Purpose
The purpose of the NASH Council is to shine a spotlight and coalesce an expanded set of stakeholders, in addition to hepatology, around the urgency of developing mechanisms for quantifying and addressing the silent epidemic of fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) in the U.S. and abroad. Current estimates are that as many as 1 in 4 people already have NAFLD or NASH yet these conditions are underrecognized, underdiagnosed, and undertreated.

Objectives
1. Create a common understanding of the health and economic impacts of NASH
2. Understand current clinical management and ongoing research
3. Identify methods to increase public and private awareness
4. Identify public and private approaches to addressing NAFLD and NASH (which may include):
   - Innovative broad-based screening
   - Alignment with/inclusion in current efforts to reduce obesity and diabetes/pre-diabetes
   - Increase nutritional options uptake
   - Medical education
   - Public and patient education

Chairs
Wayne Eskridge
Founder, Fatty Liver Foundation
Anna Mae Diehl, MD
Florence McAlister Professor of Medicine, Duke University School of Medicine

Marko Korenjak, Vice President, European Liver Patients Association, Donna Cryer, JD, GLI President and CEO, and Wayne Eskridge, President and CEO, Fatty Liver Foundation

A full list of attendees, agenda, letter of support, patient stories, and NASH Facts can be found in Appendices 1-5.
I. Welcome
Global Liver Institute President & CEO Donna R. Cryer, JD opened the inaugural NASH Council meeting at 1:00 pm EDT with a quote from Dr. Abraham Verghese's Cutting for Stone – “If the beating heart is pure theater, a playful, moody, extraverted organ cavorting in the chest, then the liver, sitting under the diaphragm, is a figurative painting, stolid and silent.” – and declared that it was our collective responsibility to be the voice so that liver issues were silent no more.

Mrs. Cryer welcomed and thanked all those assembled on behalf of the Global Liver Institute (GLI), the Fatty Liver Foundation (FLF), and the Milken Institute School of Public Health at George Washington University (MISPH), remarking that this event was the embodiment of GLI mission, vision, and operating principles, aiming to transform the culture and conversation around a liver condition by convening a broad set of stakeholders to rethink and redesign systems to generate optimal solutions for patients.

II. Introduction of Co-Chairs and Supporters
Dr. Anna Mae Diehl, Florence McAlister Professor of Medicine, Duke University School of Medicine will serve as Chair of the GLI NASH Council and sent her regrets for her inability to attend the initial meeting due to clinical commitments arising. Wayne Eskridge, Founder, Fatty Liver Foundation and NASH patient, served as inaugural Co-Chair. [Moving forward Donna Cryer will serve as the patient Co-Chair alongside Dr. Diehl and Mr. Eskridge will lead workgroups related to supporting current NASH patients].

Mrs. Cryer read a note of support from Gary Reedy, CEO of the American Cancer Society and referred to the unique joint statement of support included in the meeting materials from the Directors of both the National Institute of Diabetes and Digestive and Kidney Diseases, Griffin P. Rodgers, MD, MACP, and the National Heart, Lung, and Blood Institute, Gary H. Gibbons, MD. The NIDDK/NHLBI letter stated, in part, “We share your commitment to help people suffering with fatty liver disease improve their health and quality of life. . . . It takes a village of concerned public agencies, non-profits such as GLI, and others to improve public health through research, understanding, prevention, and management. We wish you the best of success with the GLI NASH Council and your launch event.”

III. Introduction of Council Participants
Council participants were given the opportunity to introduce themselves, the connection of their organization to fatty liver disease (NAFLD or NASH) if there was one, and what they hoped to get from participation in the meeting. The diversity of participants, including those participating remotely, from academia, local and federal government, clinical practice, medical societies, domestic and European patient organizations was noted.

IV. NASH Overview
Mrs. Cryer provided a brief introduction to non-alcoholic steatohepatitis (NASH) by describing liver functions 101, the impact on the body (by organ) of liver impairment, defining and distinguishing NAFLD and NASH, explaining risk factors including racial and ethnic disparities, highlighting the connections between NASH and other diseases, particularly those associated with metabolic syndrome, ending with the US and global prevalence of NAFLD and NASH including the 10% of American children already living with fatty liver disease.

As the global epidemic of obesity fuels metabolic conditions, the clinical and economic burden of NAFLD will become enormous. (Hepatology 2016;64:73-84)

V. NASH Patient Perspective
Wayne Eskridge described his journey as an everyman leading a typical life with a typical American diet until a diagnosis of NASH after undergoing gallbladder surgery, a myriad of tests and misdiagnoses, and shared shocking stories of other NASH patients that have compelled him to start his own organization, the Fatty Liver Foundation. Mr. Eskridge remarked that he was the rare patient who, with specific long-term support of his physician, was able to to lose more than 40 pounds and reverse his disease progression with lifestyle management. Most patients will need additional supports and therapies, but first they need to know that they have NASH and the serious, even deadly potential consequences of this disease. A key aim of FLF is to dramatically increase the number of people screened and diagnosed with fatty liver disease and NASH.
VI. NASH Advocacy in Europe

Mrs. Cryer introduced Marko Korenjak, Vice President for Coordination and Development, European Liver Patients Association, recognizing ELPA’s leadership in NASH advocacy and emphasized the importance of aligning efforts to address this global epidemic. Mr. Korenjak described ELPA’s vision, mission, and structure as a patient-driven organization with members representing 27 countries. Differences between the US and European health systems and funding mechanisms for civil society organizations, such as Horizon 2020 were acknowledged. ELPA held their first NASH/NAFLD Summit in the European Parliament in Spring 2017 co-convened with the European Association for the Study of the Liver and a member of the European Parliament. Recommendations from the clinical, economic, and political presentations are being formulated for a phase II summit in 2018, but a clear main message was formulated:

*The prevalence of NAFLD in the general population ranges from 20-30% in Europe and will become the leading cause of liver transplantation in the next ten to twenty years.*

VII. NASH Council Discussion

Mrs. Cryer facilitated a discussion by the Council participants structured around the following issues:

1. Identifying and Diagnosing Patients
2. Current Management
3. Patient Challenges
4. Supporting Future Therapies

Key elements of the discussion are detailed below without specific attribution.

**Issues in Identifying and Diagnosing Patient**

Only a small percentage of persons estimated to be living with NAFLD/NASH are diagnosed. Key Barriers are: 1) low awareness of liver and liver conditions 2) asymptomatic nature of the conditions 3) presence of other conditions/ co-morbidities in many NAFLD/NASH patients 4) “labs lie” - often liver enzyme tests are not elevated even in the presence of significant disease 5) the “biopsy barrier” - under current medical guidelines a liver biopsy, an invasive procedure with some risks, is necessary for an official diagnosis of NASH.

Discussants remarked on the need for less invasive diagnostic methods that meet standards of scientific rigor and confidence. Several detailed the current purposes and limitations of various types of imaging currently approved by FDA including Fibroscan. Regulatory distinctions in Fibroscan’s approved indications and the role of evolving real world evidence in supporting its role as a screening, if not a definitive diagnostic or staging tool were made. The point was made that research opportunities have been missed by not obtaining baseline Fibroscan scores in previous and ongoing cardiovascular, diabetes, and obesity trials. One participant involved in obesity trials offered to add liver measures beyond insulin sensitivity with assistance from other members of the Council.

The role of endocrinologists was discussed since up to 80% of type 2 diabetes patients may have some stage of NAFLD and participants stated that NAFLD/NASH was on the agenda but in nascent stages. Support and partnership in effective, scalable diagnoses and treatment strategies were welcomed.

Questions were raised as to how best to incorporate addressing social determinants of health within the context of diagnosis and management.

Another area of discussion centered on how to integrate NAFLD/NASH into electronic health records, regional health information exchanges such as CRISP (in the DC area), for example to create alerts and cascades of care as seen for Hepatitis C and other conditions in integrated healthcare models.

**Current Management**

The largest current management challenge was identified was the countering discouraging statement, “there is nothing that can be done”, now in the absence of FDA-approved medications, which disincentivizes screening, creates low urgency, and results in lack of scheduling follow up visits.

Given lifestyle change that results in sustained weight loss of 7-10% has been shown to improve outcomes in early stages of NAFLD/NASH but is notoriously hard to achieve, discussants considered various types of diets (including vegetarian/plant-based), behavioral health supports, and models such as the Diabetes Prevention Program (now
expanded through partnership with local YMCAs) and the Dr. Dean Ornish plans which have both scaled, and in the latter case receives Medicare reimbursement.

Current AASLD guidelines for management of patients with NAFLD include evidence of effectiveness of pioglitazone and vitamin E for reversing fibrosis. More controversial therapeutic uses of metformin, omega 3 fatty acids, and ursodiol. Several participants predicted the need for combinations of therapeutic approaches to combat both fibrosis and fat concentrations in the liver.

Patient Challenges
Several moving patient stories illuminated challenges in receiving a correct diagnosis, misinformation, balancing multiple conditions, medical complications including bleeding and hepatic encephalopathy, social isolation, depression, and impact on caregivers.

Supporting Future Therapies
Discussants agreed that participation in clinical trials for NASH should be considered part of current patient management as well as supporting future therapies.

Participants asked if a collaboration with metabolic/endocrine and GI divisions at FDA would be helpful to evaluating and reviewing the complexities of therapies in development for NASH. Participant, Veronica Miller, Executive Director of the Liver Forum, commented on this.

Gaps in the clinical trial experience from the patient participant perspective – lack of a culture of research participation in liver disease (as across conditions outside oncology), consent, travel distances to research sites, communication of trial opportunities by physicians, lack of emotional support through trials – were put forward.

The discussion rounded out by anticipating approval of medications for NASH and recognition of the value of involving CMS and other payers as early as possible. Both the Liver Forum and GLI agreed to align their combined contacts and ongoing efforts in this area. GLI invited input into its project to develop a patient-centered value framework for NASH.

NASH Council Moving Forward
The initial objectives of the NASH Council were reinforced and refined to:

1. Increase public understanding and appreciation of the relevance, scope, and impact of NAFLD and NASH
2. Improve physician education and prioritization of NAFLD/NASH screening, diagnoses, and management from primary care through specialists
3. Design effective patient identification, screening, education, and support strategies and content
4. Support the development of therapies to treat NASH

Specific actions discussed and supported were as follows:

1. Declaration of NAFLD/NASH as a public health emergency
2. Formalizing Membership in the NASH Council
   - Assessing internal opportunities (communications, programs) to advance objectives
   - Leveraging external networks to advance objectives
   - Referring/Recruiting new members to the Council

VIII. Closing Remarks
Mrs. Cryer closed the inaugural NASH Council meeting at 4:07 PM EDT by thanking the group and reaffirming the Global Liver Institute's dedication to and focus on this issue into 2018 and beyond.

Information on an AASLD-led Congressional briefing scheduled for Wednesday, October 25th was circulated to NASH Council participants and invitees immediately following the event.

The NASH Council Launch Event was made possible by an unrestricted educational grant from Allergan.
Appendix I: Participants

Attendees
Neal Barnard, MD, FACC, Physicians Committee for Responsible Medicine
Kathleen Corey, MD, MPH, Massachusetts General Hospital: Fatty Liver Disease Clinic
Dennis Cryer, MD, FAHA, CryerHealth, LLC
Lara Dimick-Santos, MD, Food & Drug Administration
Wayne Eskridge, Fatty Liver Foundation
Kathleen Greene, The Liver Forum
Brian Harvey, MD, PhD, Global Liver Institute
Scott Kahan, MD, MPH, National Center for Weight and Wellness/Obesity Society
Marko Korenjak, European Liver Patients Association
Michele Lentz, American Association of Clinical Endocrinologists
Veronica Miller, PhD, The Liver Forum
Cynthia Moylan, MD, American Heart Association
Shalewa Noel-Thomas, PhD, MPH, Cancer and Chronic Disease Prevention: DC Department of Health
Caitlin Ondracek, PhD, The Endocrine Society
Bennett Rosenthal, Key Antitidote
Arun Sanyal, MD, Virginia Commonwealth University School of Medicine
Rosemary Wickowski, COO, Fatty Liver Foundation

Observers
Jason Campagna, MD, PhD, Intercept
Chris Frates, Intercept
Heather Gartman, Gartman PR
Joseph Haas, The Pink Sheet
David Hartzman, Washington Talent
Brian Lee, PharmD, Bristol-Myers Squibb
Joel Lopez, JPA Health Communications
Shannon Richardson, Twist Marketing
Susan Stone, Allergan

GLI Staff
Donna R. Cryer, JD, President & CEO
Richard Gelula, MSW, COO
Jazmin Hampton, Program Director
Carrie Gelula, Creative Director
Jen DelGrande, Oncology Program Director
Fatima Khan, A3 Program Manager
## Appendix II: October 18, 2017 Agenda

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<tr>
<td>12:00</td>
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<td>Welcome&lt;br&gt;Donna R. Cryer, JD, Global Liver Institute</td>
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<td>NASH Overview</td>
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<td>NASH Patient Perspective&lt;br&gt;Wayne Eskridge, Fatty Liver Foundation</td>
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<td>NASH Advocacy in Europe&lt;br&gt;Marko Korenjak, European Liver Patients Association</td>
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<td>BREAK</td>
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<td>I. Issues in Identifying and Diagnosing Patients</td>
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<td>III. Patient Challenges</td>
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<td>IV. Supporting Future Therapies</td>
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<td>Donna R. Cryer, JD, Global Liver Institute</td>
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<td>I. Engaging the Larger Medical Community</td>
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<td>II. Educating and Supporting Patients</td>
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<td>IV. Informing Policymakers</td>
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<td>V. NASH Council Moving Forward</td>
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<td>A. Declaration of Public Health Emergency</td>
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<td>B. Commitments to workgroups</td>
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<td>C. Recruiting other members</td>
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<td>3:50</td>
<td>Closing Remarks</td>
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<td>Reception</td>
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October 11, 2017

Donna R. Cryer, J.D.
President & Chief Executive Officer
Global Liver Institute
1875 Connecticut Ave., 10th Floor
Washington, D.C. 20009

Dear Ms. Cryer,

Thank you for your letters inviting us to serve as honorary co-chairs of the Global Liver Institute’s (GLI) NASH Council and to attend its launch event on Wednesday, October 18, 2017, at George Washington University in Washington, D.C.

We applaud your initiative to address the scope of fatty liver diseases and related health conditions. Due to schedule conflicts, we regret that we are not available for your launch. We certainly wish you success in addressing nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). At this time, we are also unable to serve as co-chairs of the GLI NASH Council.

We share your commitment to help people suffering with fatty liver disease improve their health and quality of life. To better understand the causes and discover effective ways to treat NAFLD and NASH, the NIH supports and conducts a broad range of liver and biliary diseases research, including understanding how fatty liver disease is associated with obesity, diabetes, and hyperlipidemia.

It takes a village of concerned public agencies, non-profits such as GLI, and others to improve public health through research, understanding, prevention, and management. We wish you the best of success with the GLI NASH Council and your launch event.

Warmest regards,

Griffin P. Rodgers, M.D., M.A.C.P.
Director, National Institute of Diabetes and Digestive and Kidney Diseases

Gary H. Gibbons, M.D.
Director, National Heart, Lung, and Blood Institute
Patient Stories

DIAGNOSIS
Sue, age 47
I went into surgery to have my gallbladder removed. Once the Dr was in he didn't like the way my liver was looking and did a biopsy. Turns out I have NASH stage 4 grade 2 (I have no idea what grade 2 means) cirrhosis. I'm scared......

NUTRITION & SUPPORT
Kate, age 57
I have been living with NASH for several years now and have been very surprised at the lack of support and understanding from family members, friends and even the medical personnel. I try to be positive and not let it get me down but sometimes it does, and it is hard to maintain a fat free, sugar free low calorie diet when you are an emotional eater from a very young age and have been eating everything in sight for over 50 years. Food was my comfort in childhood and now the very thing that brings me comfort is killing me. My family loves me but they don't get it that I have to stay on this diet 24/7/365 for my life. When I fall off the wagon it is so hard for me to get back on it. I have never found the emotional support I needed. I am not a whiner by any means and I want to do all I can while I can but it would be so nice to have people to talk to and share with and lift each other up.

DEPRESSION
Brice, age 59
When diagnosed with NASH, I read everything I could about the fibrosis and cirrhosis. As good as the doctors are, they don't know everything about how these diseases affect each person. I have feelings of dread, loneliness, uncertainty as my doctors can't even agree as to what I have. One hepatologist thinks it is cirrhosis and the other thinks that it is a rare one called focal nodular regenerative hyperplasia. It doesn't matter, they both have told me that there is nothing that they can do for me. So, here I sit wondering if and when it will get worse. I talk to some who actually is hoping that their liver gets bad enough so that they qualify for a transplant because sometimes it is easier to think about that than the uncertainty of being ill for who knows how many years. They say there is nothing they can do for me except monitor my symptoms every six months and treat the symptoms. It is a little disheartening to hear from the ALF that they don't have much information on your disease and that they recommend going to the NIH; which doesn't have much either. Sometimes I think of suicide.

STIGMA
Terry, age 63
I have had a very rough time dealing with my liver disease. I feel sick taking my medications and I still feel sick not taking my medications. I'm on all the standard liver treatments and medications. I also have panic attacks and I am suffering again from depression. I get medical care regularly and will continue with therapy and psych medications to help me cope with this horrendous liver disease process. I have been living in the ER and cancer center for my blood, and doctors appoints. But the worst thing that has happened to me was at a recent graduation party, a family member, commented while others were asking me how I was doing, “well you did it to yourself”. “I don’t feel sorry for you and many more people feel like me”. To those who are suffering from Stage 4 decompensated liver disease either caused by NASH or alcoholism this seems to be the attitude of many people. Most people don’t comment. But she did. I have NASH….. yes I have been overweight for most of my life. Infancy, toddler, childhood, my 20, 30, 40, etc. So yes, I did it myself. But, I researched and only 25% of the world's overweight people get NASH. So there has to be other mechanisms here going on. I have been a diabetic since childhood, but the testing standards were different then. I am heartbroken.
Patient Stories

DIFFICULT MANAGEMENT

Len, age 71

In the early 90's my wife was diagnosed with diabetes and told she also had a fatty liver. They said the fatty liver was common and mostly benign but it would be good to lose a little weight. She had a hard time controlling her diabetes and a few years later her legs got big so they gave her water pills. After a while she got an irregular heartbeat so she got a pill for that and her blood pressure was getting quite high so she got a pill for that. Her left foot got very painful from the diabetes and we were afraid she might lose it but some meds helped that but walking was hard. In 2005 she started bleeding from her throat. The EMT's took her straight to ICU and 4 units of blood saved her but they said she could easily have died. They said she had esophageal varices and wondered why they hadn't been banded. We had no idea as no one ever told us. More testing and she has NASH and cirrhosis. They say stage 4 but that didn't mean much to us. Over the next year she had 7 varices banded and had a lot of pain, She also developed ascites and they drew 7 liters of fluid from her belly. In some ways this was the easy time. Her liver got worse and they put in a TIPS shunt to ease pressure on her liver but that led to ammonia in her blood and hepatic encephalopathy. It made her a crazy, mean, angry person. Not at all the woman I'd loved all these years. They gave her lactulose to control it and it did help some but it gave her frequent diarrhea. It got bad from there. One day near our anniversary she was pretty good and wanted to go out and celebrate our marriage. We went to her favorite place, she managed with a walker. It was a tender moment but she became distressed and had to leave. She had an attack of uncontrollable diarrhea. She wore an adult diaper but it failed and she left a trail of excrement on the floor as she tried to get out. She never left the house again except by ambulance. She lasted another year but it was a time of great pain and she spent her last two months in ICU with tubes everywhere. No one should have to go through that.
NASH Facts

Liver Functions 101
cellular plant, inspection station, garbage disposal, filtration system, blood clotting factor producer, catalytic converter, sex hormone converter

The body without a healthy liver
- confusion, hepatic encephalopathy
- impaired vision, jaundiced sclera
- aFib, high cholesterol, high triglycerides, vascular disease
- malnutrition
- hypertension
- osteoporosis

Connections to other diseases
IBD, Celiac disease, PCOS, sleep apnea, dyslipidemia, hypertension, obesity, diabetes, hypothyroidism, hypertension

NAFLD vs NASH
Nonalcoholic fatty liver disease (NAFLD) is a condition in which fat makes up more than 5% of the weight of the liver, not caused by alcohol use.

NASH is a form of NAFLD in which you have inflammation and liver cell damage, in addition to fat in your liver. Inflammation and liver cell damage can cause fibrosis, or scarring, of the liver. NASH may lead to cirrhosis or liver cancer.

Risk Factors
- Overweight/obesity
- Insulin resistance/ Type 2 diabetes/gestational diabetes
- Dyslipidemia
- One of more traits of metabolic syndrome
- Large waist
- High triglycerides
- Hypertension
- Hispanic ethnicity due to presence of PNPLA3 gene
- Asian Americans are more likely than people of other racial or ethnic groups to develop NAFLD when their weight is within the normal range

Prevalence
- In the US, up to two in five adults has NAFLD
- 10% of children in the US have NAFLD
- 40-80% of people with T2D have NAFLD
- 90% of bariatric surgery candidates have NAFLD
- 20% of people with NAFLD have NASH
- NASH is estimated to be #1 cause for liver transplants by 2020
- Highest in the Middle East and South America

As the global epidemic of obesity fuels metabolic conditions, the clinical and economic burden of NAFLD will become enormous. (Hepatology 2016;64:73-84).