected and who decide not to accept treatment. The Consensus Panel made recommendations aimed at reducing disparities at each of these points.

## HCV Treatment Responsiveness

Compared with Caucasians, African Americans are infected disproportionately with HCV genotype 1 and, as a result, they are less responsive to antiviral treatments than HCV genotypes 2 and 3. However, among patients with HCV genotype 1, African Americans have a significantly lower sustained virologic response (SVR) to peginterferon alfa and ribavirin than is the case with Caucasians. For example, one study found that a sustained virologic response (SVR) to peginterferon alfa and ribavirin was 52% for Caucasians but only 28% for African Americans. Multiple prospective studies have confirmed these findings. A HCV protease inhibitor combined with PEGIFN and ribavirin has been standard therapy for HCV genotype 1 since 2011.<sup>19</sup> Despite overall improvement in SVR, African Americans still have a lower SVR. Such data support the thesis of a current and impending crisis of even greater magnitude in African American communities given the lower responsiveness to treatment.

The lower response to HCV treatment within genotype 1 for African Americans is explained partly by single nucleotide

polymorphisms (SNPs) near the IL28B gene. IL28B SNP genotypes predict the likelihood of cure for all racial and ethnic groups receiving HCV treatment regimens that include interferon alfa. African Americans are less likely to have the favorable IL28B SNP (rs12979860) C/C genotype relative to Caucasians. The IL28B genotype is thought to explain approximately 50% of the disparity in treatment outcomes for African Americans. Other studies have shown a strong correlation between ribavirin drug exposure and SVR. Jin et al (2012)<sup>20</sup> reported recently lower ribavirin exposure in African Americans compared with Caucasians that was explained by aberrant ribavirin pharmacokinetics. These studies suggest that African Americans require a higher initial ribavirin dose. The Consensus Panel recommended that further research be conducted to understand the lower treatment response that is observable across different subsets of African Americans.

## The Emergence of New Therapies

The Consensus Panel reviewed recent HCV clinical trials with direct acting antiviral treatments either combined with peginterferon and ribavirin and/or interferon-free regimens. These studies show improved cure rates and better side effect profiles than current standards of care. The Consensus Panel called for greater participation of African Americans in clinical trials so that efficacy and safety in this patient group can be more rigorously studied and understood. With the development of novel HCV drugs, research is needed to determine whether the efficacy of therapy (i.e. cure rates) will continue to increase in African Americans.

## Strategies That Can Be Used to Reduce Disparities

The Consensus Panel concluded that a number of strategies can be used to reduce disparities between African Americans and Caucasians with chronic HCV. At the first level, an African American-specific campaign is needed to create awareness regarding the broad range of newer risks associated with HCV infection in African Americans. Second, providers of all races and ethnicities require adequate education and training about racial disparities in HCV epidemiology, clinical course and treatment outcomes, and barriers to care and treatment.

The Consensus Panel found that the recent increases in HCV programs, policies and initiatives also embody a number of opportunities to reduce the HCV risks that currently exist in the African American community. Nevertheless, new measures are also needed.

## SUMMARY

This executive summary provides only a few of the findings and recommendations from the full report, which follows.



# THE HEPATITIS C CRISIS IN THE AFRICAN AMERICAN COMMUNITY

## BACKGROUND

The epistemological foundations of medicine have now been expanded to include a normative commitment to the characterization, analysis, and remediation of health disparities. Despite this paradigmatic shift, however, the actualization of this goal is a complex process. For example, hepatitis C (HCV), a blood-borne viral infection that affects approximately four million Americans and which accounts for approximately 50% of liver transplants, is a condition that is not merely disparately manifested among African Americans, disparities are observable across the continuum from screening and diagnosis to treatment modalities and treatment outcomes.

Such circumstances are far from benign. America's current global status as the country whose Gross Domestic Product of \$15.851 trillion places it first in material wealth has been driven by the quality of its human capital.<sup>21</sup> The productivity of a country's human capital is a function of education and training as well as the health status of its citizens. Early mortality among any group reduces the productivity of the entire nation. Yet, HCV is closely associated with early mortality. Ly, Xing, et al (2012),<sup>22</sup> in an analysis of data from 22 million death certificates from 1999 to 2007, identified 15,106 total deaths from hepatitis C in 2007. Approximately 2,638 or 17.5% of these deaths were African Americans. Yet, African Americans were only 13% of the U.S. population. Thus, African Americans had significantly higher odds of death due to HCV than Whites. Significantly, this study found that deaths from HCV in 2007 exceeded the number of deaths from HIV. Based upon these findings, the authors concluded that chronic hepatitis C, a disease that was conservatively reported as affecting approximately 3.2 million persons in 2002 (Armstrong, 2006),<sup>23</sup> is poised to burden America's healthcare system further as these infections lead to an increase in the incidence of cirrhosis and hepatocellular carcinoma. Although the Centers for Disease Control and Prevention and HCV researchers in general continue to cite this figure today, the prevalence of HCV may now be even larger.<sup>24</sup> Thus, hepatitis C is a potentially explosive health condition towards which insufficient attention has been directed. Wong (2000)<sup>25</sup>, utilizing econometric modeling,

estimated that from 2010 to 2019, direct expenditures for HCV medical services will reach \$6.7 billion. When the indirect costs associated with lost productivity are included, the costs will be even more staggering.

However, while chronic hepatitis C infection comprises a highly serious health problem that has the potential of reducing or eliminating the labor force participation rates of large numbers of Americans, a substantial body of research suggests that the disparate nature of HCV magnifies the potential human and financial losses associated with this disease in African American communities. Metaphorically speaking, relative to African Americans and HCV, the house is, indeed, on fire, but few are taking notice of the smoke and the ash.

The National Medical Association (NMA) convened respected medical and public health expert to educate policymakers, researchers, public health officials, communities, the media, and the general public regarding the current and impending crisis of hepatitis C among African Americans.

## THE NATIONAL MEDICAL ASSOCIATION (NMA)

The National Medical Association (NMA) is the largest and oldest national organization in the world representing African-American physicians and the patients they serve. The NMA, on behalf of its 30,000 members and its partners, is seeking to develop a comprehensive set of strategies that, with the support of physicians and allied health professionals, will result in more conclusive evidence regarding racial/ethnic hepatitis C disparities as well as recommend distinct strategies for their reduction.

The NMA, a 501(c)(3) organization headquartered in Silver Spring, Maryland, is comprised of 130 local, state, and regional NMA affiliates or chapters located in 46 states. Member physicians practice in 24 specialty areas. The organization is committed to improving the health status and outcomes of minority and disadvantaged populations through professional development, community health education, advocacy, and research, in partnership with federal and private agencies and corporations.

The membership of the NMA is predominantly African American physicians. The NMA is comprised of physicians in the primary care specialties, as well as in all other medical and surgical sub-specialties, academic medicine, military medicine, and medical administration. NMA members serve a high number of patients who are African-American and/or members of other minority groups. Poor, uninsured, underinsured, and/or patients who are beneficiaries of Medicaid or Medicare are over-represented among the patients served by NMA's membership.

The NMA has an extensive national, regional, and local infrastructure to support advocacy, health promotion and disease prevention, treatment, and research initiatives. NMA's 130 state and local affiliated societies across the country are organized into six regions providing an optimum structure for the implementation of programs that have national impact.

NMA members are available to provide specialty expertise for scientific review, evaluation, and validation of project proposals and efforts through 24 scientific sections. These sections are: (1) Aerospace and Military Medicine; (2) Allergy, Immunology and Asthma; (3) Anesthesiology; (4) Basic Science; (5) Community Medicine and Public Health; (6) Dermatology; (7) Emergency Medicine; (8) Family Medicine; (9) Internal Medicine; (10) Medical Neurosurgery; (11) Medical Administration; (12) Obstetrics and Gynecology; (13) Ophthalmology; (14) Orthopedics; (15) Otolaryngology; (16) Pathology; (17) Pediatrics; (18) Physical Medicine and Rehabilitation; (19) Plastic and Reconstructive Surgery; (20) Psychiatry and Behavioral Sciences; (21) Radiology; (22) Surgery; (23) Urology; and (24) Women In Medicine. Within each of the twenty-four sections, there is significant capacity and interest to support and conduct community disease prevention and educational outreach projects including the prevention and treatment of HCV.

The organizational structure of the NMA provides an established framework of collaborative linkages within which physicians, as NMA's principal group of health professionals, can be mobilized. Through this infrastructure, physicians can address major health issues and implement national health program initiatives associated with HCV and its related comorbidities. These physicians, and the health institutions with which they are affiliated, form a natural structure and medical home for addressing concerns that disproportionately impact African-Americans and other underserved populations.

## METHODS: NMA'S HCV CONSENSUS PANEL PROCESS

The NMA identified key experts on HCV infection from academic centers, private practices, associations, research centers, and public health entities and invited them to join the HCV Consensus Panel. The purpose of the Consensus Panel

was to review the national challenge of hepatitis C, examine the evidence base on racial and economic disparities in this area, and propose a national response to such disparities that can be implemented by clinicians, policymakers, researchers, public health advisors, community organizations, and the general public. Thus, the targeted audience for this Consensus Panel Paper is quite broad.

The operational structure for the Consensus Panel was designed to assemble a collective body of practitioners, researchers, and thought leaders with extensive knowledge and experience in the area of HCV infection. The scholars selected have a demonstrated commitment to patient and physician education. NMA staff and consultants provided administrative, management, and development support. The clinical and academic concerns of practicing physicians were represented, as well as the needs and concerns of African-American patients. The body of the Consensus Panel included nationally recognized experts who provided knowledge and expertise on key clinical, research, and policy issues in the area of HCV. The HCV Consensus Panel will use findings from this scientifically comprehensive paper and make policy recommendations to the NMA House of Delegates.

The Consensus Paper and its recommendations will be disseminated to NMA member physicians, other health care providers, governmental and non-governmental agencies, policy-makers and the media. It contains recommendations that can be adopted by each key stakeholder.

## HEPATITIS C: ITS PREVALENCE AND INCIDENCE

### HCV Prevalence Rates

The crisis of hepatitis C is embedded, in part, in the absence of valid and reliable estimates of its magnitude within the United States. For example, the Centers for Disease Control and Prevention, National Center for Health Statistics, utilizes the National Health and Nutrition Examination Survey (NHANES) to estimate the prevalence of viral hepatitis A, B, C, D, and E. However, while NHANES III, which was completed from 1988–94, reported the first set of findings from serologic testing, even the findings from this dataset may have under-reported the prevalence of this infection since HCV was not discovered early enough for its inclusion in the NHANES III survey planning process. NHANES III revealed that approximately 1.8% of survey respondents were positive for HCV for the period 1988–1994.<sup>26</sup> Given the nation's population of approximately 260.3 million individuals in 1994, this represented more than 4 million persons. An estimated 75 percent of these persons did not experience spontaneous HCV clearance and, as a result, were chronically infected.



A subsequent analysis of HCV prevalence rates using NHANES 1999–2002 data revealed that 4.1 million Americans were infected with HCV and that 75% or 3.2 million of these persons were chronically infected. Such data established HCV as the nation's number one blood-borne viral infection. Indeed, this pioneer study by Armstrong (2006)<sup>27</sup> is cited often as a primary source of primary data for the prevalence of HCV despite the fact that these findings reflect data for 1999–2002. For example, Rein, Smith, Wittenborn et al (2012)<sup>28</sup> utilize these statistics as background data for their clinical study. Similarly, Conjeevaram, Fried, Jeffers et al (2006)<sup>29</sup> used the same estimates in establishing the magnitude of HCV. Likewise, Melia, Muir, McCore et al (2011)<sup>30</sup> establish the magnitude of chronic hepatitis C as a major health problem using the same citation.

Indeed, even the CDC, National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention, Division of Viral Hepatitis cites the findings from the now historic Armstrong study as the nation's official measure of the prevalence of HCV.<sup>31</sup> Such reliance upon a now dated study does not reflect poor scholarship. Rather, it documents the poverty of data used in establishing valid and reliable estimates of the breadth of HCV as a public health problem. The saturated use of the Armstrong study defines an urgent need for the development of accurate and current data on the prevalence on HCV incidence rates. Nevertheless, this pioneer analysis provides baseline data for future studies that measure the prevalence of HCV in the American population.

The analysis by Armstrong et al (2006)<sup>32</sup> of prevalence rates in 2002 reveals the patterns listed in Table 1.<sup>33</sup>

## TABLE 1: GREATER HCV BURDEN IN AFRICAN AMERICANS

The Armstrong study found that HCV rates were 100% more prevalent among African Americans (3.0%) than among Caucasians (1.5%).

Of the estimated 4,060,000 persons ever infected with HCV, 2,570,000 or 64.3% were Caucasians.

In contrast, 920,000 of the 4,060,000 persons, or 22.7% of those ever infected with HCV were African American.

Approximately 260,000 or 6.4% of those ever infected with HCV were Mexican-Americans.

Approximately 13% of the US population was African American from 1999–2002, but African Americans were 22.7% of HCV cases. Thus, African Americans were 74.6% more likely to have ever been infected with HCV relative to their representation in the overall population.

Similarly, 9.4% of African Americans 40–49 years old had ever been infected with chronic HCV compared to 3.8% of Caucasians. Thus, African Americans in this age group were 136.8% more likely to be infected with HCV.

Social determinants of health play an important role in the higher ( $p < .05$ ) HCV prevalence rates of African Americans. For example:

- The prevalence of HCV antibodies was 3.2% for persons with incomes below 100% of the poverty threshold and

only 1% for persons with family incomes equal to or greater than 200% of the federally defined poverty line.

- Thus, the probability that an impoverished person would test positive for HCV was 220% higher than for their non-impoverished counterpart.
- In 2002, the last year of the NHANES survey used by Armstrong, the poverty rate for African Americans was 24.1%. Caucasians had a poverty rate of 10.2%.
- The prevalence of HCV antibodies was 2.8% for persons with fewer than twelve years of education but only 1.3% for persons with more than 12 years of education.
- This represented a 115.4% difference.
- In 2002, 20.8% of African Americans age 25 and over had not graduated from high school compared to 11.3% of Caucasians.

Source: Calculated from data found in Armstrong GL, et al. *Ann Intern Med.* 2006; 144(10):705–714, pgs 707–8.

Source: U.S. Census Bureau, *Current Population Survey*, 2002 and 2003 Annual Social and Economic Supplements.

Source: U.S. Census Bureau, *Educational Attainment in the U.S. – 2002*. Detailed tables. Table 1a: Percent of High School and College Graduates of the Population 15 years and over by age, sex, race, and Hispanic origin, March 2002.

Source: U.S. Census Bureau, March 2001 and March 2002 *Current Population Survey*. Internet Release date: March 21, 2003.

Given such disparities in prevalence rates by race/ethnicity, poverty status, and education, one must ask “Do similar trends appear in incidence rates?”

## HCV Incidence Rates

The National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Division of Viral Hepatitis collects data on the incidence of HCV. The rate of acute HCV was 0.3 cases per 100,000 populations in 2010,<sup>34</sup> a rate that had been constant since 2006. However, the 2011 dataset reports that the incidence of acute HCV had increased to 0.4 cases per 100,000.<sup>35</sup> Table 2 summarizes this data.

**TABLE 2: REPORTED CASES OF ACUTE HEPATITIS C, NATIONALLY AND BY STATE - UNITED STATES, 2007-2011**

State	2010 % African American	2007 Rate	(No.)	2008 Rate	(No.)	2009 Rate	(No.)	2010 Rate	(No.)	2011 Rate	(No.)
Alabama	26.2	0.2	(10)	0.3	(13)	0.2	(10)	0.1	(7)	0.5	(23)
Alaska	3.3	0.1	(1)	U <sup>†</sup>	U	U	U	U	U	U	U
Arizona	4.1	U	U	U	U	U	U	U	U	U	U
Arkansas	15.4	0	(0)	0	(1)	0.1	(2)	0	(1)	0	(0)
California	6.2	0.2	(72)	0.1	(30)	0.1	(43)	0.1	(32)	0.1	(48)
Colorado	4.0	0.4	(20)	0.3	(14)	0.6	(28)	0.4	(20)	0.5	(28)
Connecticut	10.1	0.6	(20)	0.5	(19)	1.5	(53)	1.0	(37)	1.3	(47)
Delaware	21.4	U	U	U	U	U	U	U	U	U	U
District of Columbia	50.7	U	U	U	U	0.2	(1)	0.3	(2)	U	U
Florida	16.0	0.1	(16)	0.2	(32)	0.3	(53)	0.3	(56)	0.3	(64)
Georgia	30.5	0.2	(18)	0.2	(16)	0.3	(31)	0.3	(32)	0.5	(53)
Hawaii	1.6	U	U	U	U	U	U	U	U	U	U
Idaho	.6	0.3	(4)	0.2	(3)	0.5	(7)	0.7	(11)	0.8	(12)
Illinois	14.5	0.1	(16)	0.1	(10)	0	(6)	0	(1)	0	(6)
Indiana	9.1	0.2	(14)	0.2	(13)	0.3	(22)	0.4	(27)	1.3	(84)
Iowa	2.9	0	(0)	0	(0)	0.4	(11)	0	0	0	(0)
Kansas	5.9	0	(0)	0	(1)	0	(1)	0.1	(2)	0.3	(8)
Kentucky	7.8	0.7	(29)	1.6	(68)	1.5	(64)	2.5	(109)	3.2	(142)
Louisiana	32.0	0.1	(4)	0.2	(9)	0.2	(9)	0.1	(4)	0.2	(7)
Maine	1.2	0.1	(1)	0.2	(3)	0.2	(2)	0.2	(2)	0.9	(12)
Maryland	29.4	0.3	(15)	0.4	(22)	0.4	(23)	0.4	(24)	0.6	(35)
Massachusetts	6.6	0.2	(10)	0.2	(13)	0.2	(10)	0.2	(13)	0.3	(23)
Michigan	14.2	0.9	(89)	1.3	(129)	0.4	(35)	0.5	(45)	0.3	(32)
Minnesota	5.2	0.5	(28)	0.4	(22)	0.3	(15)	0.3	(16)	0.3	(17)
Mississippi	37.0	0.5	(16)	U	U	U	U	U	U	U	U
Missouri	11.6	0.1	(3)	0	(2)	0	(0)	0.1	(6)	0.1	(8)
Montana	.4	0.1	(1)	0.6	(6)	0.1	(1)	0.4	(4)	0.9	(9)
Nebraska	4.5	0.1	(1)	0.1	(2)	0.2	(3)	0.1	(2)	0.1	(2)
Nevada	8.1	0.4	(9)	0.8	(22)	0.2	(5)	0.3	(7)	0.4	(10)
New Hampshire	1.1	U	U	U	U	U	U	U	U	U	U
New Jersey	13.7	1.1	(95)	0.7	(61)	0.1	(7)	0.3	(28)	0.6	(53)
New Mexico	2.1	0.3	(5)	0.3	(5)	0.3	(6)	0.7	(14)	0.7	(14)
New York	15.9	0.2	(45)	0.2	(43)	0.3	(53)	0.3	(50)	0.3	(52)
North Carolina	21.5	0.2	(17)	0.5	(46)	0.3	(24)	0.4	(39)	0.6	(60)
North Dakota	1.2	0	(0)	0	(0)	0.3	(2)	0	(0)	0	(0)
Ohio	12.2	0.2	(20)	0.3	(40)	0.2	(26)	0.1	(10)	0.1	(6)
Oklahoma	7.4	1.4	(49)	0.5	(20)	0.7	(27)	1.1	(41)	1.4	(53)
Oregon	1.8	0.4	(16)	0.6	(23)	0.5	(19)	0.5	(19)	0.5	(20)
Pennsylvania	10.8	0.3	(34)	0.2	(27)	0.3	(39)	0.2	(26)	0.3	(35)
Rhode Island	5.7	0.8	(8)	U	U	U	U	U	U	U	U
South Carolina	27.9	0	(0)	0.1	(4)	0	(1)	0	(1)	0	(1)
South Dakota	1.3	U	U	U	U	U	U	U	U	U	U
Tennessee	16.7	0.6	(37)	0.4	(28)	0.5	(33)	0.7	(46)	1.3	(83)
Texas	11.8	0.3	(67)	0.2	(59)	0.1	(36)	0.1	(35)	0.1	(37)
Utah	1.1	0.2	(5)	0.4	(12)	0.2	(6)	0.4	(10)	0.4	(10)
Vermont	1.0	1.5	(9)	0.2	(1)	0.2	(1)	0.3	(2)	1.0	(6)
Virginia	19.4	0.1	(8)	0.1	(8)	0.1	(10)	0.2	(13)	0.3	(25)
Washington	3.6	0.3	(18)	0.4	(25)	0.3	(22)	0.4	(25)	0.6	(41)
West Virginia	3.4	1.0	(18)	1.2	(22)	1.7	(31)	1.1	(21)	2.5	(46)
Wisconsin	6.3	0	(1)	0.1	(3)	0.1	(3)	0.2	(10)	0.3	(15)
Wyoming	.8	0	(0)	0	(0)	0	(0)	0	(0)	0.4	(2)
<b>Total</b>	<b>12.6</b>	<b>0.3</b>	<b>(849)</b>	<b>0.3</b>	<b>(877)</b>	<b>0.3</b>	<b>(781)</b>	<b>0.3</b>	<b>(850)</b>	<b>0.4</b>	<b>(1,229)</b>

Source: CDC National Center for HIV/AIDS, Viral Hepatitis, STD & TB Prevention, *Surveillance for Viral Hepatitis - United States 2011*, Table 4.1; and the U.S. Bureau of the Census, Quick Facts by State (accessed Sept. 2013).

Although the 2011 dataset is incomplete, certain trends in terms of changes in the reported cases of acute HCV are suggested. For example, it appears that the number of reported acute cases of HCV increased. However, this finding is inconclusive since eight states did not submit acute HCV reports and other states submitted only partial data. Second, the finding of a 44.7% increase in the number of HCV cases may understate acute HCV trends among African Americans because many of the states that did not submit reports, and/or only submitted partial reports, include significant numbers of African Americans. For example, the District of Columbia, an area that is 50.7% African American, has incomplete data. Mississippi, a state that is 37.0% African American also has incomplete data. In addition, high percentages of African Americans live in most of those states in which the incidence rate of acute hepatitis increased, i.e. Alabama, Georgia, Maryland, North Carolina, Virginia, Tennessee, etc. These data weaknesses suggest an urgent need for accurate and complete acute HCV reporting from all states. In addition, it is important that ethnicity be included in all reported acute cases of HCV so that disparities can be identified.

Cases of HCV are defined for reporting purposes using two criteria. When chronic liver disease is diagnosed and subsequent testing reveals the presence of HCV, a clinical criteria is used for case definition. In contrast, a laboratory

criteria is said to be applied when any of the four alternative HCV screening tests are used. However, these tests do not distinguish current HCV infections from those that have been resolved. Thus, CDC also collects data on current or past HCV. This data are used as a proxy for chronic hepatitis. According to CDC's most recent report,<sup>36</sup> 185,979 chronic HCV reports were received by CDC in 2011 based upon the 34 states participating in CDC's surveillance efforts. However, for a range of reasons, only ten states – California, Louisiana, Missouri, Montana, Oregon, Pennsylvania, South Carolina, South Dakota, Vermont and Wyoming – provided their consent for their data to be included in CDC's past or present HCV data collection efforts. Additionally, some states submitted reports on HCV past or present but did not give their consent for these cases to be used for CDC's chronic HCV reporting. This decision by the other 24 states reduced the number of chronic hepatitis case reports available for the purpose of tracking HCV trends from 185,979 reports to a mere 52,286 reports. Based upon an analysis of this data so that previously reported cases could be deleted, it was determined that 32,474 newly reported cases of chronic HCV occurred in 2011. However, a full 54.2% of these reports were incomplete relative to race/ethnicity. (Only 1/10 or 1% were incomplete relative to gender and age group). Table 3 is a replication of CDC's findings from this analysis.



**TABLE 3: REPORTED CASES OF LABORATORY-CONFIRMED, HEPATITIS C (PAST OR PRESENT) INFECTION, BY SEX, RACE/ETHNICITY, AGE GROUP, AND POSITIVE LAB TESTS — EMERGING INFECTIONS PROGRAM (EIP), HEPATITIS SURVEILLANCE DEMONSTRATION SITES, 2011**

	CO N	(%)	CT N	(%)	MN N	(%)	NM N	(%)	NYS N	(%)	NYC N	(%)	OR N	(%)	SF N	(%)	Total N	(%)
Sex																		
Female	1,030	35.5	957	33.0	649	36.0	884	31.8	2,467	35.8	3,146	36.0	1,639	36.4	526	27.1	11,298	34.8
Male	1,864	64.3	1,940	66.9	1,142	63.4	1,897	68.2	4,408	63.9	5,595	64.0	2,865	63.6	1,418	72.9	21,129	65.1
Unknown/Miss	4	0.1	1	0.0	11	0.6	0	0.0	23	0.3	8	0.1	0	0.0	0	0.0	47	0.1
Race/Ethnicity*																		
AI/AN	24	0.8	5	0.2	97	5.4	46	1.7	28	0.4			63	1.4	13	0.7	276	0.8
API	16	0.6	25	0.9	50	2.8	3	0.1	59	0.9	171	2.0	46	1.0	72	3.7	442	1.4
Black	143	4.9	311	10.7	203	11.3	12	0.4	614	8.9	927	10.6	105	2.3	366	18.8	2,681	8.3
White	992	34.2	1,222	42.2	737	40.9	283	10.2	2,284	33.1	667	7.6	1,964	43.6	624	32.1	8,773	27.0
Hispanic	323	11.2	506	17.5	40	2.2	419	15.1	434	6.3	306	3.5	87	1.9	148	7.6	2,263	7.0
Other	21	0.7	5	0.2	9	0.5	0	0.0	64	0.9	287	3.3	13	0.3	37	1.9	436	1.3
Unknown/Miss	1,379	47.6	824	28.4	666	37.0	2,018	72.6	3,415	49.5	6,391	73.1	2,226	49.4	684	35.3	17,603	54.2
Age Group (years)																		
0-14	11	0.4	8	0.3	5	0.3	10	0.4	12	0.2	42	0.5	5	0.1	4	0.2	97	0.3
15-24	121	4.2	143	4.9	126	7.0	363	13.1	416	6.0	298	3.4	142	3.2	34	1.8	1,643	5.1
25-39	613	21.2	597	20.6	316	17.5	923	33.2	1,337	19.4	1,629	18.6	655	14.5	242	12.5	6,312	19.4
40-54	1,198	41.3	1,218	42.0	729	40.5	938	33.7	2,352	34.1	3,035	34.7	1,980	44.0	715	36.8	12,165	37.5
55+	948	32.7	932	32.2	626	34.7	547	19.7	2,753	39.9	3,744	42.8	1,719	38.2	948	48.8	12,217	37.6
Missing	7	0.2	0	0.0	0	0.0	0	0.0	28	0.4	1	0.0	3	3.0	1	0.1	40	0.1
Positive Laboratory Tests																		
RIBA	279	9.6	94	3.2	367	20.4	U		746	10.8	1,117	12.8	300	6.7	23	1.2	2,926	9.0
HCV RNA	1,574	54.3	743	25.6	1,315	73.0	U		3,664	53.1	4,357	49.8	2,036	45.2	1,294	66.6	14,983	46.1
Genotype	695	24.0	89	3.1	626	34.8	U		1,494	22.6	2,582	29.5	656	14.6	538	27.7	6,680	20.6
Anti-HCV & s/co ratio	1,721	59.4	2,360	81.4	534	29.6	U		3,198	46.4	7,001	80.0	1,155	25.6	1,250	64.3	17,219	53.0
<b>Total new reported cases</b>	<b>2,898</b>		<b>2,898</b>		<b>1,802</b>		<b>2,781</b>		<b>6,898</b>		<b>8,749</b>		<b>4,504</b>		<b>1,944</b>		<b>32,474</b>	
<b>Estimated pop, 2011</b>	<b>5,116,796</b>		<b>3,580,709</b>		<b>5,344,861</b>		<b>2,082,224</b>		<b>11,220,287</b>		<b>8,244,910</b>		<b>3,871,859</b>		<b>812,826</b>		<b>40,274,472</b>	
<b>Rate per 100,000 pop</b>	<b>57</b>		<b>81</b>		<b>34</b>		<b>134</b>		<b>61</b>		<b>106</b>		<b>116</b>		<b>239</b>		<b>81</b>	

Source: CDC, Viral Hepatitis Surveillance, United States, 2011, Table 4.4., Pg. 59. op. cit.

\*Categorized in the following order: 1) Hispanic; 2) AI/AN; 3) API; 4) Black; 5) White; 6) Other. Cases can be reported with more than one laboratory test result

U=No data available for reporting

The data reported were from only 8 sites—Colorado, Connecticut, New York, New York City, Oregon, and San Francisco. Therefore, the data in Table 3 above may also under-report the incidence of HCV, past or present, by race/ethnicity because, except for New York and San Francisco, African Americans are disproportionately under-represented in the other geographic areas.

Moreover, Table 3 suggests that African Americans were only 8.3% of the total reported cases of laboratory confirmed HCV, past or present. However, because 54.2% of race/ethnicity data are missing, the most appropriate denominator for such a calculation is not the 32,474 total newly reported cases. Rather, it is the 14,871 cases for which race/ethnicity was reported. Thus, African Americans, the ethnicity designated on 2,681 cases, were 18.1% of the newly reported cases of HCV, past or present. Despite the problems that attenuate this data set, African Americans were over-represented among those persons with HCV, past or present. In 2010, however, African

Americans were 21.1% of the 15,179 cases of hepatitis, past or present, for which race/ethnicity was reported.<sup>37</sup> Incidence rates for chronic hepatitis that were calculated from the above table may be in need of revision. The Institute of Medicine's now classic report, *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*, provides a discussion of some of the factors that reduce the quality of viral hepatitis reporting by states and local health departments (2010).<sup>38</sup>

## HCV Death Rates by Race/Ethnicity

Data from the Surveillance for Viral Hepatitis – United States, 2010, also reveal that African Americans died from HCV in 2004, 2005, 2006, 2007, and 2008 and 2009, and 2010 at rates that were significantly greater than all other racial groups for whom data were collected.<sup>39</sup> Table 4 describes these trends.

**TABLE 4: HCV DEATHS**

Demographic characteristic	2006		2007		2008		2009		2010	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Age Group (years)										
0–34	128	0.09	131	0.09	124	0.09	116	0.08	117	0.08
35–44	1,083	2.49	999	2.32	878	2.07	828	1.99	712	1.73
45–54	5,802	13.43	5,937	13.53	5,758	12.98	5,469	12.26	5,171	11.49
55–64	4,191	13.28	5,145	15.72	5,967	17.71	6,683	19.21	7,431	20.37
65–74	1,500	7.93	1,621	8.37	1,709	8.49	1,824	8.77	1,901	8.75
>75	1,241	6.76	1,273	6.85	1,332	7.11	1,333	7.10	1,293	6.97
Race										
White§	10,783	4.05	11,798	4.31	12,261	4.37	12,682	4.43	--	--
Black¶	2,567	7.50	2,686	7.59	2,829	7.82	2,908	7.80	--	--
Non-White, non-Black**	595	3.61	622	3.59	678	3.78	663	3.61	--	--
Race/ Ethnicity										
White, non- Hispanic	--	--	--	--	--	--	--	--	10,575	4.03
Black, non- Hispanic	--	--	--	--	--	--	--	--	2,981	7.72
Hispanic	--	--	--	--	--	--	--	--	2,318	6.83
Asian/Pacific Islander	--	--	--	--	--	--	--	--	440	3.30
American Indian/ Alaska Native	--	--	--	--	--	--	--	--	248	9.90
Sex										
Male	9,724	6.30	10,561	6.64	11,116	6.82	11,517	6.91	11,781	6.81
Female	4,221	2.52	4,545	2.65	4,652	2.65	4,736	2.65	4,846	2.63
<b>Overall</b>	<b>13,945</b>	<b>4.35</b>	<b>15,106</b>	<b>4.58</b>	<b>15,768</b>	<b>4.66</b>	<b>16,253</b>	<b>4.70</b>	<b>16,627</b>	<b>4.65</b>

\*Rates for race, sex, and overall total are age-adjusted per 100,000 U.S. standard population.

†Cause of death is defined as the underlying cause of death or one of the multiple causes of death and is based on the International Classification of Diseases, 10th Revision (ICD-10) codes B17.1 and B18.2 (hepatitis C).

§Included white, non-Hispanic and white Hispanic.

¶Included black, non-Hispanic and black Hispanic.

\*\*Included all other racial/ethnic groups. Source: CDC. National Vital Statistics System. Pg 61, Table 4.5.

In 2008, African Americans died from HCV at a rate that was 78.9% higher than their Caucasian counterparts. However, Table 4 indicates that while HCV death rates per 100,000 persons decreased for both Caucasians and African Americans from 2008 to 2010, the disparity in HCV rates increased. African Americans were 91.6% more likely to die from HCV in 2011 than in 2008 when the disparity was only 78.9% higher. Additionally, the enhanced race/ethnicity reporting indicates that American Indians/Alaskan Natives were even more likely to die from HCV than African Americans in 2011. With a death rate of 9.90 per 100,000, Native Americans died from HCV 145.7% more often than Caucasians. Additionally, Latinos died from HCV 69.5% more often than Caucasians. There may be areas in which collaborations to address HCV disparities can occur across these highly affected racial/ethnic groups.

## IMPROVING THE ACCURACY OF HCV PREVALENCE AND INCIDENCE RATES

A number of recommendations can be made in terms of the creation of greater accuracy in HCV prevalence and incidence data. First, HCV's status as the most common blood borne disease recommends its inclusion in other publicly collected datasets so that data are available for triangulation. For example, the CDC Risk Factor Surveillance Survey might collect data on HCV. Similarly, CDC's National Health Interviews Survey could also collect such data.

Second, the Consensus Panel recommends that the CDC's National Notifiable Diseases Surveillance System issue new guidelines for use by health departments at the state and local level for the reporting of both chronic hepatitis B and C. Capacity-building grants may be needed at the state and local levels so that more accurate and more complete data are collected and transmitted to CDC's system.

Third, while the Consensus Panel is aware that CDC has already taken new measures to investigate HCV outbreaks, outbreaks remain underreported and reported outbreaks of hepatitis C are not always investigated thoroughly.

The role of outbreak investigation in identifying and improving accuracy in HCV reporting is well-known. In 2011, for example, there were 1,229 case reports of acute

HCV. However, a full 447 or 36.37% of these case reports left the queries regarding risk behaviors and possible exposures unanswered. Indeed, only 513 or 41.7% of these cases identified one or more risk behaviors/exposures. Moreover, of the 782 reports that included risk factor responses, 269 or 34.4% indicated a 100% absence of known risk behaviors/exposures. Additionally, data were not disaggregated by race/ethnicity.<sup>40</sup> Thus, investigations allow CDC to link acute HCV rates with their causes and to determine the degree to which other persons from these same environments may be affected. These investigations may be as simple as interviewing the index patient or they may occur through more complex means. Nevertheless, the current paucity of data on risk behaviors/outbreaks illustrate a need to review and strengthen this area.

The NMA recommends the use of training and education to increase awareness of the importance of outbreak reporting as well as broad education about HCV risk factors, transmission, prevention, causes of serious liver disease, screening and diagnosis, and other topics. Local and state health departments may launch online marketing effort to increase use of their new tools for the support of hepatitis investigations. Measures are needed that ensure that race/ethnicity is always reported, as well.

Fourth, additional research is immediately needed that updates the Armstrong study.

Finally, existing data that are valid and reliable can be used to draw attention to the urgency of prioritizing HCV as a health issue. For example, Ly et al (2012)<sup>41</sup> found that there were 15,206 deaths from hepatitis C in 2007 but only 12,736 deaths from HIV infection. Thus, in 2007, an individual randomly selected was 18.6% more likely to die from HCV than from HIV. In addition, while CDC estimates that 1,148,200 persons age 13 and older are living with HIV infection, 3.2 million persons are living with HCV infection.<sup>42</sup> While CDC estimates that 207,600, or 18.1% of persons living with HIV are unaware of their infection, 75% of persons living with HCV do not know that they are infected. Broader publicity of these types of data is required to inform the public and healthcare communities of the urgency of programs to address HCV in general and strategies to decrease HCV racial/ethnic disparities.

## HCV: SCREENING AND DIAGNOSIS

Current guidelines also recommend HCV screening and diagnosis of the at-risk populations listed in Table 5.



## TABLE 5: PERSONS WHO SHOULD BE ROUTINELY CHECKED FOR HCV INFECTION

The more than 350,000 persons who currently receive hemodialysis<sup>43</sup> as well as those who have received hemodialysis in the past;

Children born to HCV-positive mothers (to avoid detecting maternal antibody, children should not be tested before age 18 months);

Persons with abnormal test results on the liver when tested for another reason;

All persons with HIV infection; and

Patients with signs or symptoms of liver disease; (e.g., abnormal liver enzyme tests).

Persons born between 1945 and 1965;

Injection drug users comprise 60% of all newly diagnosed cases of HCV;

Intranasal drug users;

Persons incarcerated;

Persons who engage in high-risk sexual behaviors including: multiple partners, sex with an HCV-infected person; having unprotected sex; or an injection drug user;

Persons with known exposures to HCV, such as:

- Healthcare workers after needle sticks involving HCV-positive blood;
- Recipients of blood or organs from a donor who later tested HCV-positive;

Source: CDC FAQs for Health Professionals, Last updated June 9, 2009 Available at <http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm>. Accessed 07/29/10.

The need for screening groups such as those listed is further highlighted by CDC's analysis of actual case reports from the Surveillance for Viral Hepatitis – United States, 2011. Table 6 reports findings on acute hepatitis C by risk factors.

## TABLE 6: REPORTED CASES OF ACUTE HEPATITIS C BY RISK FACTOR/EXPOSURE – UNITED STATES, 2011

Of the 646 case reports that had information about injection-drug use, 59.9% (n=387) noted use of these drugs.

Of the 624 case reports that contained information about occupational exposures, 1.4% (n=9) involved persons employed in a medical, dental, or other field involving contact with human blood.

Of the 564 case reports that had information about receipt of dialysis or a kidney transplant, 0.4% (n=2) indicated patient receipt of dialysis or a kidney transplant.

Of the 521 case reports that had information about surgery, 11.9% (n=62) were among persons who had undergone surgery.

Of the 525 case reports that included information about needle sticks, 9.0% (n=47) indicated accidental needle stick/puncture.

Of the 478 case reports that had information about number of sex partners, 31.4% (n=150) involved persons with ≥2 sex partners.

Of the 145 case reports from males that included information about sexual preferences/practices, 4.1% (n=6) indicated sex with another man.

Of the 116 case reports that had information about sexual contact, 12.9% (n=15) involved persons reporting sexual contact with a person with confirmed or suspected hepatitis C infection

Of the 116 case reports that had information about household contact, 6.9% (n=8) indicated household contact with someone with confirmed or suspected hepatitis C infection.

Source: CDC, National Center for HIV/AIDS/Viral Hepatitis, STD, and TB Prevention, Division of Viral Hepatitis, *Viral Hepatitis Surveillance*, United States, 2011

## Persons Born From 1945 to 1965: America's Most At-Risk Group

The CDC issued recommendations for birth cohort screening in 2012. The U.S. Preventive Services Task Force supported CDC's recommendation that healthcare plans and their providers offer one-time HCV testing to all persons in the age cohort 1945- 1965 in 2013.<sup>44</sup> The Consensus Panel strongly supports this recommendation and urges immediate compliance with this directive. Rein et al (2012)<sup>45</sup> suggest that birth-cohort rather than risk-based screening only, when combined with standard treatment for HCV-infected persons, can potentially prevent 82,300 deaths over the next several years and, as a result, generate cost-savings.

There are racial/ethnic disparities within the 1945 to 1965 cohort groups. As the data cited from the Armstrong study indicate, 9.4% of African Americans age 40–49 had been infected with HCV, but only 3.8% of Caucasians. Accordingly, African Americans in this age group were 136.8% more likely to be HCV infected. Thus, there is a particular need to monitor birth cohort screening utilization and impact on HCV case identification, morbidity, and mortality among African Americans.

## Injection Drug Users

As can be seen in Table 5, current practice guidelines recommend HCV screening for all persons who have injected illicit drugs at anytime, including those who are current users and those who may have injected substances only once or remotely in their lifetime. That is, this criterion is applicable to those whose injection drug use occurred decades ago as well as recently.

Data from the 2011 National Survey on Drug Use and Health revealed that in 2011, 426,000 Americans were heroin dependent.<sup>46</sup> This represents an increase of 18% from the 361,000 heroin dependent persons identified in 2010 and a 68.1% increase from the 214,000 heroin dependent persons in 2007.<sup>47</sup> This growth in the heroin dependent population suggests a critical need for greater access HCV testing through partnerships with treatment centers, homeless shelters, and other institutions that serve injecting drug users (IDU). Such partnerships can be used to expand HCV screening for IV drug users in general. The newly available rapid HCV antibody tests may be particularly applicable for testing difficult to access and transient populations such as IV drug users.

However, the Consensus Panel recommends that injection drug users as well as persons who have ever engaged in any drug use other than marijuana be considered high risk populations. As mentioned, the Armstrong study also discovered that “other drug users, except marijuana” had an HCV prevalence rate of 3.5% relative to 7/10 of 1% for persons who had no drug use or only marijuana drug use.<sup>48</sup> Thus, this group was 400% more likely to have an HCV infection than persons who did not use any drugs or who only used marijuana. This prevalence rate translated to an estimated 960,000 ever infected persons nationwide.

## HCV and Blood Transfusions

As is known, hemophilia and allied conditions, bleeding disorders secondary to platelet abnormalities, disseminated intravascular coagulation, and other conditions may require the use of clotting factor concentrates. If these products were received before 1987, pre-screening for HCV was not used. Thus, it is recommended that physicians introduce questions to their patients regarding receipt of blood clotting factor concentrates, blood transfusions, and solid organ transplants before 1987. These pre-screening questions will allow for primary care physicians to quickly and efficiently assess whether testing for HCV infection may be in order.

## Inmates of Correctional Facilities

Weinbaum, Lyster and Margolis (2003)<sup>49</sup> from the Centers for Disease Control and Prevention introduced startling evidence that supports the need to strengthen both HCV screening and treatment among current and past inmates. This study found that approximately 16% to 41% of persons in America's jails and prisons had been exposed to the HCV virus and 12% to 35% were chronically infected. Seven million persons entered, were retained, and/or left the criminal justice system *each year* during the latter years of the 1990s. These ex-inmates created a tremendous reservoir for the transmission of the HCV virus.

Spaulding and Thomas (2012)<sup>50</sup> indicate that during the current decade, more than 9 million persons enter and exit from jails and prisons each year. This criminal justice traffic further increases opportunities for the transmission of the HCV infection to the noninstitutionalized population. The Consensus Panel recommends that all persons be tested for HCV at admission and discharge from a correctional facility.

## Other Screening Issues

HCV screening is a less linear process than is the case for other medical conditions. For example, when HCV antibody screening is positive, it is also necessary to confirm HCV infection with an HCV RNA test and to identify HCV genotype (GT). Dias, Hahn, Delwart et al (2011),<sup>51</sup> in an analysis of HCV genotypes in a sample of 4600 persons with HCV infection, discovered that while HCV GT1 remained the most common among African Americans and persons born before 1970, this was not the case with young, HCV-infected persons nor with Caucasians. That is, other genotypes were observable in these subpopulations.

Similarly, HCV testing should be used in conjunction with screening to determine whether an HIV co-infection exists if HIV status is unknown. Hadigan, and Kottlilil (2011)<sup>52</sup> suggest that such screening is needed because the progression and manifestation of HCV differs when HIV/HCV co-infection exists. Since African Americans comprise 50.3% of all HIV- infected persons, dual screening is particularly important for this population.

These findings suggest that innovative programs and strategies are needed to increase HCV screenings. In

addition, the Consensus Panel recommends that existing community-based programs that serve at-risk sub-populations offer HCV education and screening to include homelessness programs, alcohol and other drug treatment programs, organizations that provide hemodialysis, programs to reduce risky sexual behaviors, and other services. Both clients and staff of programs for these at-risk populations require better education. Finally, Baby Boomers, America's most affected age cohorts, can be targeted through an intensive awareness campaign that drives them to access the one-time testing described in the June 2013 U.S. Preventive Task Force Recommendation Statement.

These recommendations are important especially when the sub-population of interest is African Americans. Trooskin, Navarro, Winn et al (2007),<sup>53</sup> in a study of 4,407 charts from four primary care sites, two community clinics, and two academically- oriented primary care practices in the City of Philadelphia, found significant racial/ethnic disparities in HCV screening. Specifically, no documentation was placed in the medical records for more than 80% of patients regarding whether they had ever engaged in injection drug use. Additionally, 95% of patients were not queried regarding whether they had ever received a transfusion. Interestingly, African Americans were more likely to have such information in their files than was the case with their Caucasian counterparts. However, when African Americans tested positive for HCV infection, they were less likely to be referred to a sub- specialist for treatment. Such findings indicate a need for physicians to be educated about HCV risk factors and screening guidelines.

## AFRICAN AMERICANS AND HCV TREATMENT

An examination of current literature reveals that HCV disparities also extend into the area of treatment. Jeffers (2007)<sup>54</sup> provides a comprehensive review of the literature on HCV treatment disparities for the period 1990–2005. A content analysis of the literature revealed that differential outcomes by race/ethnicity exist in several areas. First, the state of the infection at presentation and its progression over the life cycle may differ. Second, acute hepatitis C clears less often in African Americans rendering this sub-population subject to a higher chronicity rate. Third, African Americans are more likely to have conditions that contraindicate treatment. Fourth, African Americans are also less responsive to interferon-based treatment.

### African Americans and HCV Clearance Rates

Hepatitis C, like a number of other diseases, sometimes spontaneously clears. Seeff (2002)<sup>55</sup>, found that approximately 30% of persons with acute hepatitis C infection experience

spontaneous clearance. Thus, it becomes important to ask “Do racial/ethnic disparities exist in HCV spontaneous clearance rates?”

Thomas (2000)<sup>56</sup> found that natural clearance rates are approximately 36.4% in non-African Americans and 9.3% in African Americans. Thus, an HCV infection naturally clears 291.4% more often in Caucasians. Thomas subsequently reported that this difference is explained to a large extent by genetic variation in a single nucleotide polymorphism near the IL28B gene locus on chromosome 19 (2009)<sup>57</sup>. The IL28B SNP C/C genotype was associated with higher rates of spontaneous clearance but was significantly less frequent in African Americans than in Caucasians. Fifty-three percent of persons with the C/C genotype experienced spontaneous HCV clearance compared to 28% for persons with other genotype groups. When African Americans were found to fall within the C/C genotype group, their HCV viral clearance rates were also higher than African Americans in other genotype groups. The authors concluded that such findings suggest that the IL28B gene is a primary determinant of HCV clearance rates whether the clearance process is natural and/or medically induced.

Duggal, Thio, Wojcik et al. (2013)<sup>58</sup> also sought to identify a genetic basis for persons whose HCV infections did not spontaneously resolve. These researchers used a sample of 919 persons with spontaneous resolution, and 1482 individuals whose HCV infections persisted. They confirmed the hypothesis that biogenetic variables were operative. Chromosomes 19q13.13 near the IL28B gene locus and 6p21.32 around HLA class II genes had allele frequency variations that explained 14.9% and 15.8%, respectively, of the disparities in HCV resolution between African Americans and Caucasians.

Ge, Fellay, Thompson et al (2009)<sup>59</sup> conducted a study of HCV viral clearance after peginterferon and ribavirin treatment for HCV genotype 1. Variation in the frequency of the IL28B SNP C/C genotype could explain approximately 50% of the diversity in HCV clearance rates between African Americans and Caucasians after treatment. Again, further research is needed to address, more fully, the implications of differences in the treatment of HCV in African Americans as newer therapies emerge.

## TREATMENT EFFECTIVENESS: 2001–2011

Both the type of treatment and treatment effectiveness as measured by sustained viral response (SVR) have changed considerably over time. Table 7 describes this progress.



## TABLE 7: AN OVERVIEW OF CHANGES IN HCV TREATMENT

Year	Therapy	SVR
1991-1998	Standard IFN Monotherapy for 6 months IFN Monotherapy for 12 months	6% 16%
1998-2001	IFN+RBV for 6 months IFN+RBV for 12 months	34% 42%
2001-2011	PEG-IFN for 12 months PEG-IFN+RBV for 12 months	39% 59%
2011-present	Direct-acting antivirals+PEG- IFN+RBV	70%+
<b>Future Therapies</b>	<b>Therapies</b> Second generation HCV PIs  Nucleoside/ Nucleotides  Non-nucleoside/non-nucleotides polymerase inhibitors  Nonstructural protein 5a inhibitors  Novel IFNs  Cyclophilin inhibitors	<b>Expected Benefits</b> Higher SVR rates Fewer side effects including less anemia and neutropenia    Improved SVR rates in both treatment and treatment naïve patients   Other

Source: Constructed by NMA from data found in the following sources: 1) World Gastroenterology Organization Global Guidelines, Diagnosis, management and prevention of hepatitis C, April 2013, pg 14; 2) Yee HS, Chang MF, Pocha C; et al. Update on the management and treatment of hepatitis C virus infection: Recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program Office, *American Journal of Gastroenterology*. Jan. 2012, Vol 104, pgs. 51-2

A key question becomes, “Have these alternative pharmacologic approaches resulted in disparate treatment outcomes by race/ethnicity?”

While African Americans are often under-represented in the clinical trials used to assess the efficacy of HCV medications, a growing body of data suggests that disparity in treatment responses do occur by race. For example, during the time period 2001 to 2011 when weekly dosages of a PegIFN alfa- 2a(40kd) or PegIFN alfa-2b(12kd) in conjunction with oral RBV was the accepted standard of care for genotype 1 infection (the genotype that is most common in African Americans), SVR rates were lower than the 42-46% that prevailed among other treatment-naïve patients.<sup>60,61</sup> Indeed, research by Muir, Bornstein, and Killenberg (2004) confirmed lower treatment response rates for African Americans.<sup>62</sup>

In the VIRAHCP study Conjeevaram, Fried, Jeffers, et al (2006)<sup>63</sup> sought to re-assess previous findings that sustained virologic responses with peginterferon and ribavirin differed by race/ethnicity. This re-assessment was prompted by two factors: 1) the under-representation of African Americans in the initial clinical trials involving peginterferon and ribavirin treatment, and 2) the fact that two larger trials—Jeffers, Howell

et al, (2004)<sup>64</sup> and Muir et al (2004)<sup>65</sup>—were descriptive of racial/ethnic response rate disparities without an analysis of cause. VIRAHCP enrolled 196 African Americans and 205 Caucasians with HCV genotype 1 at multiple study sites and found a sustained virologic response of 52% for Caucasians and 28% for African Americans ( $P<.0001$ ). Thus, Caucasians with HCV were 85.7% more likely to achieve medication-based viral clearance than were their similarly treated African American counterparts.

Jin et al (2012)<sup>66</sup> analyzed outcomes for seventy-one (71) African Americans and 74 Caucasians who were infected with HCV genotype 1. Both groups of patients were highly adherent to both peginterferon and weight-based ribavirin. Nevertheless, the African Americans had significantly lower ribavirin plasma concentrations at weeks 1, 2, and 4 during treatment with peginterferon and ribavirin. A population pharmacokinetic study showed that the lower ribavirin exposure in African Americans was attributable to a larger volume of distribution. Another study by these authors revealed that African Americans were less likely than Caucasians to achieve the threshold ribavirin exposure levels associated with the SVR more common with peginterferon and ribavirin treatment. Their results

suggested that current weight-based ribavirin guidelines were not optimum for African Americans who appear to require a higher ribavirin dose. This may explain the lower efficacy of HCV protease inhibitor triple therapy for HCV genotype 1 in African Americans.

## TREATMENT SAFETY ISSUES: 2001-2011 AND BEYOND

While one primary treatment issue during the 2001–2011 period centered on treatment effectiveness as measured by response rates, another treatment issue was safety. That is, when testing revealed the presence of HCV infection, patients were referred for further evaluation and treatment by a provider with expertise in these areas to determine whether patients could be safely treated.

Melia, Muir, McCone, et al (2011),<sup>67</sup> using data from the Individualized Dosing Efficacy Versus Flat Dosing to Assess Optimal Pegylated Interferon Therapy (IDEAL) clinical trial, found that 40.2% (n=962), or 387 African Americans failed the screening evaluation. Only 28% of non- African American participants did so. African Americans were more likely than whites to be ineligible due to neutropenia (14% versus 3%,  $P < 0.001$ ), anemia (7% versus 4%,  $P < 0.02$ ), elevated glucose (8% versus 3%,  $P < 0.001$ ), and elevated creatinine (5% versus 1%,  $P < 0.001$ ).

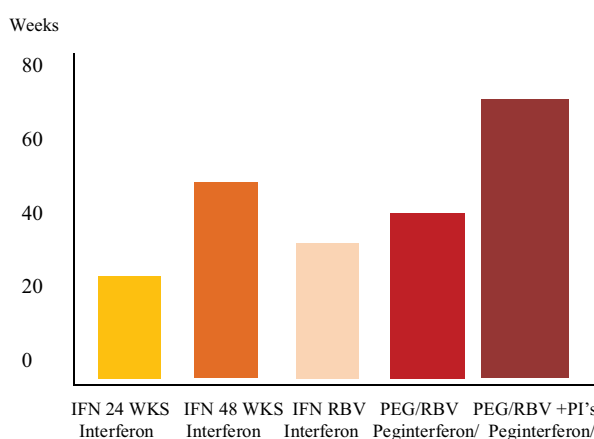
The constitutional neutropenia observed in African Americans has been identified as a barrier to participation in clinical trials of HCV with many studies excluding individuals with absolute neutrophils  $< 1500$ . To overcome this barrier, other studies have lowered the cut off to  $< 1200$  – without any apparent increase in adverse events during treatment. Thus, referral for further evaluation and management should not be denied due to neutropenia and other peripheral blood cyopenias (thrombocytopenia, anemia). Indeed, it may indicate more advanced liver disease and an even greater need for medical attention.

Howell, Jeffers, Cassidy et al (2006)<sup>68</sup> analyzed data from 78 African American patients with HCV genotype 1 infection. The pattern of medication complication was an interesting one. Careful medication monitoring resulted in dosage adjustments for peginterferon alfa-2a when neutropenia occurred in a proportion of those patients treated with ribavirin when anemia was diagnosed. However, the investigators concluded that this treatment met safety and tolerability standards when used with African Americans with HCV infections. Conjeevaram et al (2006)<sup>69</sup> also found no disparities in the incidence of dosage modifications, medication discontinuation and/or other safety issues as measured by the occurrence of adverse outcomes by race/ethnicity.

## HCV TREATMENT: 2011 AND BEYOND NEWER THERAPIES

In May 2011, the FDA approved the use of two HCV protease inhibitors plus PegIFN and RBV as the most recent combinations to be considered as the standard of care for all categories of HCV genotypes 1-infected patients who have already developed compensated liver disease. When data from clinical trials of these newer treatments are analyzed, it reveals that the SVR rates are significantly higher when all forms of triple therapy are used. Has the effectiveness of HCV treatment for African Americans as well as other populations been increased as a result of these newer therapies?

**TABLE 8: PROGRESS IN HCV TREATMENT: SVRS BY TREATMENT TYPE**



Source: Muir, Andrew, Consensus Panel Meeting Presentation, 2013

Research by Poordad, McCone, and Bacon (2011)<sup>70</sup> reveals that some of the newer therapies significantly affect SVR rates across a range of patient types. Using a double-blind study that included 938 non-African American participants and 159 African Americans, Poordad, McCone, Bacon et al. (2011),<sup>71</sup> assessed the impact of adding boceprevir to peginterferon alfa-2b and ribavirin upon treatment outcomes for persons with untreated chronic HCV genotype 1 infection.

In addition, this study—the Serine Protease Inhibitor Therapy 2 or Sprint-2 trial—also assessed whether altering the treatment period affected treatment outcomes as measured by sustained virologic response rate. Table 9 describes findings by race/ethnicity for each group.

**TABLE 9: THE IMPACT OF BOCEPREVIR UPON TREATMENT OUTCOMES BY RACE/ETHNICITY**

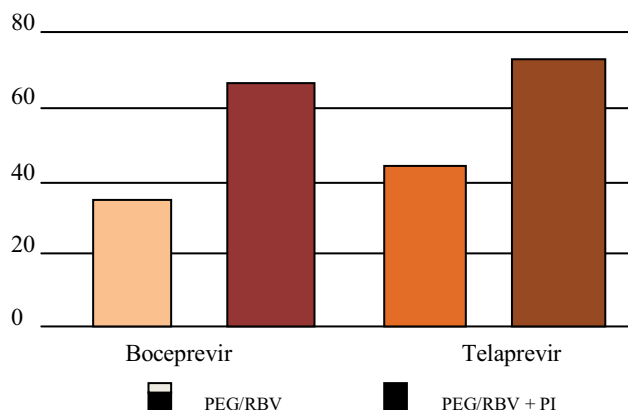
	Non-African Americans SVR	African Americans SVR
Group 1 (Control Group) Placebo+Peginterferon ribavirin for 44 weeks	40%	23%
Group 2 Boceprevir plus, peginterferon- ribavirin for 24 weeks	67%	42%
Group 3 Boceprevir+Peginterferon for 44 weeks	68%	53%

As Table 9 reveals, the addition of Boceprevir to the treatment regime has significantly improved sustained virologic response rates for non-African Americans and for African Americans. Although African American response rates remain lower than for their counterparts from other ethnic groups, the improvement in response rates has been greater for African Americans. For example, Group 3 had response rates that were 70% higher than Group 1 for non-African Americans. For African Americans, these response rates were 130.4% higher. The authors did not disaggregate data on adverse outcomes in this study by race/ethnicity.

Telaprevir, like boceprevir, is another of the new protease inhibitors that delivers improved outcomes (Liu et al. 2012)<sup>72</sup>. Table 10 compares response rates for boceprevir and telaprevir

As the above findings indicate, the use of both Boceprevir and Telaprevir in combination with PEG/RBV is associated with an SVR rate advantage. Table 11 describes outcomes from both boceprevir and telaprevir when mild and/or advanced fibrosis are present.

**TABLE 10: BOCEPREVIR AND TELAPREVIR SVR (%)**



Source: Poordad, F, Jacobson, IM, et al. NEJM 2011

**TABLE 11**

Strategy	SVR %
Base Case (boceprevir scenario)	
<b>Mild fibrosis</b>	
Standard Therapy	38
IL28B-guided triple therapy	57
Universal triple therapy	61
<b>Advanced fibrosis</b>	
Standard therapy	32
IL28B-guided triple therapy	48
Universal triple therapy	51
Telaprevir scenario	
<b>Mild fibrosis</b>	
Standard therapy	38
IL28B-guided triple therapy	63
Universal triple therapy	70
<b>Advanced fibrosis</b>	
Standard therapy	32
IL28B-guided triple therapy	54
Universal triple therapy	60

Source: Liu S, Cipriano, LE, Holodniy M, et al. New Protease Inhibitors for the Treatment of Chronic Hepatitis C: A Cost- Effectiveness Analysis. *Annals of Internal Medicine*, 2012 p. 285.

It is important to note that African American response rates also improved when Telaprevir was used in combination with PEG/RBV. The ADVANCE trials were designed to test the efficacy of the triple combination-TVV+PegIFN+RBV over three different regimens—8 weeks of TVR+24 weeks of PegIFN and RBV; 12 weeks of TVR+24 -48 weeks of



PegIFN and RBV; and PegIFN+RBV+placebo for 48 weeks. The response rates for all ADVANCE participants were 69%, 75%, and 44%. African Americans, like Caucasians, were most responsive to the 12 week treatment regimen. While Caucasians achieved an SVR of 75% relative to 44% for those receiving PegIFN/RBV+placebo, African Americans achieved a SVR of 62% relative to 25-33% for those who took PegIFN+RBV+placebo.<sup>73</sup> Thus, the response rate improved by 70.5% for all participants and 148% to 87.9% for African American trial participants.

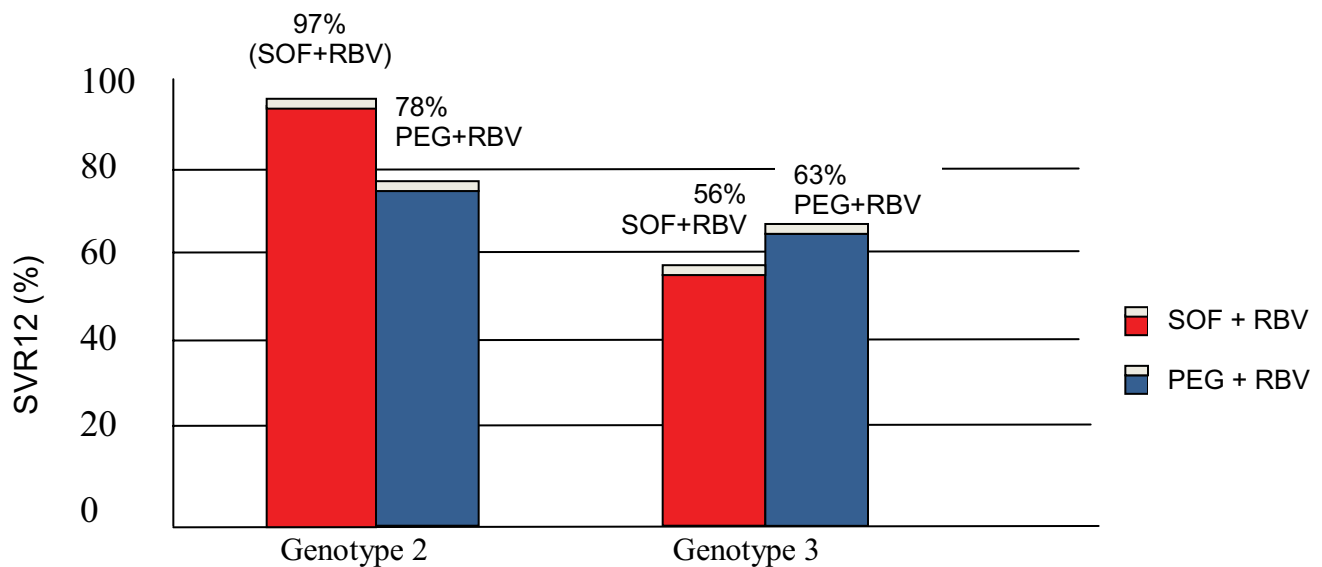
The results from Phase 3 trials have been even more encouraging relative to SVR rates. However, while African Americans, Latinos, and Asians were included in these studies at rates that roughly approximate their representation in the larger populations—15%, 11%, and 4% respectively, the baseline number of participants was so small that robust analysis is impossible.<sup>74</sup>

In general, the improvements in SVR rates with HCV protease triple therapies have been accompanied by an increase in frequency and severity of some side effects (notably anemia, neutropenia, dysgeusia, skin rash, anorectal symptoms). Fontaine, Hezode, and Dorival (2013),<sup>75</sup> identify some of these outcomes.

More research is needed that specifically assesses the impact of the triple therapy agents with African Americans. For example, Burton, Passarella, and McGuire (2012)<sup>76</sup> suggest that no reliable data are truly available on the impact of these newer agents upon African Americans because of their underrepresentation in the clinical trials for these important drugs.

In addition to the newer therapies for the treatment of genotype 1, newer agents are also being used in the treatment of genotypes 2 and 3.

**TABLE 12: SOF+RBV VS PEG+RBV BY GENOTYPE: FISSION STUDY SVR12 RESULTS**



Source: Gane et al, Abstract a5. EASL, April 2013; Lauritz et al., *N Engl J Med* 2013. DOI: 10.1056/NEJMoa121485383

Gane, Lawitz, Rodriguez-Torres et al (2013)<sup>77</sup> achieved superior SVR results for HCV infected persons with genotype 2 by combining Sofosbuvir with Ribavirin rather than by using PEG+Ribavirin alone. However, PEG+RBV maintained a slight advantage for those with genotype 3.

The Sofosbuvir/Ribavirin results were also superior to the Peginterferon Alfa- 2a/Ribavirin outcomes in terms of safety. Table 13 lists the data for key measures of safety.

**TABLE 13: SOF + RBV VS PEG + RBV: SAFETY SUMMARY**

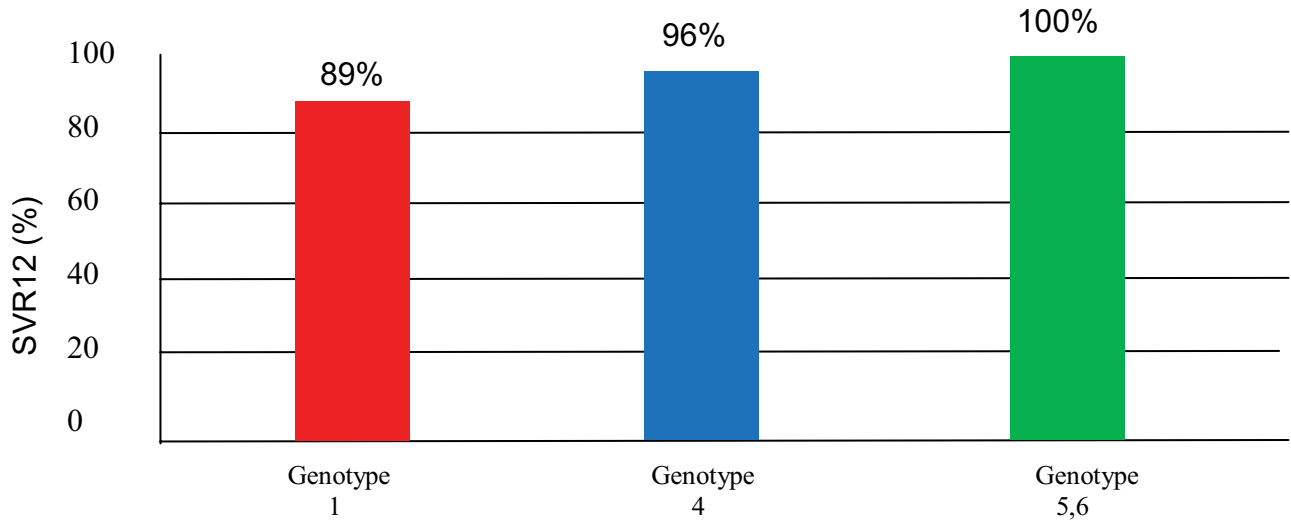
	SOF + RBV	PEG + RBV
Grade 3-4 adverse events	7%	19%
Serious adverse events	3%	1%
D/C due to adverse events	1%	11%
Hemoglobin <10 gm/dl	9%	15%
Neutrophils <750/mm <sup>3</sup>	0%	15%
Platelets <50,000/mm <sup>3</sup>	0%	7%

Source: Gane et al, Abstract 5. EASL, April 2013; Lauritz et al., *N Engl J Med* 2013<sup>83</sup>

The Neutrino Study also assessed outcomes associated with Sofosbuvir + Peginterferon + Ribavirin over a twelve-week treatment cycle for HCV-infected persons with genotypes 1, 4, 5, or 6. Lawitz, Wyles, Davis et al (2013)<sup>78</sup> found that

Sofosbuvir is highly effective with genotypes 4, 5, and 6 as well as with genotype 1. However, greater African American inclusion in clinical trials for these and other newer therapies is needed.

**TABLE 14: SOFOSBUVIR/PEGINTERFERON + RIBAVIRIN OUTCOMES BY GENOTYPE**



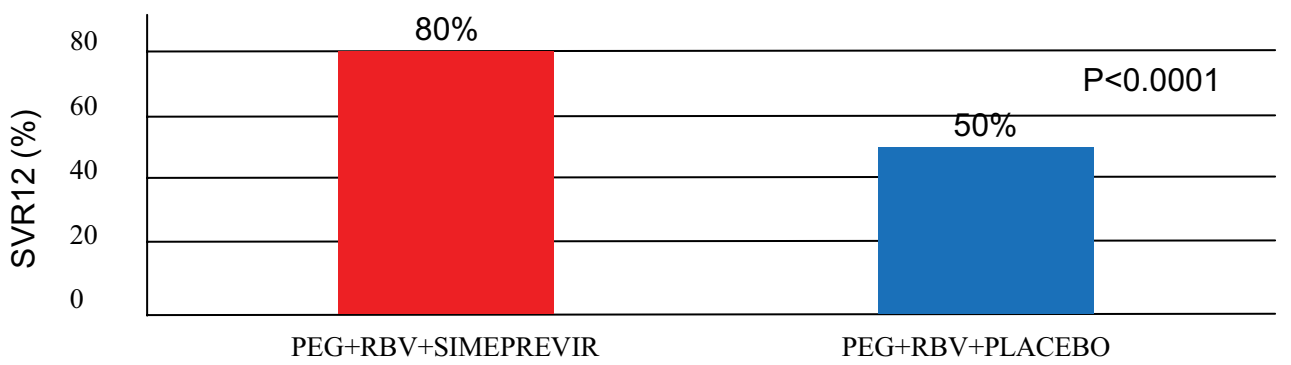
Source: Jacobson IM, Dore, Jacobson IM, Dore GJ, Foster GL, Fried MW, Radu M, Rafalskiy VV, Moroz L, Craxi A, Peeters M, Lenz O, Ouwerkerk-Mahadevan S, Kalmeijer R, Beumont-Mauviel M, Simeprevir (TMC435) with peginterferon/ribavirin for chronic HCV genotype 1 infection in treatment naïve patients: results from QUEST-1, a Phase III Trial *EASL* 2013 85

Again, because this clinical trial was specific to genotype 1, it has relevance for African Americans. However, African Americans were poorly represented in these trials.

Ferenci, Asselah, Foster et al (2013)<sup>80</sup> assessed the impact of the next generation PI, Faldaprevir, in combination with pegylated interferon alfa-2a and ribavirin versus PEG/RBV alone. As Table 16 indicates, patients treated with Faldaprevir combination had higher SVR12 rates.

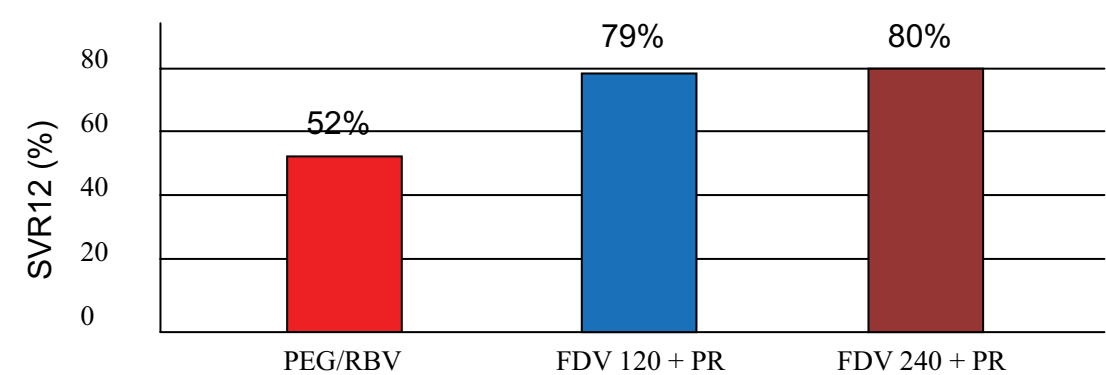
Vachon (2011)<sup>81</sup> describes these medications as ushering in a new era. The need for adequate representation of African Americans in the clinical trials of the new agents is a pressing one because of the absence of data on these outcomes that is specific to African Americans. (For example, only Caucasians and Asians were used in the clinical trials for Faldaprevir).

**TABLE 15: COMPARING SVR12 RATES BY PEG+RBV+SIMEPREVIR VS PEG+RBV+PLACEBO**



Source: Jacobson IM, Dore, Jacobson IM, Dore GJ, Foster GL, Fried MW, Radu M, Rafalskiy VV, Moroz L, Craxi A, Peeters M, Lenz O, Ouwerkerk-Mahadevan S, Kalmeijer R, Beumont-Mauviel M, Simeprevir (TMC435) with peginterferon/ribavirin for chronic HCV genotype 1 infection in treatment naïve patients: results from QUEST-1, a Phase III Trial *EASL* 2013<sup>85</sup>

TABLE 16: PEG/RBV VS FALDAPREVIR (FOV)120 + PR AND FALDAPREVIR (FOV)240 + PR



Source: P. Ferenci et al, Abstract 1416. EASL, April 201386

The ATLAS Study (2010)<sup>82</sup>, revealed positive results based upon the use of oral danoprevir (RG7227) in combination with PEGIFN-2a+ribavirin. Flisiak, Pawlotsky, Crabbe et al (2011)<sup>83</sup> analyzed the impact of alisporivir (DEB025) as a triple therapy. Gane et al (2010)<sup>84</sup>, in the INFORM-1 trial, combined a nucleoside polymerase inhibitor and danoprevir and had encouraging results.

## HCV AND AFRICAN AMERICANS: MORBIDITY AND MORTALITY ISSUES

Disparities not only exist in HCV treatment outcomes, but in the progression to liver disease and/or to primary hepatocellular carcinoma and liver-related mortality. Davila (2006)<sup>85</sup> and Sloane et al (2006)<sup>86</sup> identify some of the disparities. Table 17 describes a few of the trends that have existed over the years.



## TABLE 17: A SAMPLE OF DISPARITIES IN HCV MORBIDITY AND MORTALITY

### Disparities: Primary Hepatocellular Carcinoma

HCV incidence increased by 200% from 1975-2000.

Incidence rates and mortality rates for hepatocellular carcinoma are 200% higher in African Americans.

African Americans and Hispanics are more likely to have HCV as a risk factor for hepatocellular carcinoma.

African Americans have more advanced HCV tumor stage at diagnosis.

African Americans are less likely to receive local or surgical (resection, liver transplantation) therapy than Caucasians, even with tumors that are localized to the liver.

### Disparities: Liver Transplantation for HCV: 2002-2006

Liver disease is more severe when African Americans are placed on the wait list. This is a barrier to referral.

However, there are no differences in removal from the waitlist because of death or because the patient is too sick for a transplant.

There are no racial/ethnic differences in receiving a liver transplant within three years.

African Americans are more likely to undergo a transplantation for HCV but less likely to have a live liver donor.

African Americans have lower survival rates after transplantation. However, these differences are abolished by adjusting for the higher MELD score and older age.

Liver graft loss is more frequent in African Americans.

African Americans are more likely to have recurrent HCV and allograft rejection as causes for graft loss than Caucasians.

African Americans with graft loss are less likely to undergo repeat liver transplantation.

### Disparities: HCV Deaths: 2012

Deaths from HCV now exceed those from HIV infection. African Americans are more likely to die from HCV (Ly et al, 2012)<sup>87</sup>

Source: Davila JA, El-Serag HB. Racial differences in survival of hepatocellular carcinoma in the United States: a population-based study. *Clin Gastroenterol Hepatol*. 2006;4 (1:104-110).<sup>79</sup>

Sloane D, Chen Hegang, Howell C. Racial disparity in primary hepatocellular carcinoma: tumor stage at presentation, surgical treatment and survival. *J Natl Med Assoc*. 2006;98(12):1934-1939. <sup>80</sup>

Other differential trends also exist regarding African Americans and HCV. As indicated, HCV and HIV co-infections are more likely to exist among African Americans. Murphy, Herrmann, Osinusi, et al (2011)<sup>88</sup> sought to reduce the emergence of liver fibrosis that occurs in HCV/HIV co-infected patients by intensifying the dosages of both peginterferon and ribavirin. The treatment appeared to slow the progression to liver fibrosis without increasing side effects. However, the authors emphasize the need to assess, more carefully, the risks of double dosing through a carefully

designed clinical trial. The need for such a study is important since Rodriguez-Torres et al (2012)<sup>89</sup> found that no changes occurred in responsiveness when African Americans in their clinical trial — the Progress Study — were exposed to intensified peginterferon alfa-2a plus ribavirin dosages.

In addition to HIV/HCV co-infection, African Americans are also more likely to have co-occurring diabetes, and/or conditions that correspond to pre-diabetes. Mukhtar, Ayala, Maher et al (2013)<sup>90</sup> identified a pre-diabetes prevalence rate

of approximately 70% for Latinos, 12% for Caucasians, and 50% for African Americans in a sample of 97 HCV-infected persons. The recognition of both pre-diabetes and diabetes is important because these conditions can affect treatment responsiveness. Jin et al. (2012),<sup>91</sup> in a study of the use of weight-based dosaging for ribavirin, also found that the level of insulin resistance affected SVR rates.

In addition to diabetes mellitus and other conditions, sickle cell disease also affects the progression of both HCV and HIV infection in African Americans. Nouraie, Nekhai, and Gordeuk (2012)<sup>92</sup> analyzed 423,481 records to characterize how sickle cell affects the progression of HIV, HBV, and HCV infection. HIV prevalence rates were lower among persons with sickle cell. However, HCV and HBV infection rates were higher. In addition, HIV progressed more slowly in persons with sickle cell disease.<sup>93</sup>

All racial/ethnic disparities in HCV do not, however, disadvantage African Americans. Sarkar, Bacchetti, French et al (2012),<sup>94</sup> utilizing data from the women's interagency HIV study (WIHS), found that while it is true that African Americans are disadvantaged relative to natural HCV clearance rates and overall responsiveness to HCV treatment, the progression of liver fibrosis may be slower for African Americans. This pattern was observed among African American women co-infected with HIV/HCV who participated in this study. Despite slower liver fibrosis progression, African Americans with chronic HCV have worse outcomes relative to Caucasians, especially an increased incidence of primary HCC and a higher liver-related mortality rate.

End stage renal disease (ESRD) and HCV frequency co-occur. Thus, a natural question becomes: "Is the presence of ESRD associated with more rapid progression to severe liver fibrosis in patients with chronic HCV?" Aslinia, et al (2012),<sup>95</sup> in a cross-sectional study, compared African Americans and Caucasians with HCV infection and ESRD with HCV-infected persons without ESRD. HCV participants in the study with ESRD had a higher probability of being African American. However, these racial/ethnic disparities did not extend to liver damage. While HCV-infected persons with ESRD had lower overall likelihood of advanced liver fibrosis, African American ethnicity was independently associated with a lower probability of liver fibrosis in the sample.

This trend—a slower liver fibrosis progression and less cirrhosis—was also identified by Kohla, Iwata, Ea, et al (2012).<sup>96</sup> Using a multi-ethnic sample of 692 HCV-infected participants, these researchers found that approximately 53% of Latinos, 35% of Caucasians, 29% of Asians, but only 19% of African Americans in the sample had liver cirrhosis. Thus, African Americans with HCV infection had a lower prevalence rate of cirrhosis when the data were adjusted for duration of disease, alcohol, obesity, and other risk factors.

One issue that such data raise is that of the markers used for liver fibrosis and/or cirrhosis. Curto, Lagier, Lok, et al (2011),<sup>97</sup> for example, conducted research to determine whether a

cirrhosis risk score (CRS) with 7 single nucleotide polymorphisms is an accurate predictor/measure of fibrosis and/or cirrhosis. This study found that, indeed, this measure was valid and reliable across racial/ethnic groups.

In contrast, Zeremski, Dimova, Astemborski, et al (2011)<sup>98</sup> assessed the validity of CXCL9 and CXCL10 chemo-kines as measures of liver fibrosis in African Americans with HCV infection. This research was novel since in the past, these markers had been primarily applied to Caucasian patients. The results suggested that CXCL10 can be appropriately applied with African Americans with HCV infection. These studies suggest that the findings regarding lower progression of liver damage in African Americans may be considered as valid.

The aspartate aminotransferase to platelet ratio index (APRI) is also a marker of fibrosis and cirrhosis. Burton, Sunesara, Penman, et al (2011)<sup>99</sup> studied the utility of the APRI score to predict liver fibrosis and cirrhosis for African American and Caucasian veterans. There were no significant differences in the performance of the APRI between the two racial/ethnic groups. The utility of other biomarkers of liver fibrosis has not been studied in African Americans.

## REDUCING HCV MORBIDITY AND MORTALITY AMONG AFRICAN AMERICANS: FINDINGS AND RECOMMENDATIONS

The literature on HCV infection and racial/ethnic disparities is extensive. Moreover, despite methodological factors that can lead to the underestimation of HCV prevalence and incidence rate disparities, it appears that racial/ethnic differences in treatment outcomes exhibit greater reliability. While several of the identified disparities in liver fibrosis progression may favor African Americans, ongoing disparities in screening and diagnosis, treatment, and treatment outcomes are highly significant given that HCV mortality rates among African Americans exceed those of their Caucasian counterparts.

Indeed, when cirrhosis and/or hepatocellular carcinoma occurred in African Americans in the past, African Americans were disadvantaged relative to the receipt of a liver transplant. Moylan, Brady, Johnson, et al (2008)<sup>100</sup> in an analysis of data from the United Network for Organ Sharing Liver Transplantation waiting list, found that previous disparities in access to a liver transplant actually decreased when a policy change resulted in the adoption of an alternative approach to the distribution of available livers. This change—the introduction of the Model for End-Stage Liver Disease (MELD) score—demonstrates that some disparities in HCV morbidity and mortality are remediable. However, challenges remain.

Moylan and colleagues reported that African Americans were listed for transplantation less frequently than the burden of the disease would suggest. Once patients are listed, the disparities no longer exist, but African Americans do not have appropriate access to the liver transplant list. In addition, current research also indicates that the problem of lower 5-year survival rates for African American HCV-infected patients who receive liver transplants, can be addressed through the use of racially matched donors. However, such a strategy is not practical at this time.

Hernandez and Jeffers (2009)<sup>101</sup> completed an analysis that revealed that 15- year graft survivor rates in African American recipients of kidneys from Caucasian donors were significantly lower than with racially matched donors/recipients for HCV-infected persons. Moreover, no differences were observable when the graft recipient was HCV negative. This suggests a need to increase the number of African Americans who sign donor cards and hold family discussions. Such findings also raise the question central to the Consensus Panel process, “What types of programs, policies, and initiatives are needed to reduce HCV-related morbidity and mortality in the African American community?”

As the review of the literature demonstrates, the issues complicit in disparate HCV morbidity and mortality rates among African Americans not simple. In this section, key findings from the Consensus Panel are summarized and recommendations regarding their remediation are presented.

## Finding #1: There is a Need for Increased HCV Awareness

While accurate estimates are unavailable, the most reliable data reveal that at minimum, four million Americans nationwide are HCV-infected and 75% or 3.2 million Americans have a chronic HCV infection. Moreover, the CDC reports that approximately 75% of those with HCV infections are unaware of their condition.<sup>102</sup> Thus, there is an urgent need for an enhanced effort to increase awareness of hepatitis in general, and HCV in particular.

### Recommendations

The U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, has produced a large number of pamphlets and other materials regarding hepatitis. Because a recent study (Allison-Ottey, 2013)<sup>103</sup> revealed that few patients are familiar with the different types of hepatitis and the risks associated with hepatitis B and C, a massive educational campaign is needed that uses CDC’s informational tools to educate the public about HCV.

Allison-Ottey (2013)<sup>104</sup> completed an assessment of patients’ knowledge, perceptions and personal actions surrounding the issues of HCV. Utilizing a sample of 287 patients interviewed during routine visits to their primary care providers, an urgent need for increased HCV awareness was revealed. The sample

consisted of 62% African Americans, 28% Caucasians, and 10% Latinos. Significantly, 24% or 69 of the participants had never heard of hepatitis. Moreover, of the respondents who had heard of this infectious disease, 59.29% did not know that hepatitis was linked to liver disease. Additionally, of those who had heard of “hepatitis”, 52.1% had not heard of HCV.

Equally significant, while 24% of the participants were age 50–59, an age group that is solidly situated within the 1945–1965 age cohort group, 80.6% of respondents had never been tested for hepatitis, 14% of those who had been tested were positive, and a full 64% of those tested never returned to discover their status.

The survey particularly demonstrated the need for the recently launched campaign to promote HCV testing since 48% of the patients surveyed answered “No” to the query, “Would you like to be tested?” Culturally crafted messages may be able to reverse this position.

Moreover, the survey revealed that physicians can change the attitudes of the public towards getting tested. Almost all of the 287 respondents indicated that they would take an HCV test if their physician requested it of them. However, the fact that 92% of participants said they would be more likely to get tested if they could do so in their physicians’ office suggests a need for more physicians to conduct in-office testing. The availability of a rapid HCV test greatly facilitates in-office testing.

This recommendation is also consistent with research which indicated that physician offices may be perfect dissemination sites for HCV educational materials whether through videos or printed materials. This conclusion is based upon the fact that 93.9% of the respondents reported that they want to know more about HCV. The need for this education was demonstrated by the fact that 87.1% of respondents believed that one cannot get cancer from HCV. Such findings do, indeed, confirm the need for increased distribution of information resources to the public.

However, the Consensus Panel recommends that these materials be tested to ensure concordance with African American culture, values, and attitudes. According to the National Center for Education Statistics, approximately 14% of Americans and 24% of African Americans are functionally illiterate.<sup>105</sup> The Consensus Panel’s findings also reveal that persons with less than a high school education are at greater risk of illicit drug use and, as a result, HCV.

Therefore, the two-page fact sheets available at <http://www.cdc.gov/knowmore/hepatitis/media/factsheets.htm> may need to be pre-tested to determine whether they are appropriate for less educated individuals. It is important that these materials be tested with those African Americans who are at greatest risk of HCV.

## Finding #2: Accelerate Current Efforts to Improve Accuracy of HCV Prevalence and Incidence Data

While efforts are critically needed to increase awareness of HCV, an immediate need also exists to remediate the underestimation of the magnitude of HCV. Multiple data collection problems exist that support HCV under-estimation.

### Recommendations

Two primary data sources are currently used as a basis for assessing the prevalence and incidence of HCV. CDC's National Health and Nutrition Examination Survey (NHANES) is used to determine the prevalence of HCV. However, several factors associated with this survey may contribute to underestimation. First, NHANES only sampled America's non-institutionalized population. As a result, some of the country's higher risk populations for HCV are excluded, i.e., prisoners, the homeless, military personnel and veterans, and others. Second, while NHANES began continuing annual surveys in 1999, findings from more recent NHANES data collection on the prevalence of HCV are not annually reported.

CDC's more updated publication, *Viral Hepatitis Surveillance*, reports dated NHANES data. Thus, the Consensus Panel recommends that the Centers for Disease Control and Prevention create annual updates on HCV prevalence rates using the yearly NHANES data that are continuously collected. Even more important, we recommend that NHANES 2005-2010 data be immediately analyzed so that new findings can be baselined against the original study.

Third, the NHANES dataset does not allow a comprehensive disparity analysis for its reports. HCV infection estimates are provided for Caucasians, African Americans, and Mexican Americans only. Native Americans, Asians/Alaskan Natives, and others, have high rates of HCV infection. The Consensus Panel recommends that the NHANES survey be expanded to include these other groups.

Fourth, in addition to the NHANES dataset, which estimates HCV prevalence, the CDC National Notifiable Disease Surveillance System (NNDSS) estimates the incidence of HCV and other types of hepatitis using case reports from state and local health departments. This dataset may underestimate HCV for several reasons. First, more federal funding is needed to ensure that surveillance is comprehensive, complete, and accurate. The Consensus Panel also recommends that adequate federal funding be provided to local health departments, state health departments, and other sites to support accurate data collection. The Consensus Panel also recommends that the National Notifiable Disease Surveillance System include electronic checks for out-of-range variables, completeness and other electronic steps associated with the verification and validation of data at the point of submission. Such strategies

are commonly used by data analysts and/or statisticians as part of the data cleansing process.

Fifth, as is known, the NNDSS is not structured for the collection of data on past or present hepatitis C. Thus, the Consensus Panel recommends that CDC continue its detailed analysis of its current HCV surveillance processes and redesign these steps to enhance accuracy.

Sixth, CDC applies statistical modeling in order to express actual cases reported to CDC as incidence rates. As a part of the conversion process, adjustment modifiers are applied to each confirmed HCV case. The Consensus Panel recommends that the adjustment multipliers be revised, and that CDC's Division of Viral Hepatitis consider whether the adjustment multipliers used should be separately specified by race/ethnicity.

Seventh, the Consensus Panel is particularly concerned that the CDC's 2010 funding decisions regarding enhanced viral hepatitis surveillance sites failed to include Washington, D.C.; Atlanta, Georgia; the State of Mississippi; Detroit, Michigan; and/or other localities with large numbers and percentages of African Americans. We recommend that new enhanced viral hepatitis surveillance sites be immediately added. In addition, the Consensus Panel proposes that additional training of surveillance personnel be provided so that instances of missing data on case reports can be minimized. As discussed, race/ethnicity is missing on more than 50% of CDC's case reports.

## Finding #3: The Need to Reduce or Eliminate Under-Diagnoses of HCV

The need to more accurately estimate the prevalence and incidence of HCV is intimately related to screening and diagnosis. The Consensus Panel made a number of recommendations that can result in greater numbers of HCV-infected persons entering into treatment for this condition.

### Recommendations

A number of strategies that can reduce HCV under-diagnosis remain underfunded. At the first level, the NMA 2013 HCV Consensus Panel endorses CDC recommendation of one-time screenings for persons born between 1945 and 1965. With a roster of 30,000 African American-serving physicians and other health professionals, NMA can do much to ensure that one-time age cohort testing is implemented.

Equally important, with the availability of rapid HCV tests, the Consensus Panel recommends that physicians, nurses, and other health care professionals bring HCV screening out of their offices and into those non-traditional settings where high-need populations reside. We also suggest that public funding be made available to support such a strategy.



# Finding #4: Provide Training on HCV to Current and Future Health Providers

The study by Allison-Ottey (2014)<sup>106</sup>, On Assessing Patient Knowledge, Perception, and Personal Actions Regarding Hepatitis C, also revealed that healthcare providers need more HCV training. Thus, in the companion study, Allison-Ottey (2013)<sup>107</sup> identified the HCV training needs of African American physicians and other health professionals. Study participants felt that HCV must be advanced on the agenda of health issues currently being addressed in America, and that there is a need for improve levels of patient and provider education and awareness.

The providers who were a part of the research recommended use of the following strategies and tools: 1) Media outreach; 2) Community outreach and screening; 3) Online materials; 4) Patient information dissemination at provider sites; 5) An increased number of continuing education programs; 6) Discussions with practitioners; 7) An increased number of articles in academic journals and magazines; and 8) Direct mail.

The study also revealed that physicians want to increase their HCV screenings, but many are unaware of in-office tests that can be used. Thus, an immediate need exists for physicians to be educated on HCV screening and diagnosis including the use of rapid HIV tests.

Physicians also require education on prevention and early detection, and on the new updated treatments. Participants also reported that practice guidelines require updating so that providers can be compensated by insurance companies for making routine HCV screening panels available to persons born during the years 1945 to 1965.

## Train Physicians on the Benefits of Rapid HCV testing

Recent and future advances in the diagnosis and treatment of HCV increase opportunities to test and treat patients. The initial screening test for HCV detects the presence of antibodies (Ab) to HCV to evaluate exposure to the hepatitis C virus. In February 2011, the FDA approved the first point of care test for detection of HCV infection in at-risk individuals. The simple platform enables healthcare providers to deliver a diagnosis based on lab-accurate test results in 20 minutes using venipuncture or fingerstick blood. More recently, this test also received CLIA-waived status and can now be administered in physician offices, clinics, and public health facilities, allowing for immediate discussion with HCV positive patients about follow-up testing and care.

Primary care physicians and/or emergency department staff serve as primary points for increasing HCV screening. While primary care physicians are positioned to inquire about risk factors and/or to suggest one-time screening for the 1945–1965 age cohorts, emergency room personnel have access to

the homeless, persons with IV drug overdoses, persons with HCV/HIV co-infections, the uninsured, and insured persons without a medical home.

However, these health care professionals may need training on the screening guidelines for HCV as well as training on how and when physicians can use the latest HCV practice guidelines to address the unique needs of African American patients. The Consensus Panel recommends that the steps listed in Table 18 be taken.

## TABLE 18: EDUCATING MEDICAL PROFESSIONALS REGARDING HCV SCREENING AND DIAGNOSIS

NMA will:

- Include HCV trainings and HCV updates at its national and local meetings;
- Provide HCV screening and diagnosis training to all health care professionals including those who work in medical labs;
- Advocate for medical schools to include more modules on HCV as part of the medical training;
- Distribute HCV training tools for use by its national, regional, and local chapters;
- Train physicians to use HIV screening, diagnosis, and treatment processes that are modeled after protocols that have successfully increased HIV screening and led to decreased mortality rates;
- Train physicians to take sexual histories without being judgmental and to maintain literature and posters on HCV and other sexual issues at all times;
- Develop an HCV app for physician phones and other communication devices that includes an algorithm for screening and diagnosing HCV;
- Include information on the billing codes for various HCV-related diseases; and
- Schedule webinars and/or teleconferences on HCV.

## Other Physician Training Issues

There are key content areas that must be included in physician training modules to support reductions in HCV.

Physician training regarding HCV must cover core primary prevention issues, i.e., risk reduction; counseling the high need individuals whom they treat; directives to all patients to avoid direct exposure to blood and to refrain from the sharing of personal care or home therapy items that may transfer blood; information on the importance of covering cuts and sores; data that reinforces the urgency of engaging in safe sex; and other topics. Similarly, physician training will need to address medical management topics such as: 1) referral of patients who test positive for HCV infection to alcohol and other drug abuse programs as co- medical homes; 2) greater collaboration across medical providers so that co morbid diseases such as obesity, HIV, fatty liver disease, diabetes mellitus, chronic kidney disease or end-stage renal disease, and other conditions can be better managed; 3) screening for primary liver cancer in cirrhosis; 4) remaining current on non-invasive markers of liver fibrosis; and 5) other topics.

Physicians will require training on how to determine which patients are optimum candidates for treatment, how to manage the disproportionately high numbers of African Americans who deny treatment, and on the use of quality indicators. These are key content areas that must be included in physician training modules to better support reductions in HCV.

## **Finding #5: There is a Need for the Greater Inclusion of African Americans in Clinical Trials**

The Consensus Panel recommends that NMA expand its intensive training to prepare even more physicians serving African American communities to participate in clinical trials. Whether the topic for consideration is oncology or HCV, a recurring theme is that of increasing minority participation in clinical trials. While training to increase physician participation in clinical trials research has been used, NMA has disproportionately centered its training on patient recruitment in the past. While patient recruitment is important and strategies are needed which send electronic alerts to health care providers about ongoing and new HCV clinical trials, a more intensive supply-side strategy is also required. Beginning at the level of medical training, a greater emphasis upon research design and statistical analysis is needed so that more African American physicians will have the tools needed to participate in clinical research. At the level of medical schools, relationships with pharmaceutical companies can begin to be built. Medical professionals who graduate with a greater knowledge base in ethno-pharmacology across medical specialties will be better prepared to participate in clinical trials. The intensive recruitment of African American patients into clinical trials is more effective when culturally concordant researchers are a part of a key team.

The Consensus Panel recommends that the described efforts be combined with other strategies such as those listed in Table 19.

## **Finding #6: Increase Access to Care and Treatment for HCV-Infected Persons**

Whether the health issue is HCV and/or another health area, access to care and treatment has been linked to identifiable disparities in screening, treatment, and treatment outcomes. Therefore, the Consensus Panel supports enhancing access to care and treatment for persons with HCV infections and co-infections.

### **Recommendations**

Given the aggressive processes currently underway for the implementation of the Patient Protection and Affordable Care Act, the Consensus Panel recommends that NMA support the enrollment of populations at high risk of HCV into an insurance plan under the Affordable Care Act. For example, IV drug users are disproportionately represented among persons with HCV infections. IV drug use correlates with homelessness, unemployment, and other circumstances that affect access to income and, as a result, health care. Given these intricate relationships, the Consensus Panel recommends that all providers train at least one person on staff to directly provide benefits establishment, and/or link uninsured patients to organizations that engage in benefits establishment. Through this process, Medicaid and/or Medicare-eligible patients can be linked with public insurance and other patients can acquire private insurance through the Exchanges. This service will pay for itself through reductions in uncompensated care.

It is also important to note that the Exchanges that have been created as part of the Affordable Care Act may not be a point of access for some HCV-infected persons. The Exchanges serve only persons whose incomes are 33% to 300% *above* the federally defined poverty line. However, expanded Medicaid coverage as proposed under the ACA will support and advance access to care and treatment for large numbers of persons who are at risk of HCV.

Yet, even with insurance, additional actions may be needed to: 1) implement birth-cohort screening and continue risk- based screening among high-risk populations; 2) monitor persons tested so that they obtain their results; 3) motivate those who test positive to accept treatment if eligibility screening reveals that they are eligible for treatment; 4) report symptoms that suggest that treatment may be having an adverse effect; and 5) complete the entirety of the physician-recommended treatment schedule.

The Consensus Panel recommends that family members of persons who are HCV-infected solicit a person to serve as a peer mentor to accompany the patient to appointments, serve as a point of triangulation for scheduled appointments, and become an overall guardian who ensures that the access provided through the ACA is fully utilized. The implementation of such strategies is important. Stein,

## TABLE 19: OTHER STRATEGIES TO SUPPORT THE INCREASED OVER-REPRESENTATION OF AFRICAN AMERICANS IN HCV CLINICAL TRIALS

Urge regulatory authorities to review clinical

trial requests and approvals within the context of the degree of inclusion of minorities when the illness or disease involves disparate rates of morbidity and/or mortality.

Educate the scientific community and pharmacies about the most recent findings regarding HCV and African Americans so that they can disseminate information regarding clinical trials.

Hire a social media campaign team to target high need populations on how to access clinical trials.

Conduct new clinical trials in communities with large numbers of African Americans.

With each encounter with an HCV-infected person, review their medical records to determine: 1) whether the individual's treatment needs recommends their inclusion in a clinical trial; 2) whether a clinical trial is recruiting that is a match for the patient's needs; and 3) how that individual's inclusion in an appropriate clinical trial can be facilitated.

The inclusion of lower thresholds for the neutrophil count in eligibility criteria for clinical trials can increase representation in HCV trials since current findings indicate that this can be safely done.

Maintain an electronic database of MDs and/or PhDs from various practice settings with the training and background needed for participation in current and upcoming HCV clinical trials.

Increase the awareness of the public about the urgent need for HCV medications that includes greater all-phase representation of African Americans.

Schedule a meeting with the Congressional Black Caucus and present the Consensus Panel's findings with an identification of the exact support needed by Congressional representatives.

Negotiate with the Food and Drug Administration to require the mandatory reporting of drugs with disparate minority outcomes to treatment providers.

Continue NMA's practice of sponsoring community outreach programs that explain clinical trials to the African American community. However, for HCV, target these outreach programs to those sub-segments of African Americans who are at high risk.

Engage in advocacy with the FDA to request Phase IV commitments for upcoming new HCV drugs.

NMA experts involved in HCV clinical trials can develop community-based participatory research projects.

Anderson, Robertson, and Gelberg (2012),<sup>108</sup> in a sample of uninsured homeless person in Los Angeles, found that 43% of clients tested positive for HCV and 72% of this group did not know that they were HCV-infected. However, medical visits were significantly *less* likely among those persons who tested positive for HCV.

### Finding #7: Hepatitis C in the Criminal Justice Population Needs to Be Addressed

Spaulding, Seals, McCallum et al (2011),<sup>109</sup> in a study of 15½ year survival rates for persons imprisoned in the State of Georgia, found that mortality during their prison years was relatively low, but post-release mortality was higher than for their age cohorts who had not been imprisoned. Moreover, HIV, cancer, and cirrhosis were variables that contributed

to post-release deaths. Research such as these findings re-emphasize the need for specialized strategies to address the HCV needs of incarcerated persons.

### Recommendations

Latimer, Hedden, Floyd et al (2009)<sup>110</sup> analyzed data from injection drug users from the City of Baltimore with "...a life-time history of jail or correctional facility incarceration." Interestingly, HCV was 200% higher among the incarcerated Caucasians than among African Americans. Additionally, the overall rate of sero-positivity was 260% higher among the incarcerated than the general population. Within the ranks of those incarcerated, the HCV infection rate was 740% higher among prisoners who had used injection drugs for five years or more relative to those who had engaged in injection drug use for less than one year. Given these and other findings, the NMA 2013 HCV Consensus Panel makes the recommendations in Table 20.

## TABLE 20: RECOMMENDATIONS REGARDING HCV AND THE INCARCERATED

Mandatory HCV screening for all persons in jails or prison upon entry.

Revise prison and jail intake sheets so that long-time injection drug users, persons with

HIV/infection, and other very high-risk groups can be identified.

All persons incarcerated should be screened for HCV upon release and provided HCV education and linkages to treatment.

A curriculum that is specifically targeted towards the criminal justice population is needed. This multi-media curriculum should include video-lessons, and exercises for group discussions so that the varying literary levels of the inmates do not reduce educational effectiveness.

Create linkages with in-custody and post-custody programs for the criminal justice population and provide the HCV curriculum to them for use in their programs.

Collaboration between the Congressional Black and Hispanic Caucuses, and the Directors of Federal and State prisons to identify and address unique barriers to screening and treatment for prisoners is needed.

Federal, state, and local officials should review their jails and prisons and assess the adequacy of resources for treating those with HCV infection and co-infections.

Urge the Department of Justice to provide funding to conduct new research, data collection, and analyze HCV screening, care, and treatment in jails and prisons.

## Finding #8: Increase Monitoring of Outcomes of HCV Screening

DiBisceglie et al (2000)<sup>111</sup> tracked the natural progression of HCV infection and found that approximately 15% of acute phase HCV infections naturally resolved while 85% became chronic. Of those who became chronic, approximately 20% developed into cirrhosis within approximately fifteen years after the initial infection. Of those persons whose HCV progressed to cirrhosis, 6% developed end-stage liver disease and 4% experienced hepatocellular carcinoma. Thus, approximately 50% of those with cirrhosis required a liver transplant and/or experienced death. The five-year survival rate for those with hepatocellular carcinoma was less than 5%. Such detailed monitoring and tracking allows a patient to experience maximum treatment. However, monitoring of this type on a patient-by-patient basis is uncommon. The presence of co-occurring illnesses and risky lifestyles can further truncate the progression. Thus, there is a need for greater monitoring of outcomes associated with HCV.

### Recommendations

Research introduced earlier indicates that African Americans are less likely to have their HCV detected at an early stage. They are also less likely to know they are infected, less likely to accept treatment, less likely to respond to treatment, and more likely to have co-occurring illnesses/ diseases. The Consensus Panel recommends that medical professionals utilize electronic medical records to track and monitor the outcomes of African Americans infected with HCV. This monitoring data can be combined with other data and, through statistical analysis, used to better understand HCV's progression patterns among African

Americans. The Consensus Panel proposes that NMA organize a team to pursue funding to create a demonstration that tests the impact of improved monitoring on HCV outcomes.

## Finding 9: There is a Need to Analyze and Apply New Treatments

There is a need to understand the promises and challenges that are implicit to new treatments and new treatment approaches. This need is significant since the current standard of care for treatment is less effective in African Americans. Remaining current is a requirement in many fields. Medical professionals must manage challenging schedules while addressing the highly critical need to remain current on new treatments and treatment approaches. This is particularly true for primary care physicians who provide medical homes for IV drug users, the homeless, Baby Boomers, the incarcerated, persons with co-occurring disorders, and other groups at high risk for HCV infection. Indeed, because the standard treatment of HCV requires knowledge of HCV genotypes, treatment algorithms, risks of treatment, and other clinical issues, remaining aware of new treatment approaches is critical. In addition, primary care physicians who provide a medical home for HCV-infected patients also need knowledge of community linkages to whom referrals for nonmedical services can be made.

Although specialists manage the overall treatment process, the primary care physician must remain current regarding the challenges, potential benefits, and side effects of the newer triple treatments that are being used in order to increase treatment responsiveness. In this regard, the Consensus Panel makes the recommendations listed in Table 21.



## TABLE 21: REMAINING CURRENT ON THE PROMISES AND CHALLENGES OF NEW TREATMENT AND TREATMENT APPROACHES

Maximize use of electronic, digital media, and social networking to remain current on new treatments.

Explore new service delivery options associated with HCV such as the development of liver clinics in very high-risk areas.

Review sample sizes, data collection processes, and overall designs of research on new treatments and treatment approaches to ensure the robustness of the findings.

While this Consensus Paper has focused upon race/ethnicity, there is also a need to analyze and respond to gender disparities that exist in terms of HCV screening and diagnosis, treatment, and treatment outcomes.

### Recommendations

Data from the CDC, Division of Viral Hepatitis, *Viral Hepatitis Surveillance*, United States, 2011, reveal that males remain at higher risk of past and present hepatitis. Thus, there is a need to design and implement gender-specific primary and secondary prevention programs.

For example, Ufearo, Kambal, Onojobi et al (2010)<sup>112</sup> analyzed HCV seropositivity among 143 African American males and females who regularly used alcohol. The results of this study indicated that African American women in the study had a higher rate of HCV seropositivity than did the males—29% vs. 23%. Accordingly, the Consensus Panel recommends that more researchers disaggregate their work by gender so that the unique needs of both African American males and females can be characterized.

## HCV AND AFRICAN AMERICANS: THE ROLE OF CURRENT AND PROPOSED POLICIES

The described findings and recommendations are far from exhaustive. However, these recommendations comprise an agenda that will guide NMA's HCV implementation process

over the next year. Utilizing these recommendations, NMA and its membership will schedule meetings, distribute press releases, submit funding proposals, and establish partnerships to ensure that this Consensus Paper serves as an action plan for change. This action will necessarily include advocacy in support of policy. A number of current and proposed policies hold promise as tools for reducing HCV disparities in the African American community. This section briefly outlines the Consensus Panel's recommendations regarding current and/or proposed initiatives.

### The Patient Protection and Affordable Care Act

Passed in March 2010 after a number of modifications and adaptations, the Patient Protection and Affordable Care Act holds tremendous promise as a tool to contain and reduce HCV infections. First, it expands Medicaid coverage and in doing so, it will allow more Americans in general, and more African Americans in particular, to access health insurance. However, advocacy is needed with the Centers for Medicare and Medicare Services (CMS) to make one-time HCV screening a core health service for all Medicaid beneficiaries who embody multiple HCV risk factors.

Second, the Patient Protection and Affordable Care Act also allows behavioral health providers to serve as a medical home for persons with substance use disorders and/or mental health disorders. Because traditionally defined primary care providers are not equipped to provide treatment to IV drug users, a primary risk group for HCV, the Consensus Panel recommends that IV drug users maintain their substance abuse and/or mental health treatment providers as their medical home while receiving HCV treatment through the coordinated care and case management services which medical professionals are urged to provide under this law that is currently being implemented.

### Expanding Hepatitis C Legislative Awareness Days to Other Communities

In addition to the National Hepatitis Day every May, the NMA 2013 HCV Consensus Panel recommends that advocates for HCV issues organize hepatitis C Days in all states with large numbers of at-risk populations. As a part of this activity, elected officials and their staff can be briefed on key issues.

### Syringe Access Programs

Syringe access programs for IV drug users have been controversial since their origins. The Consensus Panel urges activists to increase support for syringe access as part of the effort to reduce HCV.

### S2750-2013: Requiring Hospitals to Offer Hepatitis C Tests

The Consensus Panel fully supports Bill Number S2750. This highly critical Bill makes the offering of HCV testing mandatory for hospitals, primary care providers, clinics, and others who treat persons born between 1945–1965.

### The Viral Hepatitis Testing Act of 2011

The Viral Hepatitis Testing Act of 2011<sup>113</sup> provided \$25,000,000 in funding for fiscal year 2012, \$35,000,000 for fiscal year 2013, \$20,000,000 for fiscal year 2014, and \$30,000,000 for fiscal years 2015–2016 combined. This funding will be used to improve Viral Hepatitis Testing. However, to date, African American health institutions have not participated fully in this grant program. The Consensus Panel recommends that NMA monitor this effort and encourage more minority applicants.

## SUMMARY

The use of Consensus Panels in the field of healthcare is quite common. Moreover, the deliverables produced by these panels of experts have, over time, contributed much to spur and provide direction to policymakers, researchers, community-based organizations and other entities. Through the 2013 HCV Consensus Paper, the National Medical Association has committed its staff, resources, membership, and partners to active participation in transforming the described recommendations into actions that will result in saved lives.

# END NOTES

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