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Health Disparities in Liver Disease:

Time to Take Notice and Take Action

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Health disparities between various groups in the United States have received increasing attention over the past decade, and solving this problem has become a major public health priority. The Federally-sponsored *Healthy People 2010*, our nation's health promotion and disease prevention initiative, calls to "eliminate health disparities, including differences that occur by gender, race or ethnicity, education or income, disability, geographic location, or sexual orientation" (1). These health disparity populations constitute a large proportion of patients with liver disease (2,3), and evidence suggests that these populations are disproportionately affected by several common hepatic disorders that include viral hepatitis (4-7), non-alcoholic fatty liver disease (8,9), and hepatocellular carcinoma (10-13). Health disparities, therefore, have special relevance to the field of hepatology. This policy statement aims to inform the hepatology community about the importance of health disparities in our field, provide a framework for approaching health disparities in research and clinical practice, and recommend ways the AASLD and its membership can work toward the reduction and elimination of health disparities in patients with liver disease.

The importance of health disparities to liver health

As acknowledged in *Healthy People 2010*, health disparities have become one of the nation's most pressing public health concerns. The Institute of Medicine's groundbreaking report "Unequal Treatment", that described significant disparities in health between various groups in the United States, was a call to action in the medical community (14). Commitment to improving health disparities is shared by many organizations including the Centers for Disease Control and Prevention (15), the Department of Health and Human Services (16), many academic and community medical centers, as well as professional, political, philanthropic, and patient organizations. Furthermore, numerous health care systems and payers, including Centers for Medicare and Medicaid Services and private insurers, are placing increasing emphasis on quality care initiatives, including the promotion

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of health equity. In December 2008, the National Institutes of Health (NIH), which shapes our nation's research agenda and scientific funding priorities, convened a Health Summit *The Science of Eliminating Health Disparities* to address the best ways to integrate "science, policy, and practice" to solve this growing problem (17). Taken together, these examples underscore the mounting professional, political, payer and public support of programs to reduce health disparities.

Multiple definitions of health disparities exist in the literature and in practice (18,19). Broadly defined health disparities are "clinically and statistically significant differences in health outcomes or health care use between socially distinct vulnerable and less vulnerable populations" (20). A more specific definition is provided in the Minority Health and Health Disparities Research and Education Act of 2000 (21):

> "[a] population is a health disparity population if there is a significant disparity in the overall rate of disease incidence, prevalence, morbidity, mortality or survival rate in the population as compared to the health status of the general population."

In order to optimize our understanding of health disparities, we must be mindful that there are many determinants of health beyond access to and provision of health care. Studies suggest that the provision of health care accounts for only a small proportion of an individual's overall health state (22,23). Genetics, the external and social environment, socioeconomic status, education and literacy, cultural norms, and personal behavior all contribute powerfully to an individual's health (22). Thus, health disparities can occur due to differences between groups in any of the aforementioned determinants. The World Health Organization Commission on Social Determinants of Health recently issued a report describing the important role social and environmental factors have in shaping health inequity worldwide (24). Moreover, an in-depth assessment of the non-medical contributors to health status in the United States is currently being undertaken by the Commission to Build a Healthier America sponsored by the Robert Wood Johnson Foundation (25). Hence, public policy as it relates to non-medical determinants of health can strongly influence the propagation or elimination of health disparities.

Health disparity populations traditionally derive from groups that have been disadvantaged or underserved, and are often referred to as "vulnerable populations" (26). The *Healthy People 2010* agenda is inclusive of many such patient groups, including those that differ by gender, race, ethnicity, sexual preference, geography, or socioeconomic status. Patients who are uninsured or underinsured, and thus lack adequate access to health care (27), represent a growing vulnerable patient population. The AASLD's mission statement recognizes the importance of socioeconomic influences on health outcomes by ensuring "the provision of liver health care to all Americans, regardless of ability to pay" (28). However, as discussed above, health disparities will persist even with equalization of access to health care. This further highlights that there are multiple causes of health disparities other than medical care, including genetic, behavioral, cultural, environmental, and social determinants.

Health disparities have been described for diverse liver diseases (2,3), including viral hepatitis (4-7), nonalcoholic liver disease (8,9), and hepatocellular carcinoma (10-13), which together account for the greatest burden of liver disease facing hepatologists today (29). Indeed, a recent review article in this journal by Nguyen and Thuluvath provides a comprehensive overview of racial and ethnic disparities in liver disease (2). Disparities due to socioeconomic status -- regardless of race and ethnicity -- have also been demonstrated for important hepatic risk factors such as injection drug use (30), obesity and diabetes (31). Our goal in this article is not to provide an extensive overview of health disparities in liver disease; but rather we hope to emphasize the substantial impact of health disparities on the field of hepatology and highlight their special importance to our organization.

Promotion of an integrated and multidisciplinary approach to addressing health disparities

Partnership between researchers, clinicians, public health workers, payers, policymakers, philanthropic organizations, and patients is imperative to achieve a thorough understanding of when and why disparities exist, and to develop and implement programs to reduce health disparities. The NIH roadmap espoused by Elias Zerhouni, former NIH Director, focuses on three research funding initiatives to improve the nation's health: 1) *new pathways to discovery*, 2) *research teams of the future*, and 3) *reengineering the clinical research enterprise* (32). The NIH roadmap emphasizes pre-translation or fundamental scientific research (which we will term T0 research), upon which diagnoses, treatments, and prevention can be based; phase 1 translation (T1) research, which transfers fundamental scientific knowledge to health applications; and phase 2 translation (T2) research, which determines the value of health applications to establish evidence-based guidelines. This approach to improving health by concentrating on T0, T1, and T2 research is echoed in the National Institute of Diabetes and Digestive and Kidney Diseases' Action Plan for Liver Disease Research (33).

However, to address health disparities, T0, T1, and T2 research pathways are necessary but not sufficient. Improvements in health, and therefore reductions in health disparities, will require extension of the NIH roadmap to include T3 and T4 translation pathways (Table 1). Phase 3 translation (T3) research studies delivery, dissemination, and diffusion of evidence-based guidelines into health practice (34), and phase 4 translation (T4) research assesses health outcomes of T1 and T2 health applications in actual practice (35). Bench to bedside research (i.e., T0, T1, and T2) allows for understanding the underlying biologic and genetic differences between groups and for developing targeted therapeutics and novel diagnostics. In parallel, bedside to community research (i.e., T3) is necessary to move proven health interventions to clinical practice. Finally, to address the problem of health disparities it will also be necessary to determine the effectiveness of diagnostics and treatments in 'real world' clinical settings, and to evaluate how interactions between the patient, provider, and healthcare system affect health outcomes (i.e., T4).

The importance of this continuum of translation research is mirrored in several proposed models for approaching health disparities in research and clinical practice (16,20,26). Since health disparities result from a complex interplay of medical and non-medical factors, these models recognize that an integrated, interdisciplinary approach is required. A useful framework adapted from Kilbourne and colleagues is presented in Table 2 (20). The key steps in this approach include: 1) measuring and identifying health disparities, 2) investigating and understanding the causes of disparities, and 3) developing, implementing, and evaluating interventions aimed at reducing disparities. In the past, health disparities research has largely focused on documenting that disparities exist; however, emphasis must be placed in the future on understanding the causes of disparities and implementing programs aimed at their reduction.

Case study in health disparities research: hepatitis B virus control in Alaska Natives

Hepatitis B virus is a major public health concern worldwide, and the disease is concentrated in several high risk groups in the United States, including foreign born immigrants and Alaska Natives (4-6,36). The remarkable success over the past four decades of the hepatitis B virus control program in Alaska serves as a superlative example of the effectiveness of a multidisciplinary approach to addressing health disparities.

Although the symptoms, signs, and complications of hepatitis B virus had been well-recognized for hundreds of years, it was only after fundamental scientific advances in T0 research -- including blood protein analysis, immunology, and virology -- that efforts to manage hepatitis B virus could begin (37). These pre-translation research discoveries permitted the development of key clinical applications. The identification and characterization of the Australia antigen (38), now known as the hepatitis B surface antigen (HBsAg), permitted creation of the first diagnostic test for hepatitis B virus (39-41). With improved understanding of immunological responses and the pathobiology of hepatitis B virus, T1 research advances were made including the creation and application of a successful vaccine (42). Elucidation of hepatitis B virology allowed development of effective treatments that include interferon and several nucleotide and nucleoside analogs (43). Clinical trials with these medications and the development of clinical guidelines to treat hepatitis B virus are excellent examples of T2 applications in this field (44,45). As illustrated here in the advances realized in the diagnosis, prevention, and treatment of hepatitis B virus, T0, T1, and T2 research play an important role in improving health care and provide an essential foundation for T3 and T4 research pathways.

These scientific discoveries allowed epidemiologists and clinicians to begin to measure the burden of hepatitis B virus in diverse populations in the United States that included Alaska Natives. Although this population is in fact racially diverse, from a functional standpoint they represent a distinct health disparity population based on socioeconomic, environmental and geographic factors (46). Epidemiologic surveys, done by applying the newly available HBsAg radioimmunoassay, demonstrated that a disparity existed in Alaska Natives in the incidence and prevalence of hepatitis B virus and its complications, as compared to Caucasians in the United States or to other non-Alaska Native American populations (47,48). Researchers also documented an increased incidence of hepatocellular carcinoma (HCC) with a higher mortality rate among Alaska Natives when compared to the overall population (49,50). The measurement of these differences in incidence, prevalence, and outcomes brought about efforts to identify the causes of the disparities and to develop programs aimed at their reduction.

Identification of the causes underlying the increased disease burden in Alaska Natives included elucidation of differences in viral transmission as compared to other populations. Studies in Alaska Natives showed that child-child transmission was a major form of infectivity in Alaska as compared to other parts of the world where vertical transmission dominated (36,51). Knowledge of the unique infection patterns and geographic distribution of hepatitis B in different Alaskan communities helped officials design and implement a comprehensive vaccination program in the early 1980s to control transmission of hepatitis B virus (51). Extensive effort and partnership between health workers, researchers, and the community was required to make this program a success. Studies have shown that the prevalence of hepatitis B virus in Alaska Natives born after program implementation dropped to nearly zero (52,53). Another aspect of this comprehensive program included population-based surveillance for HCC in chronically infected individuals using serial alpha fetal protein (AFP) measurements (54). This program has resulted in increased survival from HCC over a 16 year follow-up period as compared to a historical cohort (55). The promising results shown here in reducing disparities through T3 and T4 based studies and interventions underscore the importance of identifying the factors contributing to observed differences and implementing programs that address population specific trends and needs.

Recommendations for action

Health disparities are a growing public health imperative and an important problem within the field of liver disease. As illustrated in the case of hepatitis B virus disparities in Alaska

Natives, an integrated, multidisciplinary partnership between basic scientists, clinical and health services researchers, practitioners, public health workers, policy makers, payers, and patients is an effective approach to the complex challenge of identifying, understanding, and reducing health disparities in liver disease. The AASLD and its membership have the opportunity to take action to reduce health disparities and improve health for vulnerable patient populations with liver disease. With these goals in mind, the Public Policy Committee will:

1. Work toward organizing a multidisciplinary program at the Liver Meeting® (e.g., focused study group, mini-symposium, or workshop) to establish priority areas in liver health disparities that should be targeted for future study and intervention.
2. Support the AASLD's development of funding for basic science, clinical, and health services research that specifically addresses health disparities in liver disease.
3. Advocate for vulnerable patient populations to receive adequate private, local, and federal support for access to liver health care and enrollment in clinical trials.
4. Encourage the education of hepatology trainees and practitioners about health disparities and how to provide culturally sensitive and language appropriate health care.

These recommendations mirror the goals and mission of the AASLD (56). Hence, we propose that these recommendations be considered for adoption by the AASLD for implementation through its member committees, including basic research, clinical research, NIH liaison, practice guidelines, public policy, scientific program, and training and clinical policy. Efforts to understand and eliminate health disparities in patients with liver disease are essential to achieve the AASLD's vision, "to prevent and cure liver disease."

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List of Abbreviations

(AASLD)	American Association for the Study of Liver Disease
(NIH)	National Institute of Health
(T0)	pre-translation research
(T1)	phase 1 translation research
(T2)	phase 2 translation research
(T3)	phase 3 translation research
(T4)	phase 4 translation research
(HBsAg)	hepatitis B surface antigen
(HCC)	hepatocellular carcinoma
(AFP)	alpha fetal protein

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Table 1

Bench-to-Bedside Research Pathways

Pre-translation (T0) research	elucidate pathogenesis and pathophysiology of disease
Phase 1 translation (T1) research	seeks to move a basic discovery into a candidate health application
Phase 2 translation (T2) research	assesses the value of T1 application for health practice leading to the development of evidence-based guidelines
Phase 3 translation (T3) research	attempts to move evidence-based guidelines into health practice, through delivery, dissemination, and diffusion research
Phase 4 translation (T4) research	seeks to evaluate the “real world” health outcomes of T1 and T2 applications in practice

Modified from Zerhouni (31), Westfall (33), and Khoury (34).

Table 2

Systematic Approach to Health Disparities Research

Steps	Goals	Research Pathways
Measurement of disparity	Document differences in incidence, prevalence, natural history, and outcomes	Epidemiologic and patient centered research
Identification of causes of disparity	Determine social, environmental, biologic, cultural, and behavioral contributors	Basic science, clinical, health services, and qualitative research
Implementation of programs to reduce disparity	Develop interventions in academic and community hospitals, health centers, physicians offices, communities, public health and public policy venues	Clinical trials and health services research
Evaluation	Debrief on intervention effectiveness	Health services and qualitative research

Adapted from Kilbourne et al (19)