August 8, 2012

Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
c/o
Scientific Resource Center, Oregon EPC
Mail code: BICC
3181 S.W. Sam Jackson Park Road
Portland, Oregon 97239-3098

Re: AHRQ Comparative Effectiveness Review on Adherence to Hepatitis C Treatment Interventions

On behalf of approximately 200 organizations representing the chronic viral hepatitis community, the National Viral Hepatitis Roundtable (NVHR) thanks the Agency for Healthcare Research and Quality (AHRQ) and the Oregon Evidence-Based Practice Center (EPC) for the opportunity to comment on its draft Comparative Effectiveness Review on Adherence to Hepatitis C Treatment Interventions. The NVHR appreciates AHRQ’s decision to focus this systematic review on the benefits and harms of treatment adherence interventions for adults receiving combination antiviral therapy for chronic hepatitis C (HCV). We agree with AHRQ that such reviews form the foundation of evidence-based practice and improve the applicability of study findings to clinical practice. We also thank AHRQ for its commitment to transparency and for the value it places on broad stakeholder input.

Societal Impact of Chronic Hepatitis C

As AHRQ knows, the societal impact of HCV is far-reaching. HCV is the most common chronic blood-borne infectious disease in the U.S., with 2.7 to 3.9 million persons living with the infection. In the absence of treatment, up to 40% of these individuals may develop liver cirrhosis or liver cancer. At a time when most cancers are on the decline, rates of liver cancer have tripled over the last several decades, and in the decade to come, mortality rates are expected to increase ten-fold, with more than 150,000 Americans dying from viral-hepatitis associated liver cancer or end-stage liver disease. Viral hepatitis also remains the leading cause of liver transplantation in the U.S.

The aging of the baby boom population is of particular concern to our community since they account for 80% of all Americans infected with chronic HCV. If immediate attention is not paid to this aging population, it may pose a significant threat to Medicare and the healthcare system as a whole. The NVHR supports the Centers for Disease Control and Prevention’s (CDC) recently updated HCV screening guidelines, which includes one-time HCV testing for all adults born between 1945 and 1965. We hope that the broader healthcare community will further improve future HCV screening rates by adopting similar policies targeting high-risk individuals.
General Comments on AHRQ’s Comparative Effectiveness Review

Goals of the Study

The NVHR appreciates that the report sets out to gather data on both the intermediate and final health outcomes related to antiviral therapy treatment adherence interventions. The NVHR finds great value in studies that evaluate final health-related outcomes—such as HCV-morbidity, mortality, and quality of life—and we support follow-up periods that account for longer-term health outcomes. We also recognize the benefit of studying intermediate outcomes. The FDA’s recent approval of protease inhibitors to treat chronic HCV infection, as well as future regimens currently under development, make issues such as sustained viral response, resistance, and side effects increasingly important. The NVHR welcomes AHRQ’s attention to these issues.

Study Results

The NVHR supports the report’s conclusion that the strength of the current evidence is low and that more adequately powered and rigorously conducted RCTs are needed to test HCV adherence interventions on intermediate and health outcomes, as well as in genotype-1 patients receiving a triple therapy. We are especially pleased that AHRQ highlights the limitations of cohort studies, including their susceptibility to selection bias and challenges accounting for unknown prognostic factors, versus the more optimal randomized controlled trial (RCT). At the same time, we appreciate AHRQ’s recognition of instances in which cohort studies may prove more valuable than RCTs, including the collection of longer-term outcomes data, such as cirrhosis and hepatocellular carcinoma, through patient registries.

While the identification of gaps in current research helps point to areas of future investment, it also signifies the large amount of work that still needs to be done in this field and the continuing lack of conclusive evidence regarding best practices. Therefore, we caution the public and private sector against using this report or the data it contains for payment decisions. All too often in healthcare we see inappropriate interpretations and applications of weak evidence. For example, data on specific hepatitis screening strategies remains spotty and inconclusive, yet is often relied on by insurance companies, which limits our ability to identify patients in need of treatment and to control infection rates.

Future Research

While it is unfortunate that the current set of available data on this topic is poor and of limited focus, we are grateful that AHRQ calls attention to the need for additional investments in high quality research on this topic by pointing out gaps in the evidence. Just about every clinical trial currently has a component that evaluates adherence, yet adherence is rarely, if ever the primary focus of these studies. We call on the healthcare community as a whole, including larger health systems and public and private payers, to invest in this work. In fact, we view research on adherence to HCV treatment interventions as an ideal priority for funding under the newly created Patient-Centered Outcomes Research Institute (PCORI).

The current lack of data also points to more inherent challenges. The field of adherence research related to HCV is largely underdeveloped and often fails to recognize that problems with treatment adherence are often the result of side effects and other problems associated with drug therapy. For example, most studies to date are limited in that they evaluate compliance...
with the full dose prescribed, which results in inaccurate classifications of non-adherence among patients who follow a physician’s order and take less than the recommended dose because of side effects such as anemia. The NVHR supports AHRQ’s call for future studies that clearly distinguish between physician-initiated dose-reduction and discontinuation from true patient non-adherence. We also encourage public health researchers, working with the hepatitis community, to be more forward thinking and to develop more accurate, but also more standardized instruments, methodologies, and definitions to measure intervention adherence and outcomes in both clinical trials and real world settings. Adherence research related to other disease states and interventions is more fine-tuned, and policymakers and researchers may find helpful models in the fields of chemotherapy drugs, HIV treatments, and TB treatments. Again, we believe the development and evaluation of more innovative and standardized methodologies and definitions for HCV treatment adherence research would be an ideal target for PCORI funding given its great potential to advance public knowledge and improve patient care.

As AHRQ and the healthcare community consider future study strategies, the NVHR urges it to consider other complementary domains. For instance, we view retention in care and management of comorbid conditions (e.g., the use of concurrent treatments) as natural extensions of the adherence research agenda since these factors may further interfere with treatment adherence.

Conclusion

The NVHR appreciates your consideration of our comments. We are a strong supporter of evidence-based medicine and believe that the best available evidence should inform all healthcare decision-making. When properly understood and applied, evidence-based medicine enhances the overall quality of care, benefiting both the healthcare system and our patients. The NVHR looks forward to working with AHRQ and its EPC network to develop a stronger evidence base regarding hepatitis C treatment adherence interventions and to presenting the results of these studies in a format that is easy to understand for patients, caregivers, and healthcare providers.

Should you have specific questions about our comments, please feel free to contact Martha Saly, Director of the NVHR, at 707-242-3333 or mbsaly@nvhr.org.

Sincerely,

Martha Saly
Director
National Viral Hepatitis Roundtable