Hepatic Encephalopathy: Current Pathway for Care Resolution and Best Practices for 2025…What Every Case Manager Should Know.

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Learning Objectives

- Explain the physical and psychosocial impacts that a diagnosis of hepatic encephalopathy (HE) imparts on the patient, family and caregivers as well as all healthcare delivery systems.
- Consider how frequent recurrences of HE may cause nonreversible patient organ dysfunction resulting in both reduced patient quality of life and an increased economic burden for both patients and healthcare delivery systems.
- Review established Standards for Transitions of Care and avenues for implementing those Standards in patients diagnosed with HE to minimize the number of potentially avoidable readmissions.

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- The guide is available for download
  https://cmsa.org/hepatic-encephalopathy-cmag/

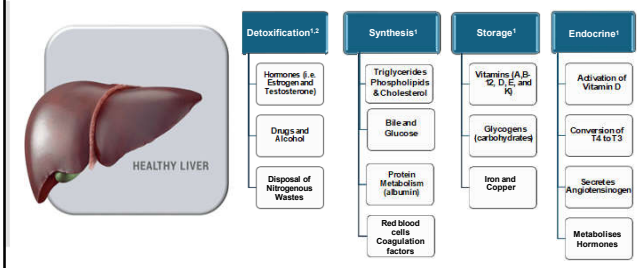
It All Starts with the LIVER

Some functions of the Liver

- Performs many critical metabolic functions including producing bile
- Converts glucose to glycogen
- Regulates blood clotting
- Produces cholesterol
- Regulates levels of amino acids in blood
- Processes drugs and other toxic substances
- Converts ammonia, made during digestion, to urea

www.niddk.nih.gov

Normal Healthy Liver Functions



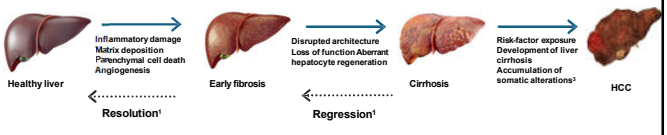
1. Ozougwu. *Int J Res Pharm Biosci.* 2017;4(8):13-24. 2. Trefts et al. *Curr Biol.* 2017; 27(21): R1147-R1151.

Liver Damage Can Lead to Progressive Liver Disease

Causes of chronic liver injury[1]

- NASH/NAFLD (MASH/MASLD)[2]
- Alcohol consumption
- Viral infection
- Autoimmune disorders
- Cholestatic disorders
- Metabolic diseases

Liver insufficiency
Portal hypertension



MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction–associated steatotic liver disease; HCC, hepatocellular carcinoma
1. Pellicoro et al. *Nat Rev Immunol.* 2014;14:181-194. 2. Rinella et al. *J Hepatol.* 2023;79:1543-1565. 3. Toh et al. *Gastroenterology.* 2023;164:766–782.

Defining MASLD/MASH – Metabolic Dysfunction–associated Steatotic Liver Disease and MASH - metabolic dysfunction-associated steatohepatitis -

MASLD

- A buildup of fat in the liver that has become the most common liver disorder in the United States.
- Two thirds of obese adults and one third of obese children have fatty livers[1].

MASH

- A leading cause of liver failure prompting an increasing need for transplant costing the United States health care system about $100 billion annually.
- It is estimated that nine to 15 million adults have MASH.

1. MASLD. https://gi.org/topics/steatotic-liver-disease-masld/

MASLD/MASH/MetALD

- MASLD is asymptomatic and frequently undiagnosed.
- Diagnosis of MASLD requires liver steatosis together with at least one out of five cardiometabolic criteria, e.g. presence of impaired glucose regulation, type 2 diabetes, overweight or obesity, hypertension or dyslipidemia[1].
- MASH may prompt scarring of the liver, cirrhosis and liver failure.
- MetALD describes those with MASLD who consume greater amounts of alcohol per week
- REZDIFFRA (resmetirom) tablet thyroid hormone receptor-beta (THR-beta) agonist indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis. Avoid use of REZDIFFRA in patients with decompensated cirrhosis[2].
- Additional resources are available at www.aasld.org

1. Hagström, et al. 99% of patients with NAFLD meet MASLD criteria and natural history is therefore identical. Journal of Hepatology, Volume 80, Issue 2, e76 - e77
2. REZDIFFRA-PI_14Mar2024_final-revised-clean-SPLPPI.pdf

Burden of Chronic Liver Disease (CLD) and Cirrhosis in the United States[1,2]

PREVALENCE

- As of 2018, **4.5 million** people, or **1.8% of US adults**, were diagnosed with liver disease[1]
- Prevalence of cirrhosis increased from **0.20%** in 2006 to **0.45%** in 2020[2]

HEALTHCARE UTILIZATION

- Over **1 million** outpatient visits and **325,000** ED visits for CLD in 2014[4]
- Cirrhosis-related hospitalizations and related costs increased from **$4.8 billion** in 2001 to **$9.8 billion** in 2011[4,5]
- CLD patients typically require more hospital-based care than those with other chronic disease[6]

HOSPITAL READMISSIONS

- **High readmission** rates in cirrhosis patients, particularly driven by **HE** (adjusted **odds ratio 1.77 each** for 30- and 90-day readmission)[3]

MORTALITY for CLD and Cirrhosis Combined

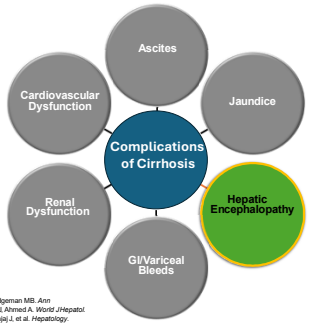
- Mortality increased from **11.0 per 100,000** persons in 2017 to **13.8 per 100,000** persons in 2020[8]
- **56,585** deaths annually, with **17.0** deaths per **100,000** persons in 2021[1]
- **9th** leading cause of death as of 2021[1]
- Deaths associated with cirrhosis are expected to triple by 2030[7]

1. National Center for Health Statistics. https://www.cdc.gov/nchs/fastats/liver-disease.htm. Accessed April 14, 2023. 2. Wong et al. Poster presented at: Digestive Disease Week; May 6-9, 2023; Chicago, IL. 3. Tapper et al. Clin Gastroenterol Hepatol. 2018;16:1161-1169. 4. Moon et al. Clin Gastroenterol Hepatol. 2020;18:2650-2658. 5. Kim et al. Clin Gastroenterol Hepatol. 2021;19:2804-2666. 6. Asrani et al.Increasing health care burden of chronic liver disease compared to other chronic disease, 2004-2013. Gastroenterology 2018; 155:778-729. CLD patients typically require more hospital-based care than those with other chronic disease 7. Estes et al. Modeling the epidemic of nonalcoholic fatty liver disease.Hepatology 2018;67:123-133.

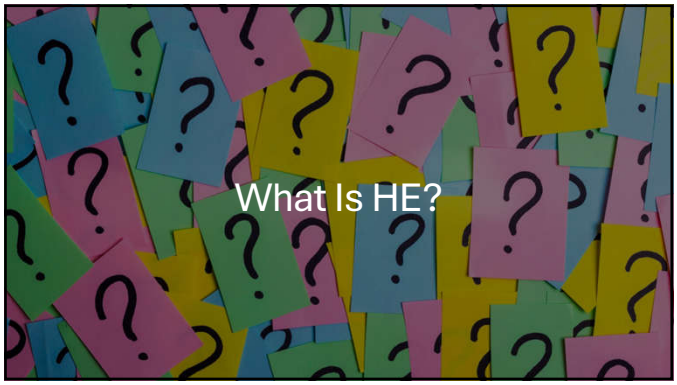
Complications of Decompensated Cirrhosis

- Decompensated cirrhosis is associated with serious complications due to hepatic insufficiency and portal hypertension[1]
- Hepatic encephalopathy (HE) is a primary complication of decompensated cirrhosis[1-4]

- **Up to 80% of patients will develop HE, ranging from minimal to overt[2,5,6]**



1. James J, Liou IW. *Med Clin North Am*. 2015;99(5):913-933. 2. Jawaro T, Yang A, Dixit D, Bridgeman MB. *Ann Pharmacother*. 2016;50(7):569-577. 3. Liu A, Perumpail RB, Kumari R, Younossi ZM, Wong RJ, Ahmed A. *World J Hepatol*. 2015;7(29):2871-2879. 4. Saab S, *Int J Gen Med*. 2015;8:165-173. 5. Vilstrup H, Amodio P, Bajaj J, et al. *Hepatology*. 2014;60(2):715-735. 6. Flamm SL. *Am J Manag Care*. 2018;24(4 Suppl):S51-S61.



Overview of HE

Hepatic encephalopathy (HE) is a progressive cognitive disorder caused by liver insufficiency or portosystemic shunting (PSS), which manifests as a wide range of neurological or psychiatric impairments[1]

Reversible neuropsychiatric syndrome encountered in patients with cirrhosis of the liver.

- OHE may occur in **30% to 45%** of patients with cirrhosis[2]
- Among patients with cirrhosis, the rate of overt HE (OHE) in the United States increased from **11.8**% in 2006 to **21.4%** in 2020, with an estimated **200,000 adults with OHE in 2020**[3]
- Cognitive impairment results in utilization of more health care resources in adults than other manifestations of liver disease.

CMS implemented HE-specific ICD-10 code K76.82 on October 1, 2022[4]

CMS, Centers for Medicare & Medicaid Services; ICD, International Classification of Diseases.
1. Vilstrup et al. *Hepatology*. 2014;60:715-735. 2. Poordad. *Aliment Pharmacol Ther*. 2007;25(suppl 1):3-9. 3. Wong et al. Poster presented at: Digestive Disease Week; May 6-9, 2023; Chicago, IL.
4. Klein. AJMC. http://www.ajmc.com/view/new-icd-10-code-aims-to-provide-more-insight-into-hepatic-encephalopathy. Accessed May 8, 2023.

Healthcare Resource Patterns With OHE

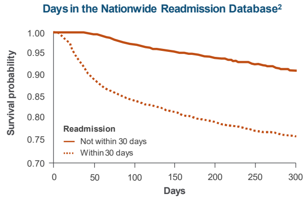
Adults with OHE commonly experience long-term care (LTC) stays and inpatient admissions, representing substantial healthcare resource burden

- Among adult patients with OHE in a Medicare population
  - **63%** had ≥1 LTC stay
  - **95%** were transferred to a skilled nursing facility from an inpatient stay
  - After a skilled nursing facility stay, **19%** were admitted to an inpatient hospital stay
  - Inpatient readmissions within 30 days of skilled nursing facility discharge were commonly related to OHE **(36%)**

OHE, overt hepatic encephalopathy.
Heimanson et al. Poster presented at: Digestive Disease Week; May 6-9, 2023; Chicago, IL.

OHE Is Associated With Increased Mortality

Calendar-Year Survival of Patients Readmitted Within 30 Days in the Nationwide Readmission Database[2]



- In a study of hospitalized patients with cirrhosis, grade III/IV OHE had significantly higher 30-day mortality (**38%**) vs grade I/II HE (**8%**) or no HE (**7%**)[1]
- Among 24,473 patients with cirrhosis hospitalized with HE, **32%** were readmitted within 30 days[2]
  - Early readmission was a highly significant predictor of calendar-year mortality

CI, confidence interval; HE, hepatic encephalopathy; HR, hazard ratio; OHE, overt HE.
1. Bajaj et al. *Clin Gastroenterol Hepatol*. 2017;15:565-574. **2.** Kruger et al. *Ann Hepatol*. 2019;18:310-317.

Readmission Rates With OHE

Recurrent HE underlies elevated rates of hospital readmission

- **53%** of patients with cirrhosis experienced ≥1 readmission within 90 days, with HE as the primary reason for readmission (NACSELD cohort)[1]
- **36%** of patients with ≥3 complications of cirrhosis were readmitted within 90 days, with HE as a significant predictor of 30- and 90-day readmissions (State Inpatient Databases[a])[2]
significant predictor of 30- and 90-day readmissions
(State Inpatient Databases[a])[2]

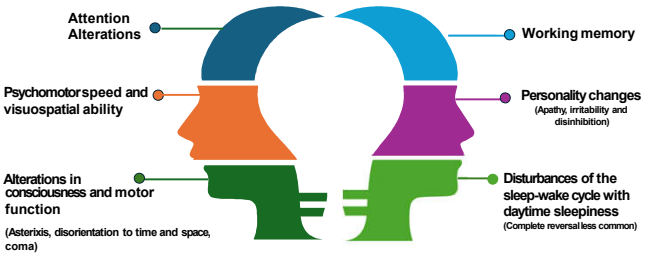
Factors contributing to HE-related readmission include[3,4]

- Failure to refill prescription
- Lack of follow-up
- Limited social support
- Limited access to transitional education
- Other disease factors (eg, hypertension)

HE, hepatic encephalopathy; NACSELD, North American Consortium for the Study of End-Stage Liver Disease; OHE, overt HE.
[a]Adult patients with cirrhosis admitted to hospitals in California, Florida, Massachusetts, Mississippi, and New York in 2011 were included.
1. Bajaj et al. *Hepatology*. 2016;64:200-208. **2.** Tapper et al. *Clin Gastroenterol Hepatol*. 2016;14:1181-1188;1188.e1-1188.e2. **3.** Neff. *Hepatology*. 2013;58(S1):390A-391A. **4.** Rassameehiran et al. *South Med J*. 2016;109:365-369.

Clinical Features of Hepatic Encephalopathy (HE)

HE manifests a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma



Vilstrup H, et al. *Hepatology*. 2014;60(2):715-735.

Symptoms of HE

- Anxiety or irritability
- Cognitive impairment
- Shortened attention span; difficulty concentrating
- Flapping hand motions (asterixis)
- Muscle twitching (myoclonus)
- Reduced alertness
- Sleep problems
- Slurred speech
- Bizarre or inappropriate behavior
- Coma

https://cmsa.org/hepatic-encephalopathy-cmag/

Common Triggers for HE

- Binge drinking alcohol
- Constipation
- GI bleeding
- Infection
- Kidney disease
- Portosystemic shunting
- Primary hepatocellular cancer
- Medication nonadherence
- Electrolyte imbalance
- Thrombosis in the portal vein
- Respiratory distress
- Medications that impact the nervous system (opiates, benzodiazepines, antidepressants, and antipsychotic agents)
- Sudden change in diet

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West Haven Criteria

COVERT HE		OVERT HE		
Minimal	**Grade I**	**Grade II**	**Grade III**	**Grade IV**
✓ No observable symptoms ✓ Detectible solely by psychometric testing	✓ Trivial lack of awareness ✓ Euphoria or anxiety ✓ Shortened attention span ✓ Impairment of addition or subtraction ✓ Altered sleep rhythm	✓ Lethargy or apathy ✓ Disorientation for time ✓ Obvious personality change ✓ Inappropriate behavior ✓ Asterixis	✓ Somnolence to semi-stupor ✓ Responsive to stimuli ✓ Confused ✓ Gross disorientation ✓ Bizarre behavior	✓ Coma

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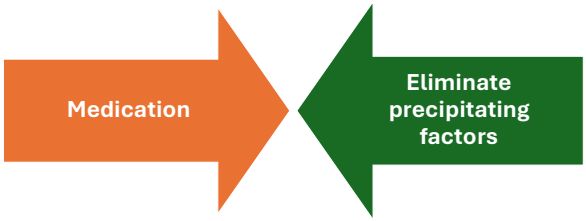
Treatment of HE



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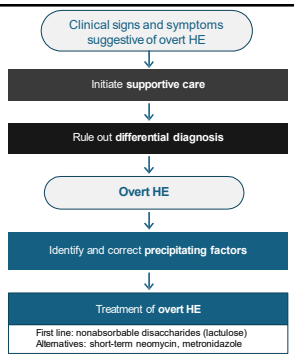
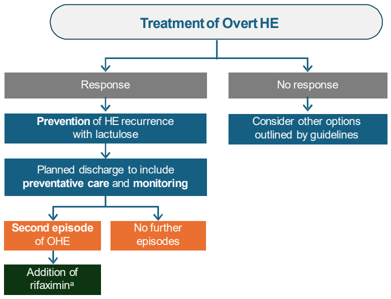
Management of an Overt HE Episode[1,2]



HE, hepatic encephalopathy
1. Vilstrup et al. Hepatology. 2014;60:715-735.
2. Rahimi et al. Eur J Gastroenterol Hepatol. 2009;21:1405-1412.

Prevention of Recurrent Overt HE[1,2]



BID, twice daily; HE, hepatic encephalopathy; OHE, overt HE.
[a]Rifaximin 550 mg BID is indicated for the reduction in risk of overt HE recurrence in adults.

1. Vilstrup et al. *Hepatology*. 2014;60:715-735. 2. Shawcross et al. *Eur J Gastroenterol Hepatol*. 2016;28:146-152.

Treatment of HE

- **First-line medical treatment: lactulose**
  - Lowers ammonia levels by causing bowel movements
  - Elimination of ammonia-producing bacteria from the intestines
  - Lowers the absorption time of ammonia
  - Administered orally or per rectum (enema) during an acute episode
- **Rifaximin for breakthrough episodes**
  - Minimally absorbed antibiotic than decreases the risk for additional episodes
  - Decreases ammonia production in the intestine
  - AASLD/EASL* Guidelines state Rifaximin is an effective add-on therapy to lactulose to reduce the risk of another overt HE recurrence

* American Association for the Study of Liver Disease/European Association for the Study of Liver Disease
https://cmsa.org/hepatic-encephalopathy-cmag

The Role of the Case Manager in Supporting a Patient Diagnosed with HE

The Case Management Process for the Management of HE: Client Selection

- Would a patient who is diagnosed with cirrhotic liver disease benefit from case management intervention with education about liver disease and the serious complications associated with that disease including hepatic encephalopathy?
- Provide information to family and caregivers regarding the symptoms of hepatic encephalopathy.
- Review medications to determine if lactulose was previously prescribed.

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The Case Management Process for the Management of HE: Comprehensive Assessment

Conduct a biopsychosocial assessment
- Physical conditions(s) and symptoms
- Presence of psychological challenges
- Social and health system challenges

Concerns and preferences
- What worries the patient and family/caregiver?
- What is most important to them?

Health experiences
- How has liver disease impacted their lives?
- What do they know about liver disease?
- What do they want to know?

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The Case Management Process for the Management of HE: Comprehensive Assessment

Current and past treatment
- What treatment has been recommended?
- What was the response to the prescribed treatments?

Other barriers or concerns
- Presence of behavioral or mental health symptoms or disorders

Presence of health-related social needs
- Financial
- Living environment

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The Case Management Process for the Management of HE:
Comprehensive Assessment

- Readily available social supports
- Trusted providers
- Ability to obtain medications
- Nutritional status
- Ability to drive
- Triggers
- Adherence to prescribed treatment regime
- Level of engagement
- Primary decision maker

The Case Management Process for the Management of HE:
Comprehensive Assessment

The CAGE questionnaire is a four-question screening tool used to identify potential alcohol use disorder in adults:

•**C**: utting down on drinking
•**A**: nnoyance by criticism of drinking
•**G**: uilty feeling about drinking
•**E**: arly-morning drink (eye-opener)

To score the questionnaire, you assign one point for each "yes" answer.
A higher score indicates a greater risk for alcohol misuse.
A total score of two or more is considered clinically significant.

file:///Users/nancyskinner/Downloads/CAGE_questionaire.pdf

The Case Management Process for the Management of HE:
Development of a Case Management Plan of Care

- Define the patient/family/caregiver challenges
- What challenges are most important to the patient/family/caregiver?
- What is the primary goal the patient/family/caregiver wish to achieve
- Develop interventions to achieve identified goals
- Evaluate the results of the care plan at regular intervals

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The Case Management Process for the Management of HE

Implementation and Coordination of the Case Management Plan of Care

- Consult with hepatologist or transplant center
- Availability of prescribed medications
  - Part D annual out-of-pocket drug spending cap is $2,000
- Physical and Occupational therapy
- Consult to registered dietician
- Counseling
- Home health care
- Assisted living or skilled nursing facility
- Advancing adherence

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Important Safety Considerations

Outpatient Management

- Monitor for the patient's capability to manage their care.

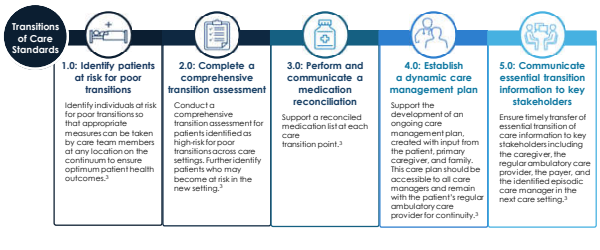
Capacity to drive

- Increased risk of driving accidents in the presence of cognitive deficits.
- Restrict driving for those whose condition suggests the patient is at risk.
- Neuropsychiatric testing may be required to determine fitness to drive.
- With disease progression, re-evaluation to drive may be necessary.

The loss of independence may be very difficult- be supportive but firm in safety recommendations.

https://cmsa.org/hepatic-encephalopathy-cmag

Transitions of Care



ED, emergency department.
American Case Management Association. Transitions of care guiding principles. https://transitionsofcare.org/standards/guiding-principles/. Accessed June 19, 2020.

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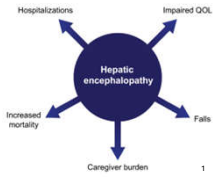
Readmission Rates for Patients with HE

- 30-day readmission rates ranging from 10% to 50%, with a pooled estimate around 26%
- Patients experiencing hepatic encephalopathy are more likely to be readmitted to the hospital compared to other complications of cirrhosis[1].
- According to one study, the 30-day readmission rate for patients with hepatic encephalopathy (HE) is around 30-35%[2].



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1.Frenette et al. Hepatic Encephalopathy-Related Hospitalizations in Cirrhosis: Transition of Care and Closing the Revolving Door. Dig Dis Sci. 2022 Jun;67(6):1994-2004.. 2. Pusateri et al. Randomized intervention and outpatient follow-up lowers 30-d readmissions for patients with hepatic encephalopathy, decompensated cirrhosis. World J Hepatol. 2023 Jun 27;15(6):826-840

Reducing Readmissions

The primary cause of readmissions for patients diagnosed with overt hepatic encephalopathy is recurrence of the hepatic encephalopathy itself, often due to poor medication adherence or failure to manage precipitating factors like infections, electrolyte imbalances, or dietary indiscretions.

Frenette et al. Hepatic Encephalopathy-Related Hospitalizations in Cirrhosis: Transition of Care and Closing the Revolving Door. Dig Dis Sci. 2022 Jun;67(6):1994-2004.

Reducing Readmissions

Or

The patient, family or caregiver does NOT does not understand information regarding

- Their diagnosis
- What they need to do about it
- The value of adherence and the consequences of nonadherence

Based on HCAHPS data, only 52% of patients nationally indicated that they "Strongly Agree" they understood their care when they left the hospital.

www.medicare.gov/care-compare

Reducing Readmissions

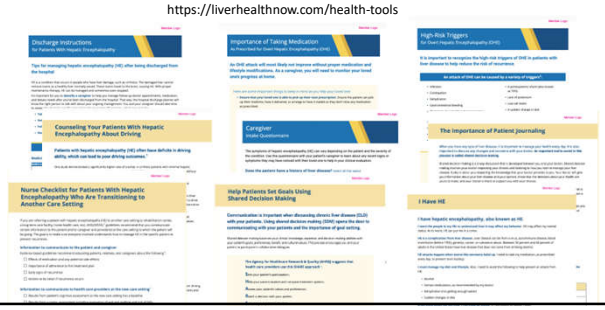
Establish a multidisciplinary approach involving collaboration among
- Hepatologists, gastroenterologists, PCPs and transplant centers
- Physical and occupational therapists
- Dieticians
- Pharmacists across the care continuum
- Case managers in acute & post-acute care and managed care
- Social workers
- Behavioral health professionals
- Patient educators
- Support groups

In order to address potential contributing factors and optimize treatment plans

Patient Education Resources

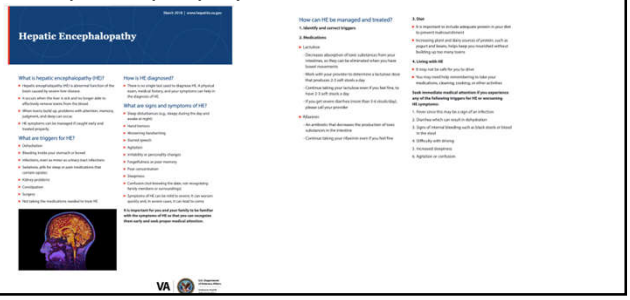
Liver Health Now Tools (*requires registration*)

https://liverhealthnow.com/health-tools



Patient Education Resources

Hepatic Encephalopathy https://www.hepatitis.va.gov/pdf/HE-fact-sheet.pdf



Patient Education Resources

Understanding HE https://www.understandinghe.com/he-resources/