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Evidence-based Care and Therapeutic Updates to Reduce the Risk for Rapid Progression and Recurrence of Hepatic Encephalopathy

INTEGRITY CONTINUING EDUCATION

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A DIVISION OF ULTIMATE MEDICAL ACADEMY

Supporter Acknowledgment

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Learning Objectives

- Describe a plan of care for patients hospitalized with HE that is consistent with updated evidence-based recommendations
- Review the efficacy and safety of therapies for treatment of acute episodes of overt HE and prevention of their recurrence
- Identify crucial components of a transitional care plan to prevent future hospitalizations among patients with HE

HE, hepatic encephalopathy.

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Overview of HE

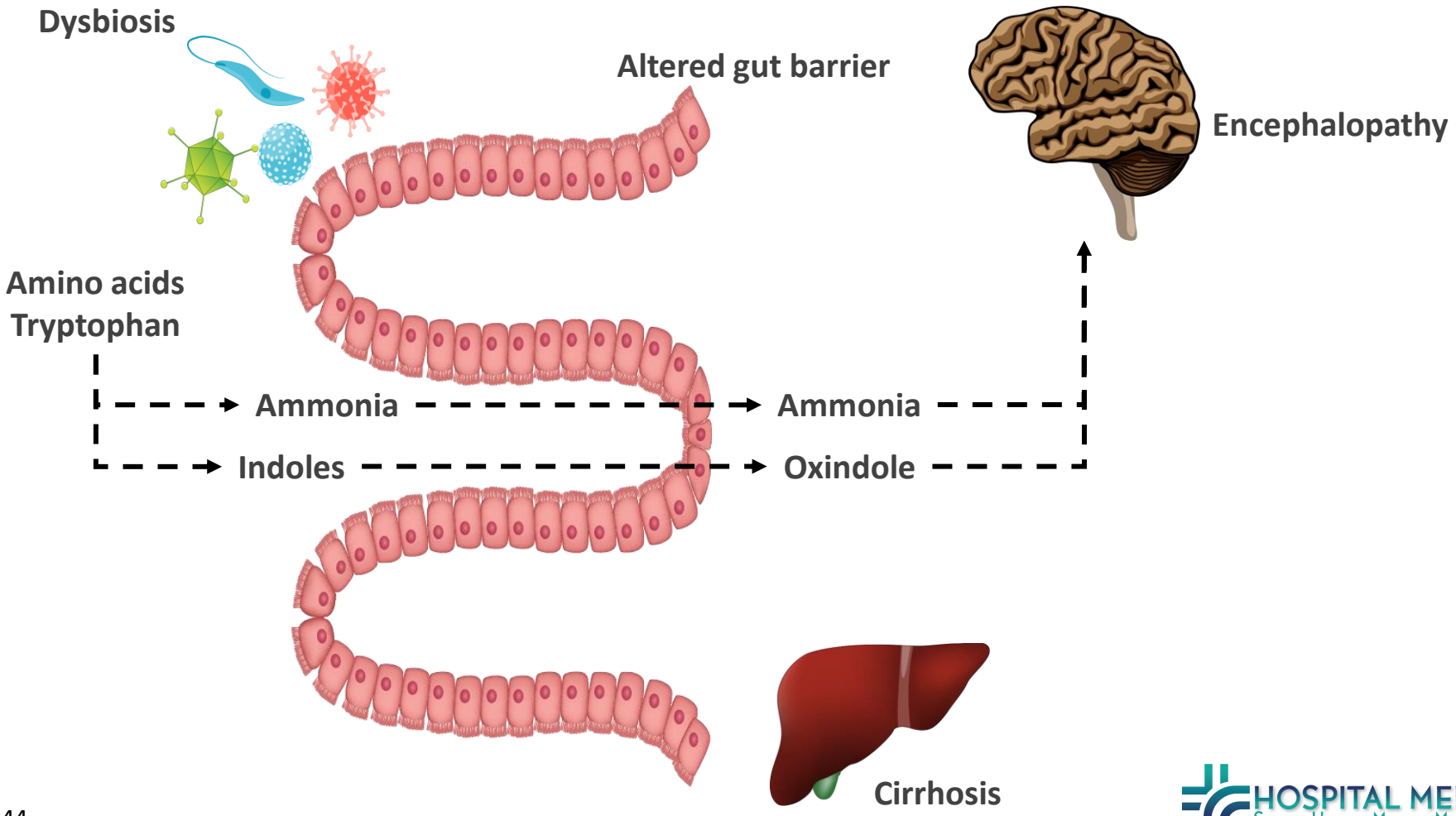
Hepatic Encephalopathy

- Important neuropsychiatric complication caused by liver insufficiency and/or PSS
- 30%–45% occurrence in patients with cirrhosis
- Affects an estimated 202,000 adults in the US (2018)
- Symptoms range from subclinical neurological or psychiatric alterations to coma
- High risk of recurrence, diminished HRQOL, and poor survival

HRQOL, health-related quality of life; PSS, portosystemic shunt.

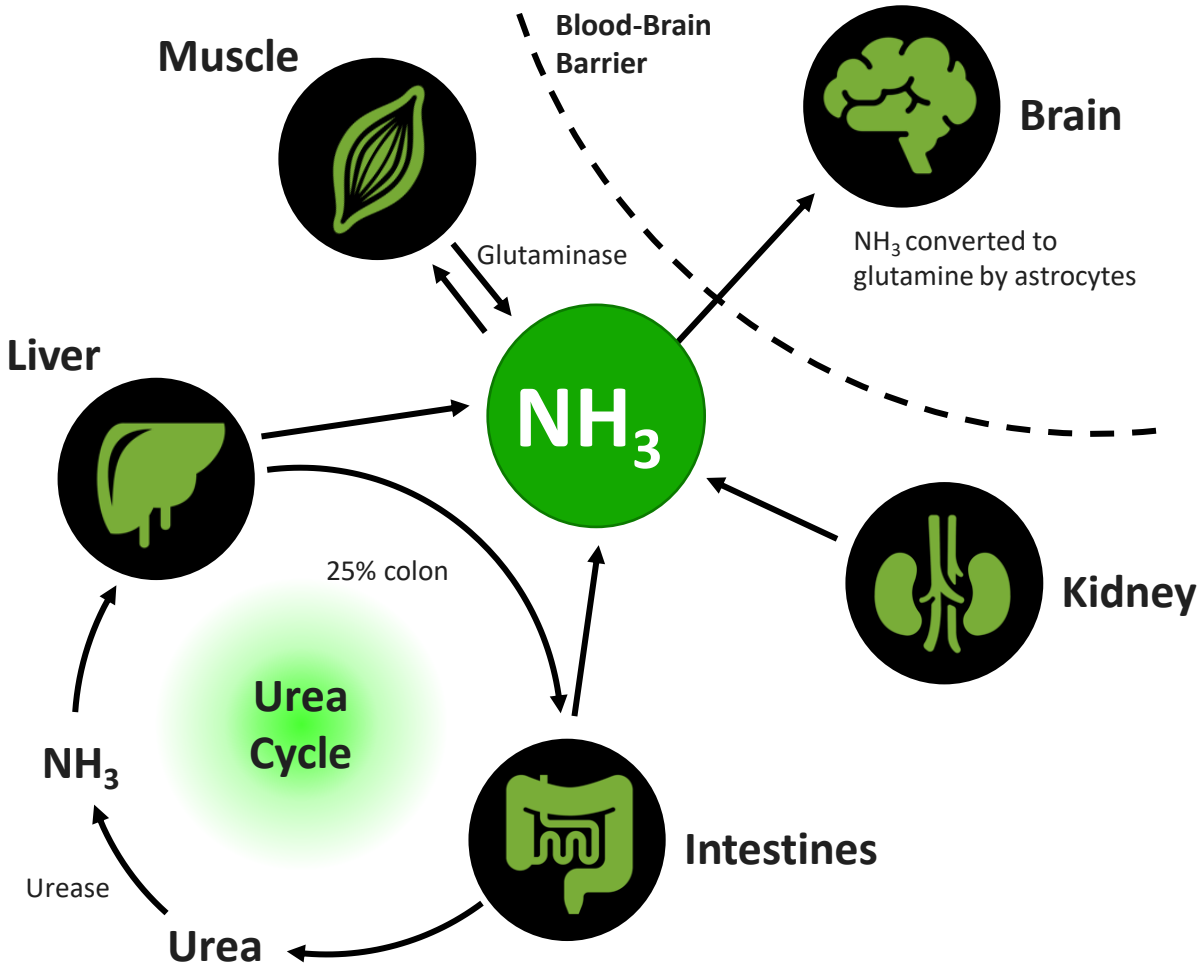
Chacko KR, et al. *Hosp Pract*. 2013;41(3):48-59; Poordad FF. *Aliment Pharmacol Ther*. 2007;25(suppl 1):3-9; Potnis A, et al. *Int J Hepatol*. 2021;2021:8542179. eCollection 2021; Vilstrup H, et al. *Hepatology*. 2014;60(2):715-735.

The Role of Gut Microbiota in Liver Disease and HE



Tilg H, et al. *Gut*. 2016;65(12):2035-2044.

Ammonia (NH_3) Underlies the Primary Pathophysiologic Mechanism of HE



- NH_3 is produced by bacterial metabolism of urea and proteins (gut) and deamination of glutamine (small intestine)
- Impaired hepatic metabolism of NH_3 and portal hypertension ➔ shunting of NH_3-rich portal blood to systemic circulation
- NH_3 crosses blood-brain barrier and is metabolized by astrocytes to glutamine
- Glutamine accumulation ➔ cerebral dysfunction

Elwis S, Rahimi RS. *J Clin Transl Hepatol*. 2017;5(2):142-151; Swaminathan M, et al. *Hepatic Med*. 2018;10:1-11.

Characteristics Associated With Poor Outcomes Following a Diagnosis of HE

Baseline Variable	Death		Hospital Days	
	Adjusted HR (95% CI)	*P* Value	Adjusted IRR (95% CI)	*P* Value
Age (per year)	1.02 (1.02, 1.03)	<0.001	1.01 (1.01, 1.01)	<0.001
Male	1.21 (1.19, 1.24)	<0.001	1.03 (0.99, 1.06)	0.116
End-stage renal disease	1.08 (1.01, 1.14)	0.015	1.15 (1.06, 1.25)	<0.001
Urban	1.01 (0.98, 1.04)	0.707	1.04 (1.00, 1.09)	0.063
Race (relative to White)				
Black	1.00 (0.96, 1.04)	0.960	1.17 (1.10, 1.23)	<0.001
Other	0.90 (0.87, 0.94)	<0.001	0.97 (0.92, 1.03)	0.353
Cirrhosis etiology				
Alcohol	0.82 (0.79, 0.85)	<0.001	1.01 (0.94, 1.09)	0.692
Hepatitis C	0.87 (0.85, 0.90)	<0.001	1.20 (1.15, 1.25)	<0.001
Hepatitis B	1.19 (0.88, 1.61)	0.980	0.79 (0.75, 0.83)	<0.001
Nonalcohol, nonviral cirrhosis	1.07 (1.02, 1.12)	0.004	0.98 (0.93, 1.03)	0.427

CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio.

Tapper EB, et al. *Aliment Pharmacol Ther*. 2020;51:1397-1405.

Characteristics Associated With Poor Outcomes Following a Diagnosis of HE (Continued)

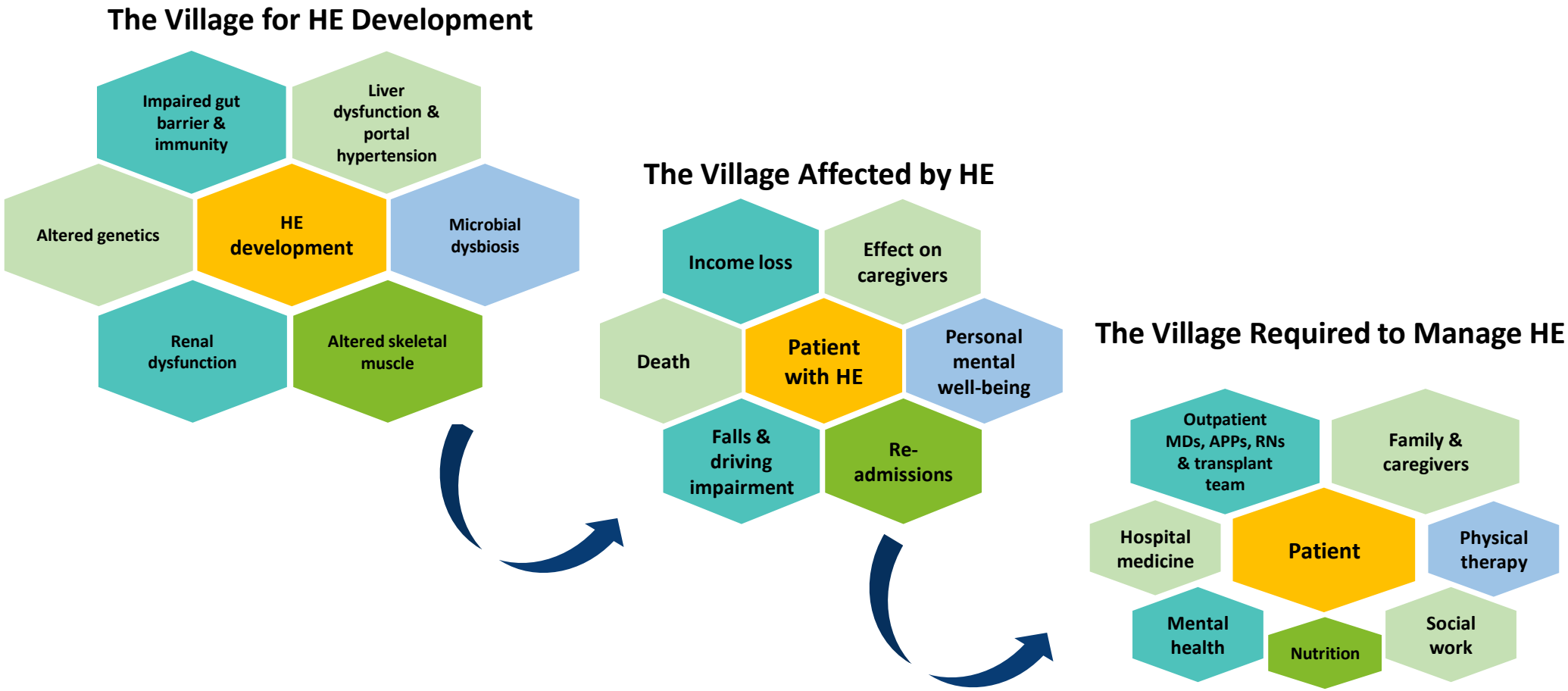
Baseline Variable	Death		Hospital Days	
	Adjusted HR (95% CI)	*P* Value	Adjusted IRR (95% CI)	*P* Value
Time-varying covariates				
Gastroenterology consult	0.73 (0.67, 0.80)	<0.001	1.07 (1.00, 1.14)	0.056
Rifaximin	0.40 (0.39, 0.42)	<0.001	0.35 (1.33, 0.37)	<0.001
Ascites	4.20 (4.08, 4.32)	<0.001	1.86 (1.79, 1.93)	<0.001
Varices	1.03 (1.00, 1.06)	0.029	0.77 (0.74, 0.80)	<0.001
TIPS	1.15 (1.08, 1.23)	<0.001	1.14 (1.05, 1.24)	0.002
Hepatocellular carcinoma	2.27 (2.19, 2.34)	<0.001	0.95 (0.91, 1.00)	0.057
Charlson Comorbidity Index (CCI: relative to CCI 0)				
CCI = 1	1.20 (1.17, 1.24)	<0.001	1.17 (1.13, 1.22)	<0.001
CCI = 2	1.26 (1.22, 1.30)	<0.001	1.28 (1.23, 1.34)	<0.001
CCI ≥3	1.42 (1.35, 1.48)	<0.001	1.33 (1.24, 1.42)	<0.001

TIPS, Transjugular intrahepatic portosystemic shunt.

Tapper EB, et al. *Aliment Pharmacol Ther*. 2020;51:1397-1405.

The Multilayered Impact of HE

The Three Villages of HE



Bajaj JS. *Am J Gastroenterol*. 2021;116:1184-1186.

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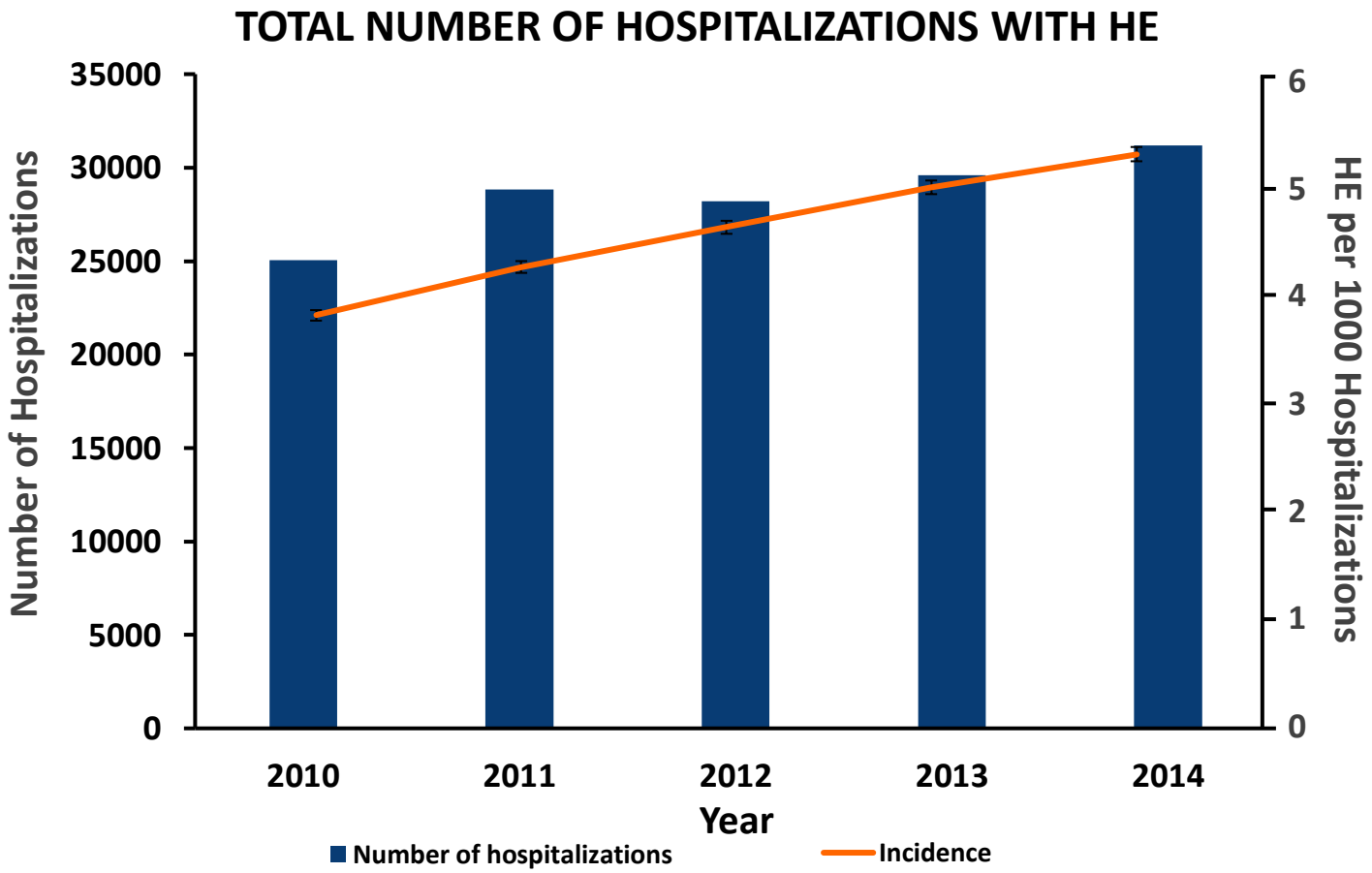
HE in the Hospital Setting

Trends in Hospitalizations With HE in the US



Hospitalized patients with cirrhosis and HE (2010 – 2014):

- Total hospitalizations ↑ **24.4%** (*graph*)
- Prolonged hospitalizations* ↑ **38%**
- In-hospital mortality ↑ **45%**

*Prolonged hospital stay was defined by a length of stay in the 75th percentile or higher.

Al-Taee AM, et al. *Eur J Gastroenterol Hepatol*. 2019;31(9):1165-1166; Hirode G, et al. *Dig Dis Sci*. 2019;64(6):1448-1457.

Factors Associated With Greater Risk for HE Among Hospitalized Patients With Cirrhosis

Portal hypertension

AHR: 3.42 with vs without

Cause of cirrhosis

AHR: 1.44 for alcohol-related vs NAFLD-related

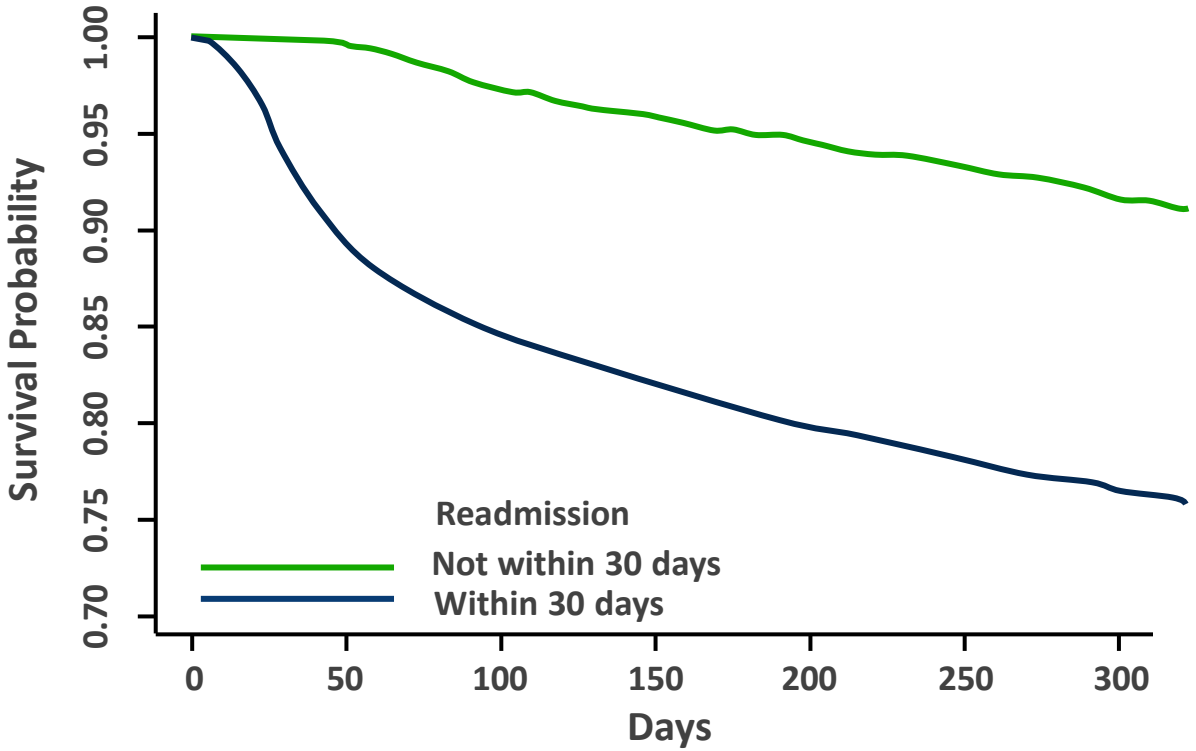
Medication use

Benzodiazepines – AHR: 1.19
GABAergics – AHR: 1.17
Opioids – AHR: 1.24
PPIs – AHR: 1.41

AHR, adjusted hazard ratio; GABA, gamma-aminobutyric acid; NAFLD, nonalcoholic fatty liver disease; PPIs, proton pump inhibitors.
Tapper EB, et al. *Hepatol Commun*. 2019;3(11):1510-1519.

30-Day Readmission Is Associated With Poor Survival in Hospitalized Patients With HE

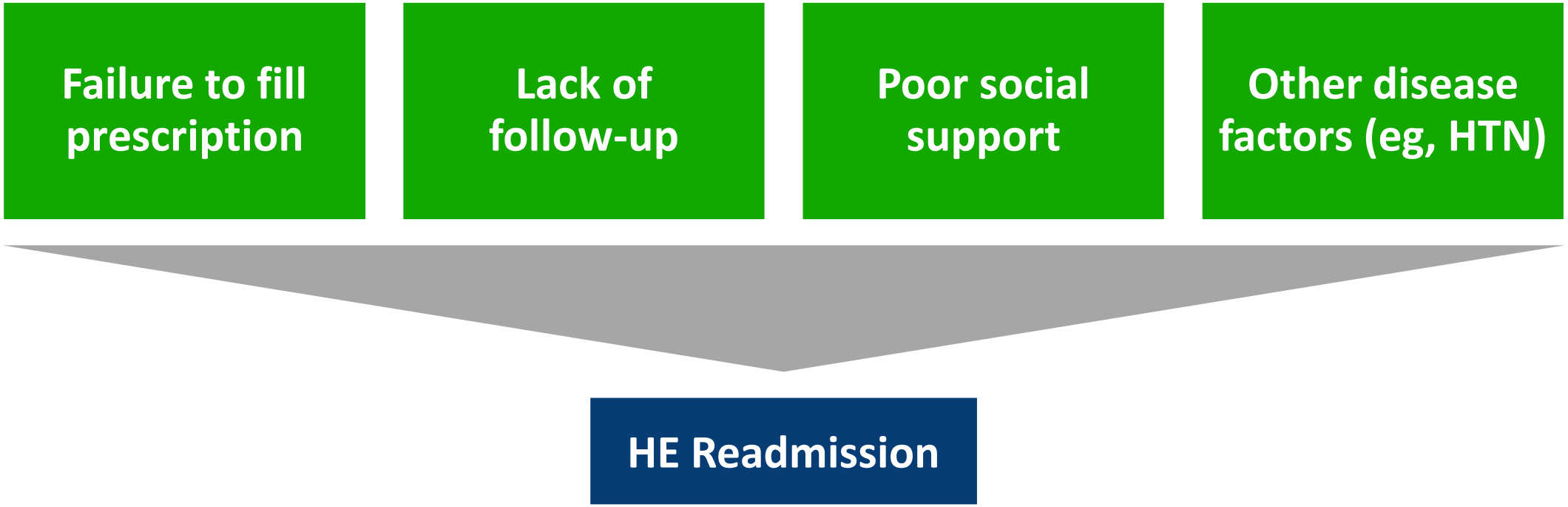
Probability of survival with vs without readmission within 30d among patients with HE



Patients readmitted ≤30d of index hospitalization had significantly lower calendar-year survival vs those not readmitted ≤30 d (HR, 4.03; 95% CI, 3.50-4.66).

Kruger AJ, et al. *Ann Hepatol*. 2019;18(2):310-317.

Factors Contributing to HE Readmission



HTN, hypertension.

Neff G. *Hepatology*. 2013;58(S1):390A-391A; Rassameehiran S, et al. *South Med J*. 2016;109(6):365-9.

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Recognition and Diagnosis of HE

HE Types Based Upon Underlying Disease

Type	Underlying Disease
A	Acute liver failure
B	PSS or bypass
C	Cirrhosis

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

West Haven Criteria Minimal and Grade I HE

WHC	Description	Operative Criteria
Unimpaired	▪ No encephalopathy, HE history	▪ Normal test results
Minimal	▪ Alterations in psychomotor speed/executive functions or on neurophysiological measures ▪ No clinical evidence of mental change	▪ Abnormal results on psychometric or neurophysiological tests ▪ No clinical manifestations
Grade I	▪ Trivial lack of awareness ▪ Euphoria or anxiety ▪ Shortened attention span ▪ Impairment of addition or subtraction ▪ Altered sleep rhythm	▪ Orientation in time and space ▪ Cognitive/behavioral decay with respect to standard on clinical examination, or to caregivers

All conditions are required to be related to liver insufficiency and/or PSS.

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

West Haven Criteria Grades II, III, and IV HE

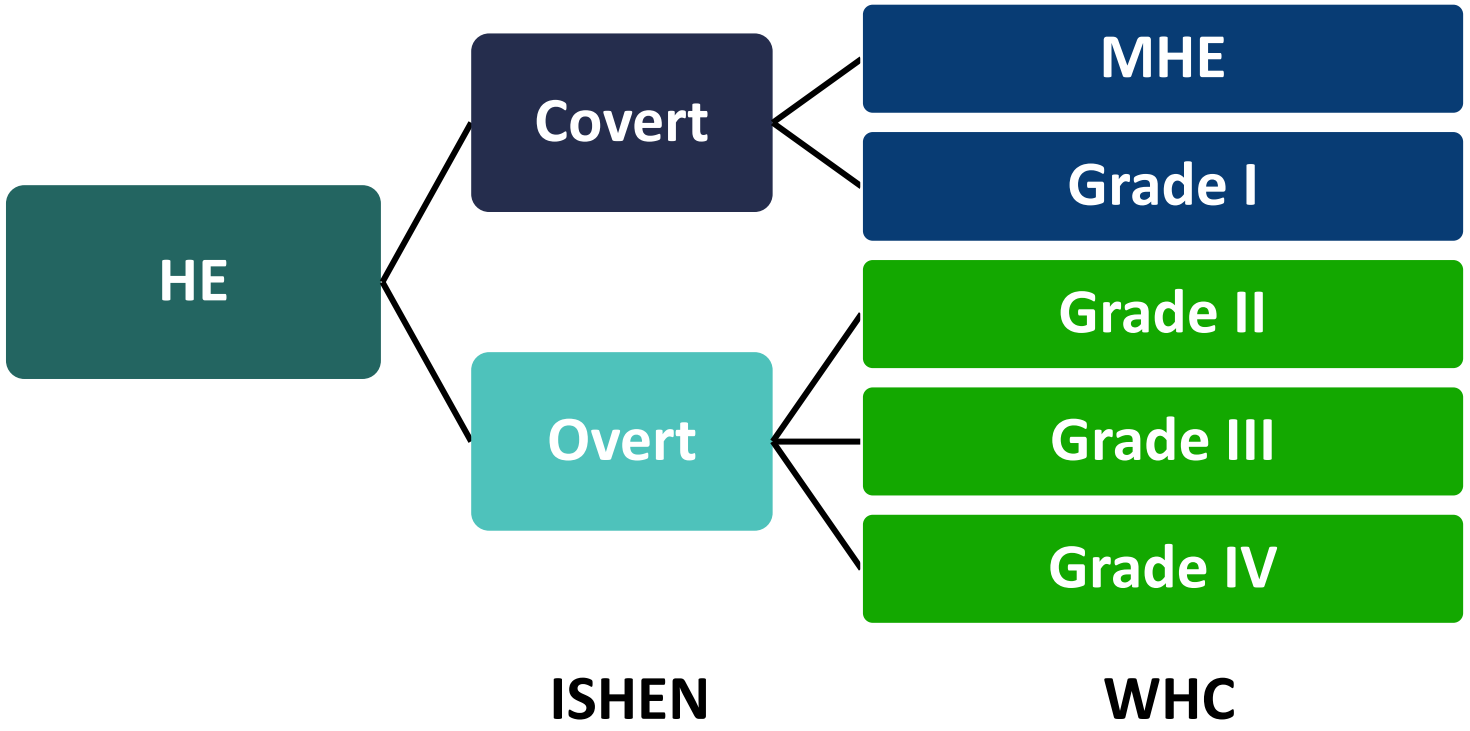
WHC	Description	Operative Criteria
Grade II	▪ Lethargy or apathy ▪ Disorientation for time ▪ Obvious personality change ▪ Inappropriate behavior ▪ Dyspraxia ▪ Asterixis	▪ Disoriented for time (≥3 of the following errors: day of month or week, month, season, or year) ▪ ± Other symptoms
Grade III	▪ Somnolence to semi stupor ▪ Responsive to stimuli ▪ Confused ▪ Gross disorientation ▪ Bizarre behavior	▪ Disoriented for space (≥3 of the following errors: country, state [or region], city, or place) ▪ ± Other symptoms
Grade IV	▪ Coma	▪ Does not respond even to painful stimuli

All conditions are required to be related to liver insufficiency and/or PSS.

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

Covert vs Overt HE

Poor reliability of *Grade I* staging has led to the classification of covert vs overt HE:



ISHEN, International Society for Hepatic Encephalopathy and Nitrogen Metabolism; MHE, minimal HE.
Vilstrup H, et al. *Hepatology*. 2014;60(2):715-735.

Diagnosis and Staging of HE

Clinical Examination

Reliable markers

- Disorientation
- Asterixis

Easily overlooked markers

- Mild hypokinesia
- Psychomotor slowing
- Attention deficits

Staging Disease Severity

West Haven Criteria (gold standard)

Quantitative Testing

Only in study settings

2014 AASLD/EASL Practice Guidelines. *Hepatology*. 2014;60(2):715-735.

Precipitating Factors for Overt HE

Precipitating Factor	%	Precipitating Factor	%
Dehydration	76	TIPS	13
Acute renal failure	76	GI bleeding	13
Lactulose nonadherence	53	Hyponatremia	13
Infections	42	Large-volume paracentesis	9
Constipation	40	High protein diet	0
Opioids and benzodiazepines	27	Unknown	0
Hypokalemia	20		

GI, gastrointestinal.

Pantham G, et al. *Dig Dis Sci*. 2017;62:2166-2173.

Diagnostic Tests

- Complete blood count
- Comprehensive metabolic panel
- Blood cultures
- Urine analysis and culture
- Chest x-ray
- Paracentesis
- Alcohol level/drug screen if suspicion arises based on history

Differential Diagnosis of HE

Overt HE or Acute Confusional State

- Diabetes
- Alcohol
- Drugs
- Neuroinfections
- Electrolyte disorders
- Nonconvulsive epilepsy
- Psychiatric disorders
- Intracranial bleeding and stroke
- Severe medical stress

Other Presentations

- Dementia
- Brain lesions
- Obstructive sleep apnea

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

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Treatment of Acute Overt HE

Approach to the Management of Overt HE (2014 AASLD/EASL)

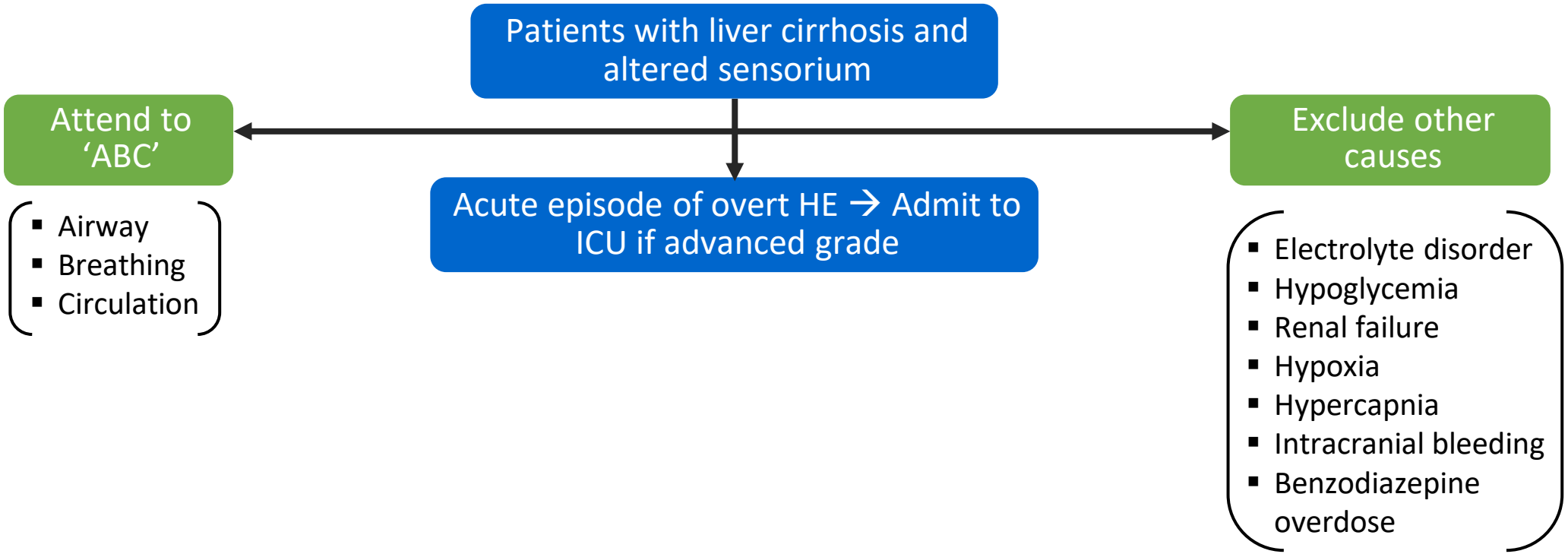
2014 AASLD/EASL Practice Guidelines. *Hepatology*. 2014;60(2):715-735.

Algorithm for the Management of Overt HE (2020 ISHEN Consensus)

Patients with liver cirrhosis and altered sensorium

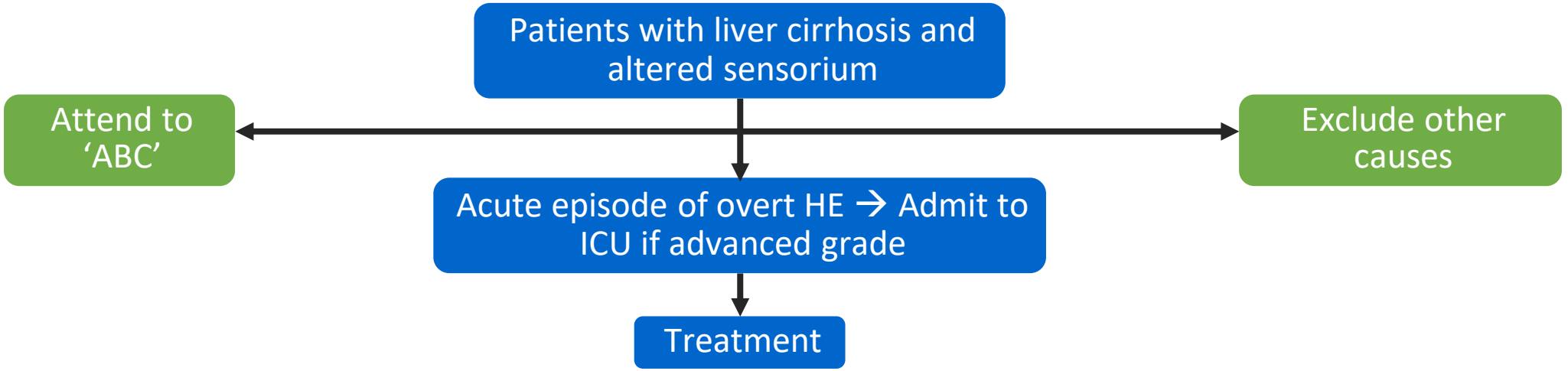
Bajaj JS, et al. *Am J Gastroenterol*. 2020;115(7):989-1002.

Algorithm for the Management of Overt HE (2020 ISHEN Consensus)



Bajaj JS, et al. *Am J Gastroenterol*. 2020;115(7):989-1002.

Algorithm for the Management of Overt HE (2020 ISHEN Consensus)



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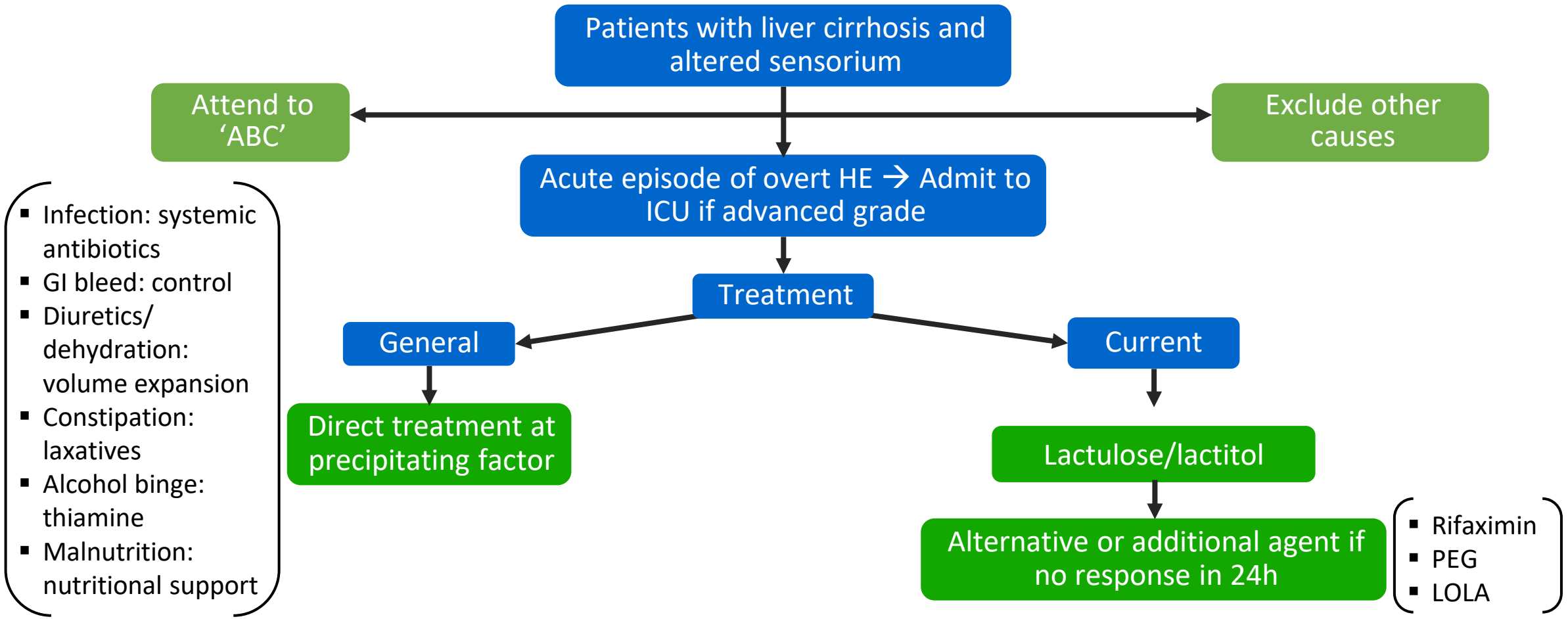


LOLA, L-ornithine L-aspartate; PEG, polyethylene glycol.

Bajaj JS, et al. *Am J Gastroenterol*. 2020;115(7):989-1002.

Therapies for Acute Overt HE

	Agent	Mechanism of Action/Comments
Available	Nonabsorbable disaccharides	Promotes NH_3 conversion to NH_4^+ in the colon, shifting flora from urease- to non-urease-producing bacteria; exerts a cathartic effect
	Rifaximin	Reduces NH_3 by eliminating NH_3-producing colon bacteria; indicated for reducing risk of OHE recurrence in adults
	Zinc	Enhances urea formation from NH_3 and amino acids
Emerging	PEG 3350-electrolyte solution	Purgative; causes water to be retained in the colon, produces a watery stool
	Ornithine Phenylacetate	Ammonia scavenger; lowers ammonia levels independent of gut action (ie, by a different mechanism) in patients with cirrhosis

NH3, ammonia; NH4, ammonium; OHE, overt hepatic encephalopathy.

Elwir S, et al. *J Clin Transl Hepatol*. 2017;5(2):142-151; Flamm SL. *Ther Adv Gastroenterol*. 2011;4(3):199-206; Lynn AM, et al. *Liver Transpl*. 2016 Jun;22(6):723-31; Leise MD, et al. *Mayo Clin Proc*. 2014;89(2):241-253.

Lactulose for the Reduction of NH3 in Patients With OHE

Dosing

- Initial dose: 30 mL orally, tid
- 300 mL in 700 mL water or normal saline as an enema retained for 30–60 minutes every 4–6 hours

Adverse events*

- Aspiration
- Dehydration
- Hypernatremia
- Severe perianal skin irritation
- Precipitation of HE with overuse

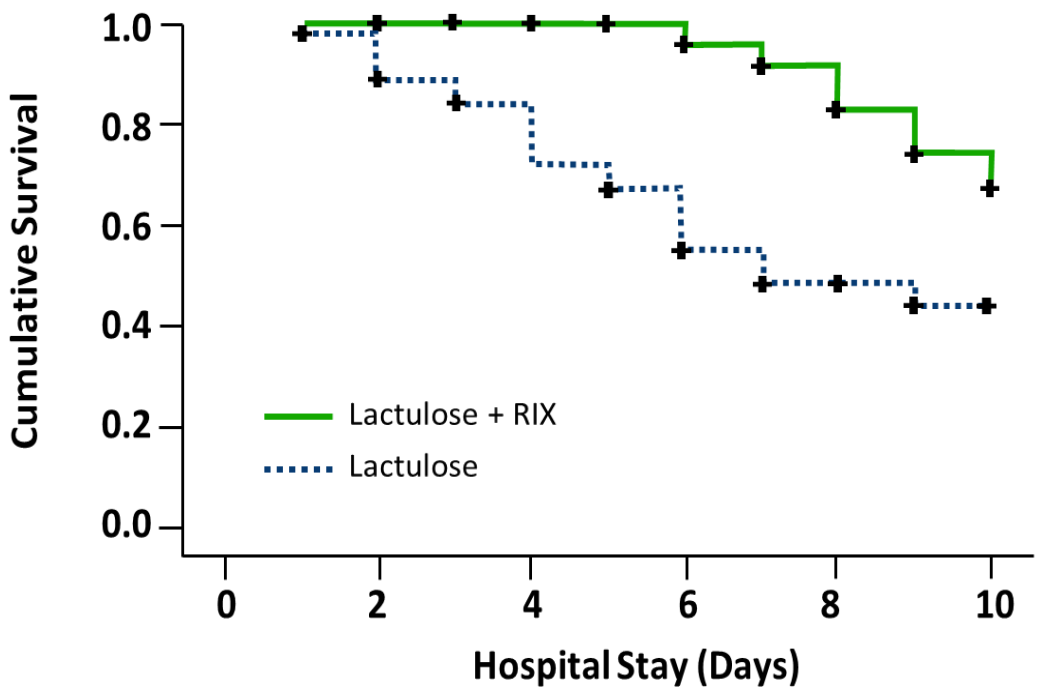
*Data for precise frequency of AEs are not available.

tid, three times a day.

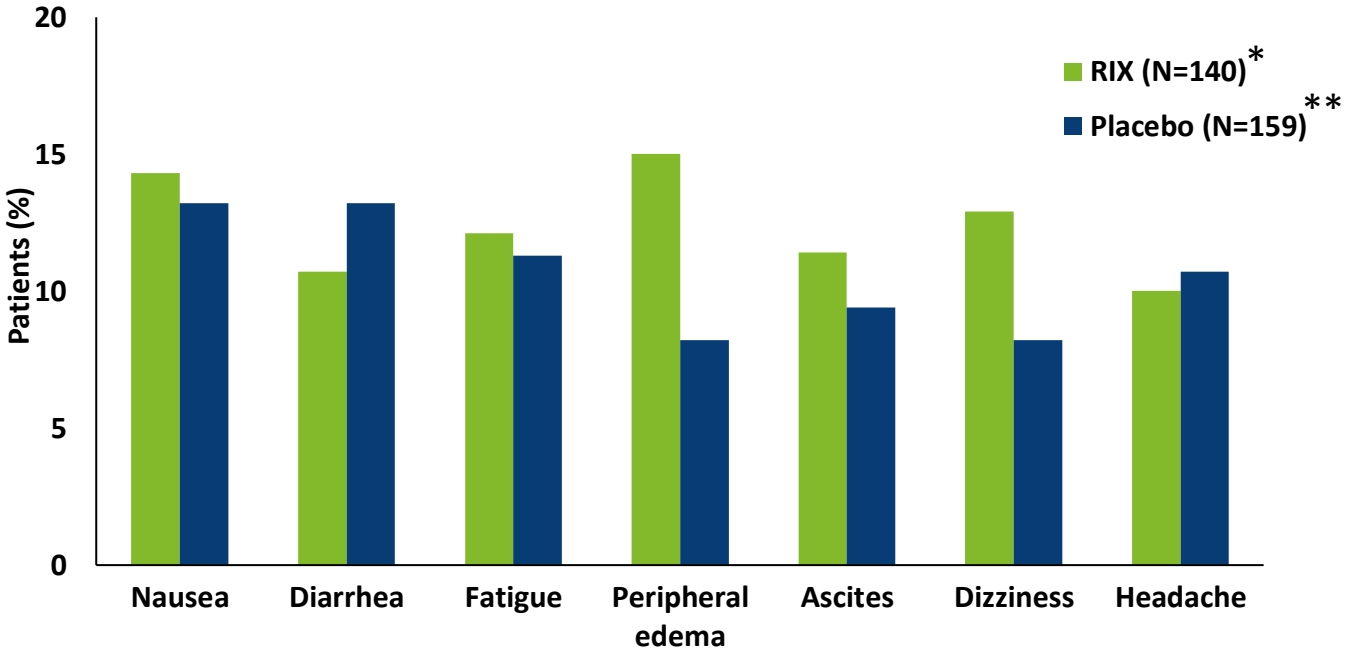
Enulose® [package insert]. Baltimore, MD: Actavis Mid Atlantic LLC; 2006; Vilstrup H, et al. *Hepatology*. 2014;60(2):715-735.

RIX Added on to Lactulose for the Treatment of Acute Overt HE

Survival



Safety and tolerability

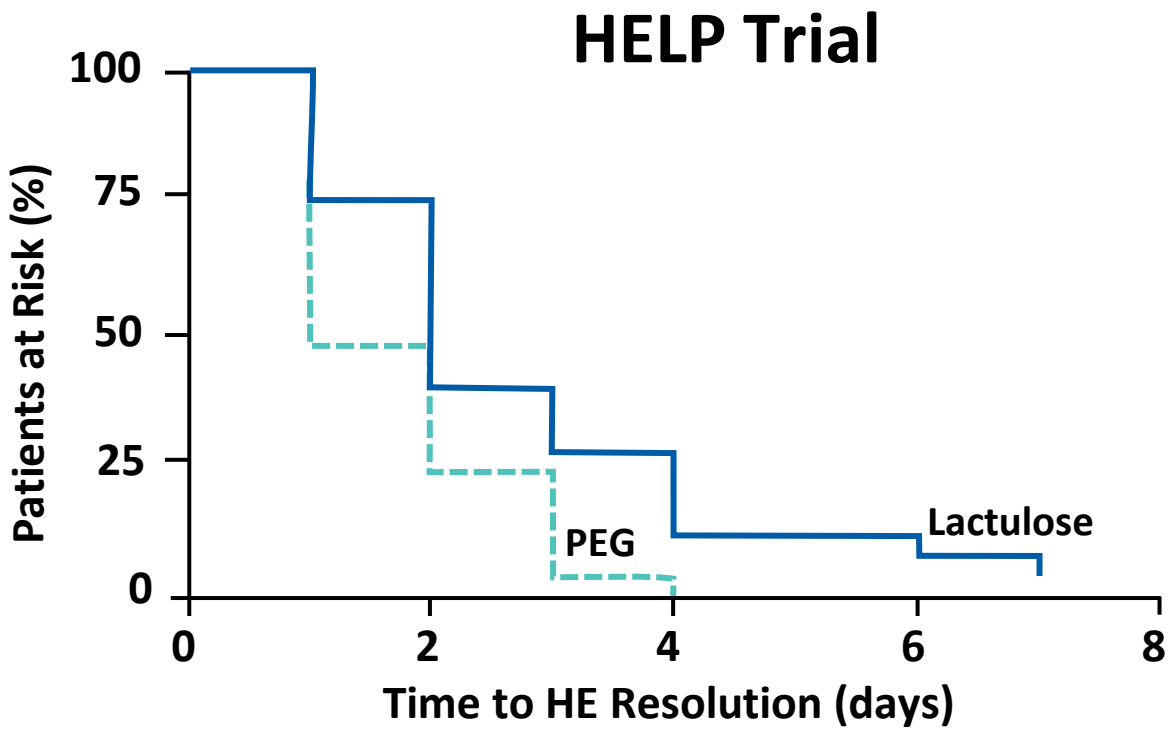


The incidence of common AEs† did not differ significantly between groups.

*91.4% receiving concomitant lactulose; ** 91.2% receiving concomitant lactulose; †AEs occurring at an incidence rate of ≥10% in the rifaximin group.

Sharma BC, et al. *Am J Gastroenterol*. 2013;108(9):1458-1463; Bass NM, et al. *N Engl J Med*. 2010;362(12):1071-1081.

PEG-3350 Treatment in Patients With Cirrhosis Hospitalized for HE



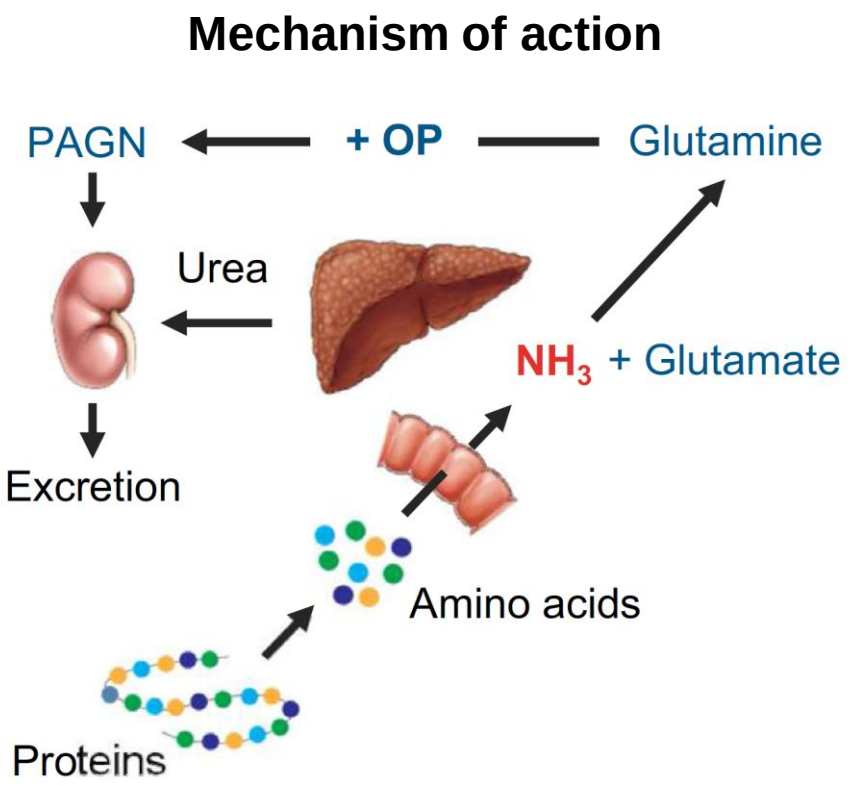
- PEG vs standard lactulose increased:
  - **Rate of HE resolution**‡ (*graph*)
  - % patients with **HESA score improvement ≥1***
  - Mean **HESA score at 24h**†

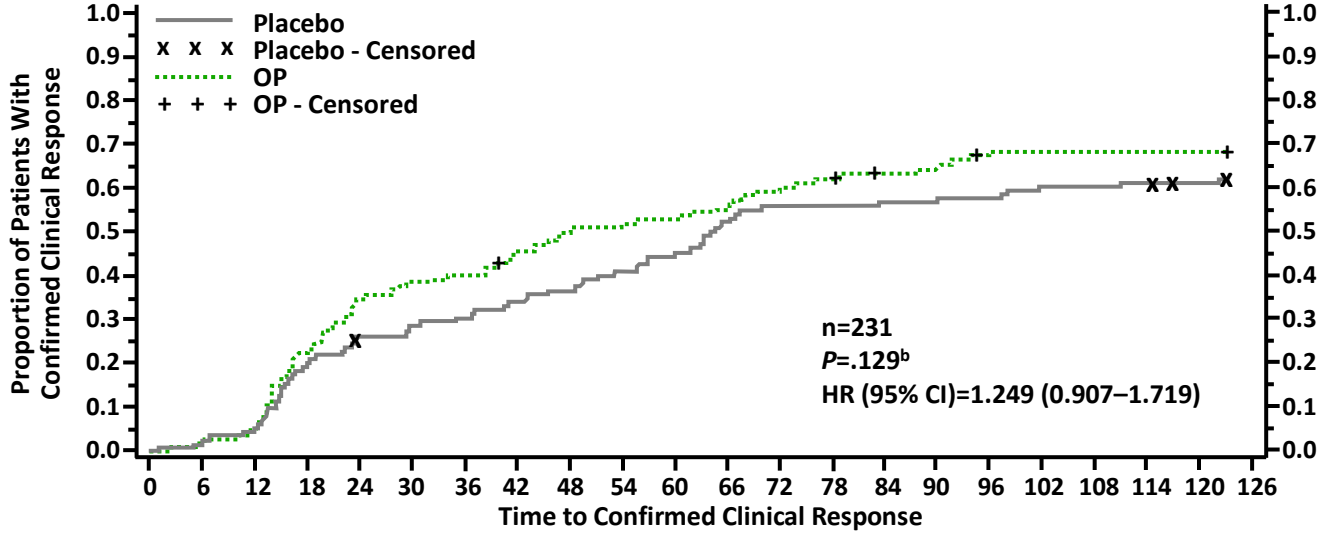
*P<.01; †P=.002; ‡P=.01.

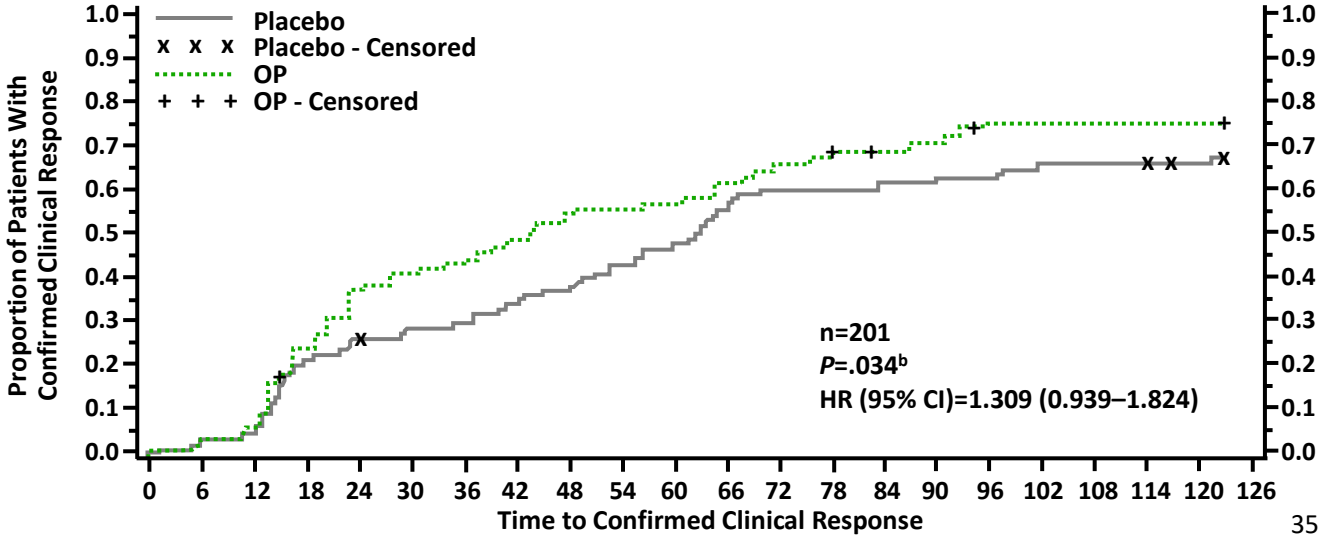
PEG, polyethylene glycol 3350-electrolyte solution; HESA, hepatic encephalopathy scoring algorithm.

Rahimi RS, et al. *JAMA Int Med*. 2014;174(11):1727-1733.

Ornithine Phenylacetate in Hospitalized Patients With Cirrhosis, Increased Ammonia Levels, and Acute OHE







OP, ornithine phenylacetate; PAGN, phenylacetylglutamine.

Rahimi RS, et al. *Clin Gastroenterol Hepatol*. 2020;S1542-3565(20)31432-4.

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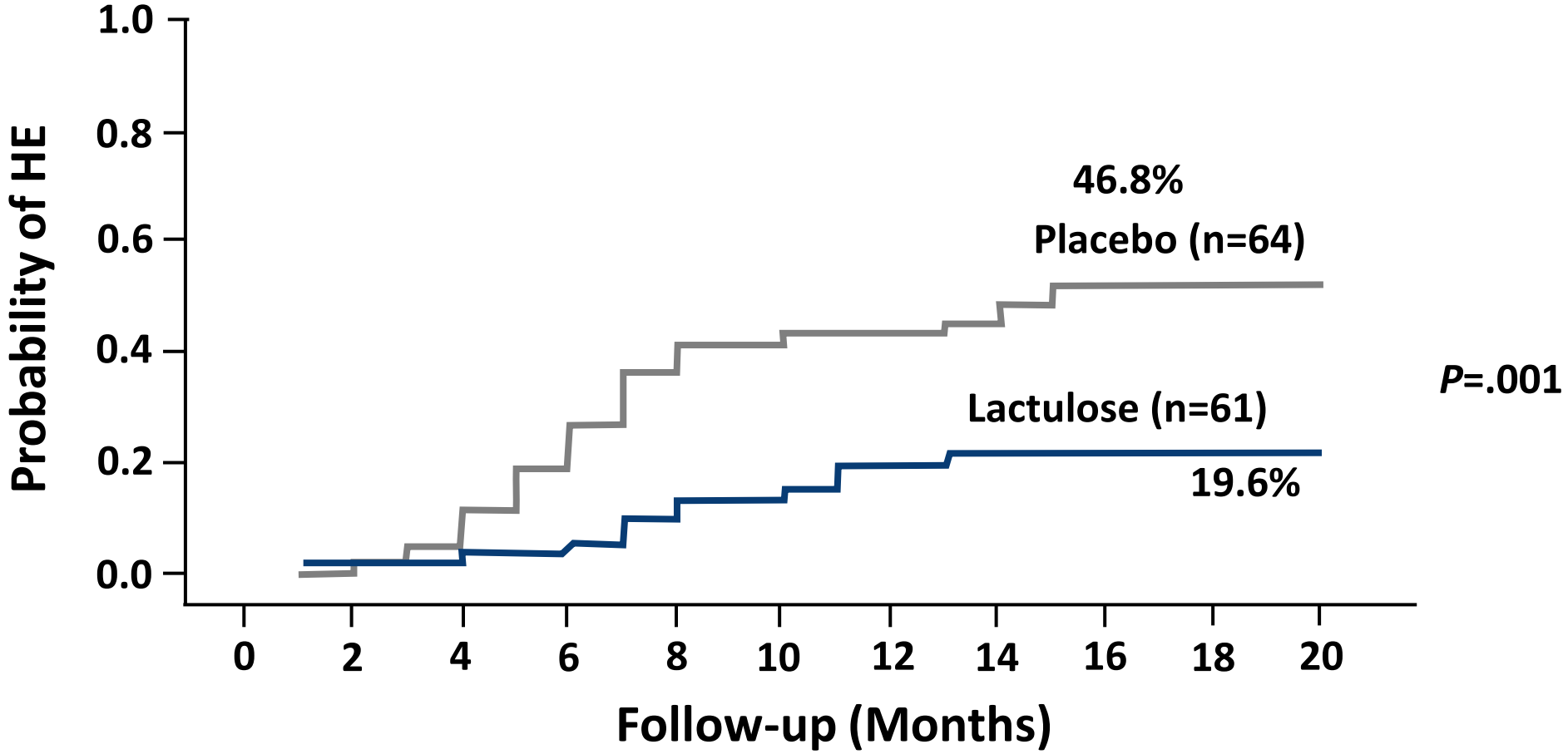
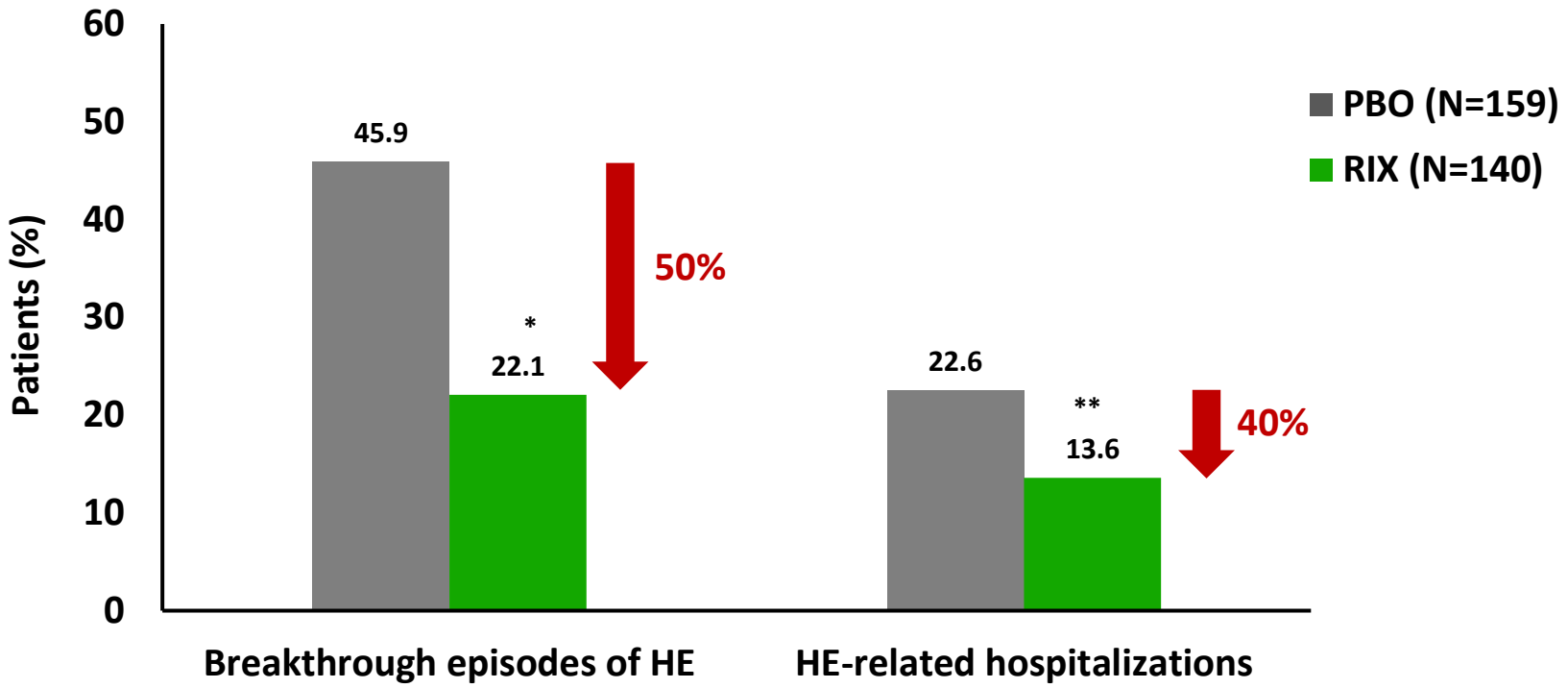
Prophylaxis of Recurrent Overt HE

Lactulose Prevents Recurrence of HE in Patients With Cirrhosis



Sharma BC, et al. *Gastroenterology*. 2009;137(3):885-891.e881.

Effect of RIX on Breakthrough HE Episodes and HE-related Hospitalizations



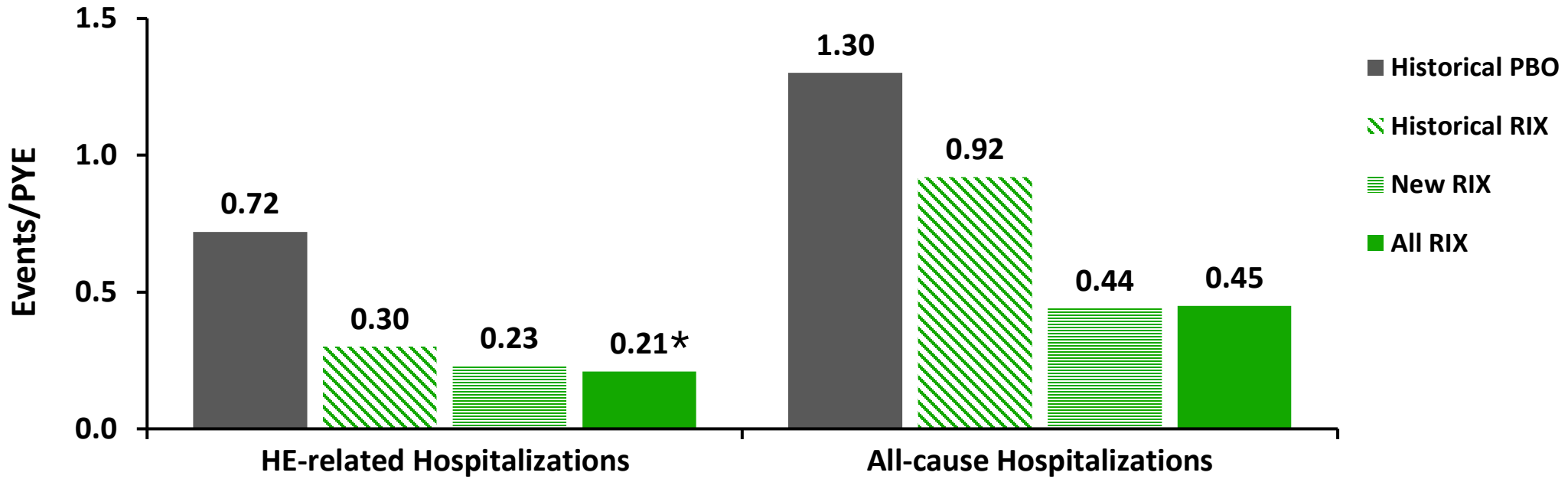
Over a 6-month period, treatment with RIX resulted in lower rates of both OHE breakthrough and HE-related hospitalizations vs PBO.

*P<0.001 vs PBO; **P=0.01 vs PBO

Note: >90% of patients received concomitant lactulose during the study period.

Bass NM, et al. *N Engl J Med*. 2010;362(12):1071-1081.

Long-term Maintenance of Remission From Overt HE With RIX



Treatment with RIX for ≥2 years reduced the rate of HE-related and all-cause hospitalization, without increasing AE rates.

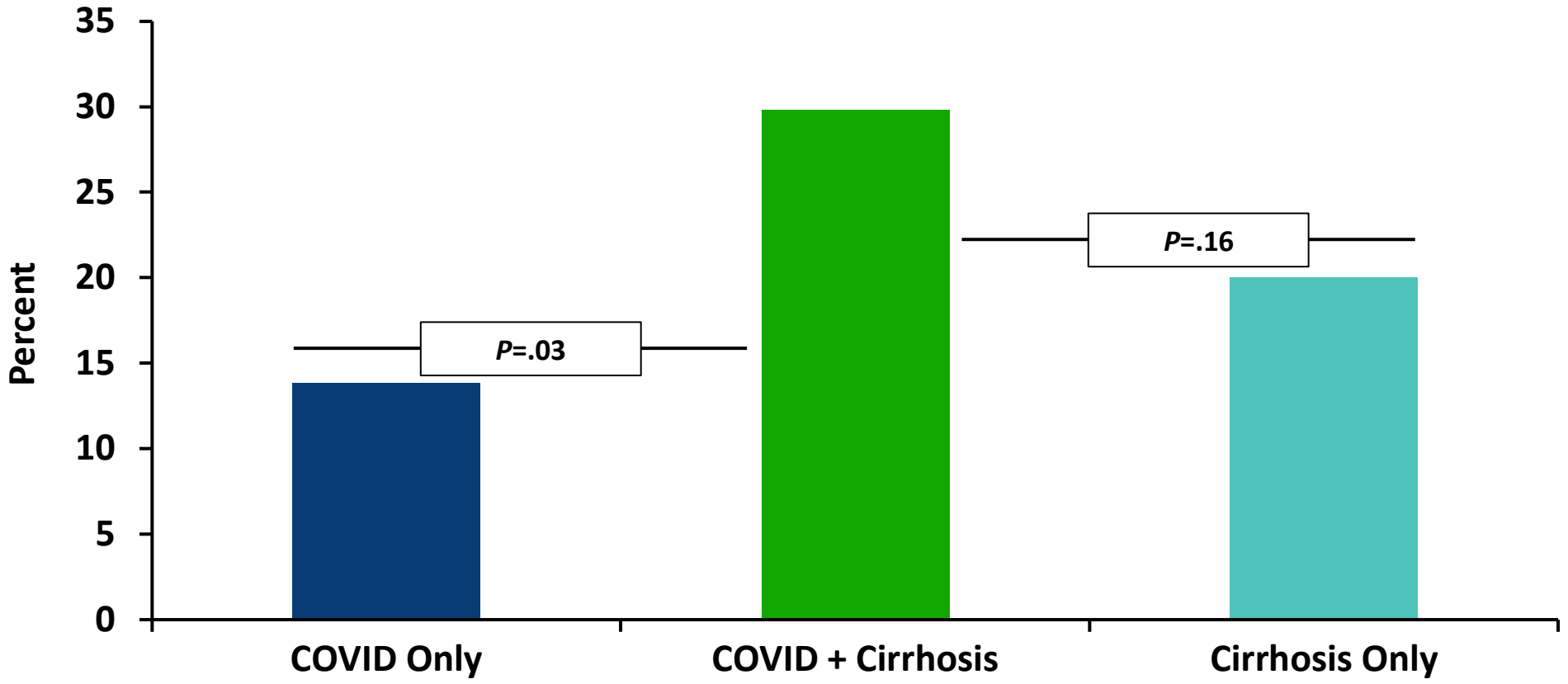
*P<.001 vs PBO.

PYE, person-years of exposure.

Mullen KD, et al. *Clin Gastroenterol Hepatol*. 2014;12(8):1390-1397.e1392.

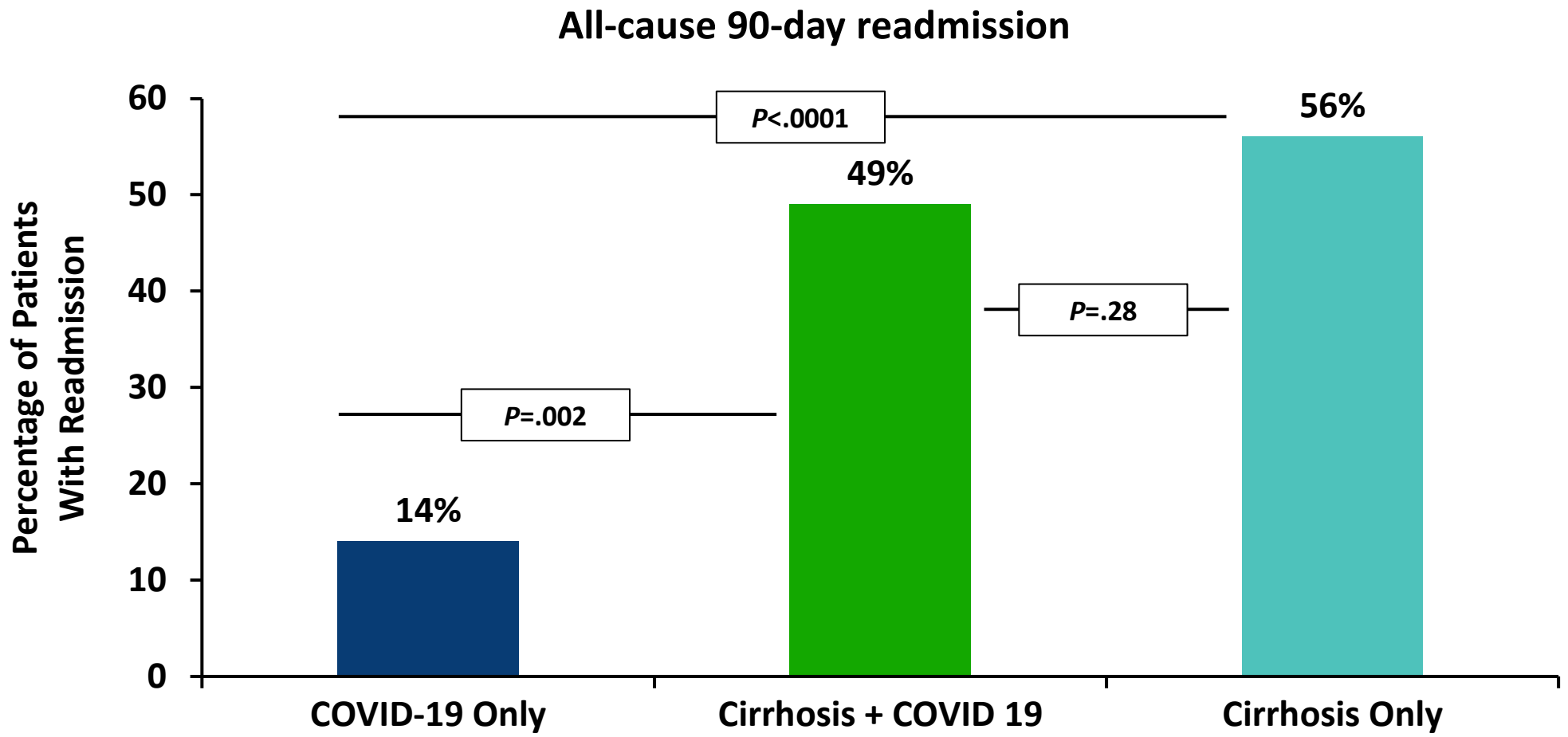
Care of Hospitalized Patients With Cirrhosis and HE in the Era of COVID-19

Patients With Cirrhosis and COVID-19 Are at Increased Risk for Mortality



Bajaj JS, et al. *Gut*. 2021;70:531-536.

Readmission Rates Among Patients With Cirrhosis and COVID-19



Bajaj JS, et al. *Liver Transpl*. 2021.

mRNA COVID-19 Vaccination in Patients With Cirrhosis

Vaccine + Control	Day 0-7		Day 7-14		Day 14-21		Day 21-28		Day 28-Onward		Efficacy Day 28 on, % (95% CI)*	*P* Value
	Vaccine	Control	Vaccine	Control	Vaccine	Control	Vaccine	Control	Vaccine	Control		
COVID-19 infection												
No.	183										64.8 (10.9–86.1)	
Events, no.	25	36	21	32	17	12	14	8	6	17		
Cumulative events, no.	25	36	46	68	63	80	77	88	83	105		0.03
No. at risk	20037	20037	18109	18073	15991	15935	13731	13678	12059	12012		
Cumulative incidence, %	0.12	0.18	0.25	0.38	0.39	0.50	0.56	0.64	0.69	0.87		
Hospitalization for COVID												
No.	57										100.0 (99.3–100.0)	
Events, no.	4	8	8	7	6	5	10	6	0	3		
Cumulative events, no.	4	8	12	15	18	20	28	26	28	29		0.20
No. at risk	20037	20037	18109	18073	15991	15935	13731	13678	12059	12012		
Cumulative incidence, %	0.02	0.04	0.07	0.08	0.11	0.13	0.20	0.19	0.23	0.24		
COVID-19–related death												
No.	13										100.0 (99.3–100.0)	
Events, no.	1	3	2	1	0	2	1	1	0	2		
Cumulative events, no.	1	3	3	4	3	6	4	7	4	9		0.20
No. at risk	20037	20037	18109	18073	15991	15935	13731	13678	12059	12012		
Cumulative incidence, %	0	0.01	0.02	0.02	0.02	0.04	0.03	0.05	0.03	0.07		

mRNA vaccine administration was associated with a delayed but modest reduction in COVID-19 infection and a reduction in COVID-19–related hospitalization or death in patients with cirrhosis.

John BV, et al. *JAMA Intern Med*. 2021.Online ahead of print.

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COVID-19, Cirrhosis, and HE

- Patients with cirrhosis and COVID-19 infection are at increased risk:
  - More severe COVID-19 illness
  - Greater complications related to existing liver disease
  - Prolonged hospitalization
  - Increased mortality
- 47% of patients with cirrhosis and COVID-19 present with acute hepatic decompensation
  - Typically worsening ascites and encephalopathy
- Prompt recognition and accurate diagnosis are crucial to avoid poor health outcomes

Tapper EB, et al. *J Hepatol*. 2020;73:441-445; Bajaj JS, et al. *Liver Transpl*. 2021; Bajaj JS, et al. *Gut*. 2021;70:531-536.

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Transition of Care Following Acute OHE Resolution

Planning for Patient Discharge

Neurological Status

- Confirm status
- Assess other contributing causes
- Inform caregivers of potential changes after acute illness resolution & need for monitoring

Patient & Caregiver Education

- Identify and discuss precipitating factors
- Plan for future HE management
  - Role of nutrition
  - Importance of prophylaxis
  - Driving considerations
  - Recommended vaccinations

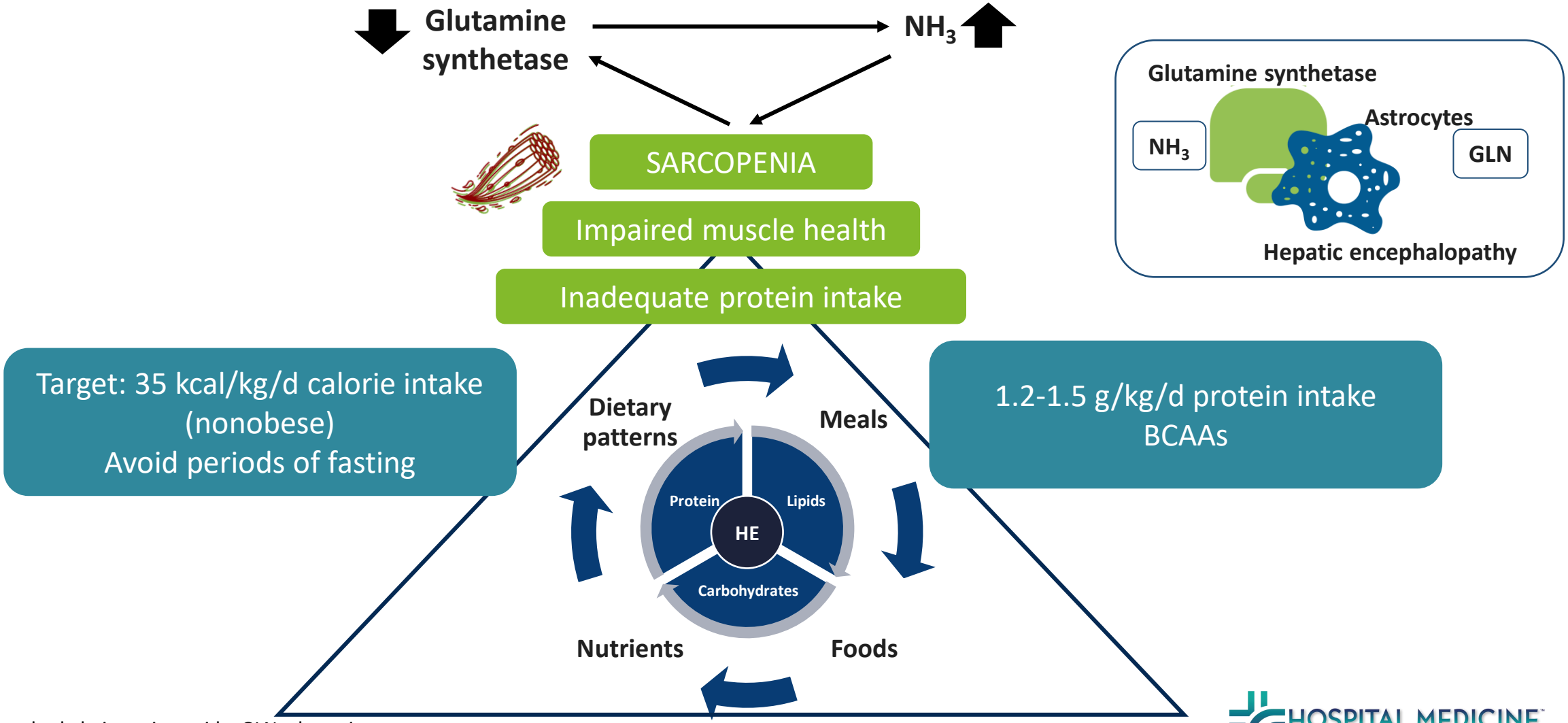
Postdischarge Follow-up

- Ensure follow-up with PCPs who can:
  - ✓ Adjust prophylactic treatment
  - ✓ Advise on avoiding precipitating factors
  - ✓ Act as liaison between patient's family, caregivers, & HCPs
- Discuss GI consult

HCP, healthcare provider; PCP, primary care provider.

2014 AASLD/EASL Practice Guidelines. *Hepatology*. 2014;60(2):715-735.

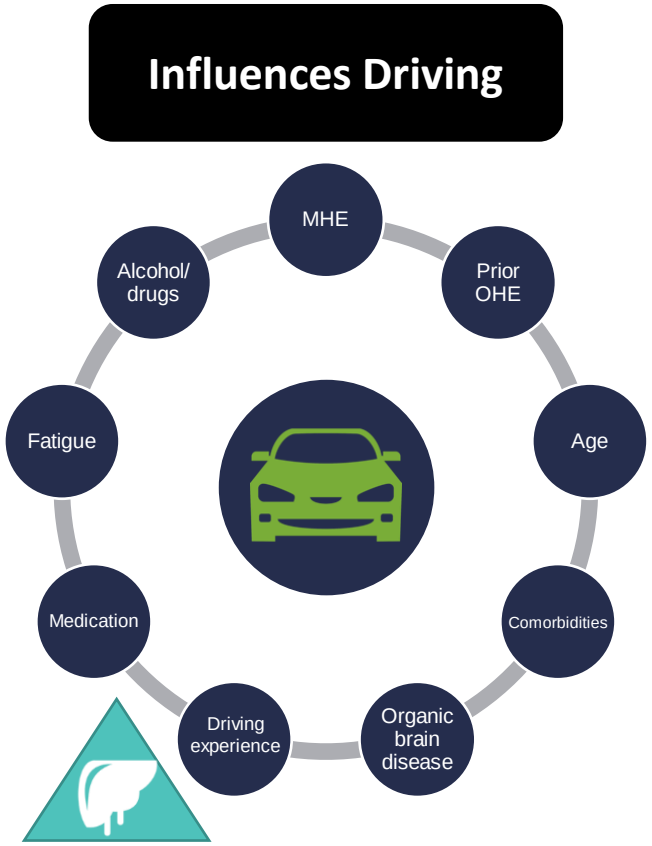
The Central Role of Nutrition in HE Management



BCAA, branched-chain amino acids; GLN, glutamine.

Bajaj JS, et al. *Am J Gastroenterol*. 2020;115:989-1002.

Contributing Factors, Consequences, and Management of Driving Impairment in HE



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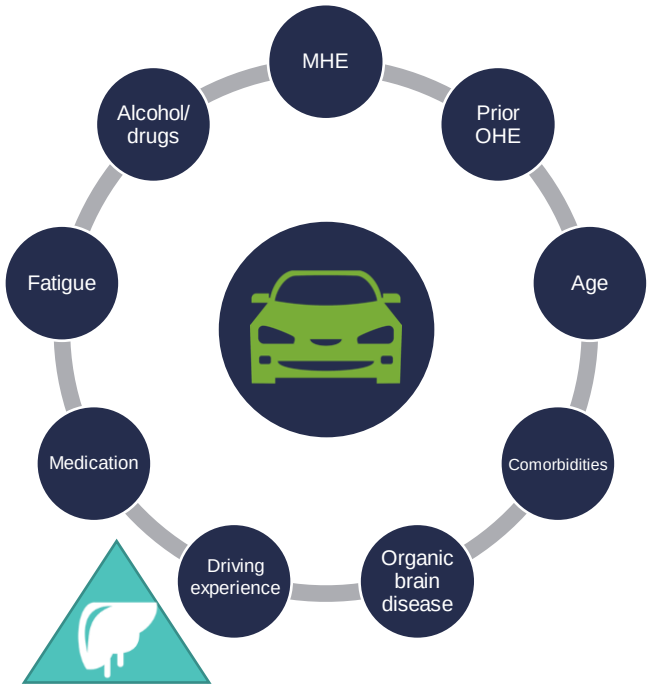
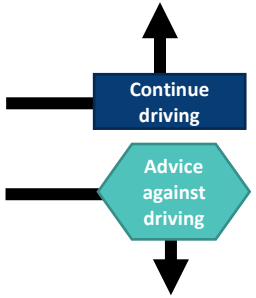
Contributing Factors, Consequences, and Management of Driving Impairment in HE

Influences Driving



Consequences

- Accidents
- Near misses
- Getting lost



- Isolation
- Lower self-sufficiency
- Damage to patient-doctor relationship

Bajaj JS, et al. *Am J Gastroenterol*. 2020;115:989-1002.

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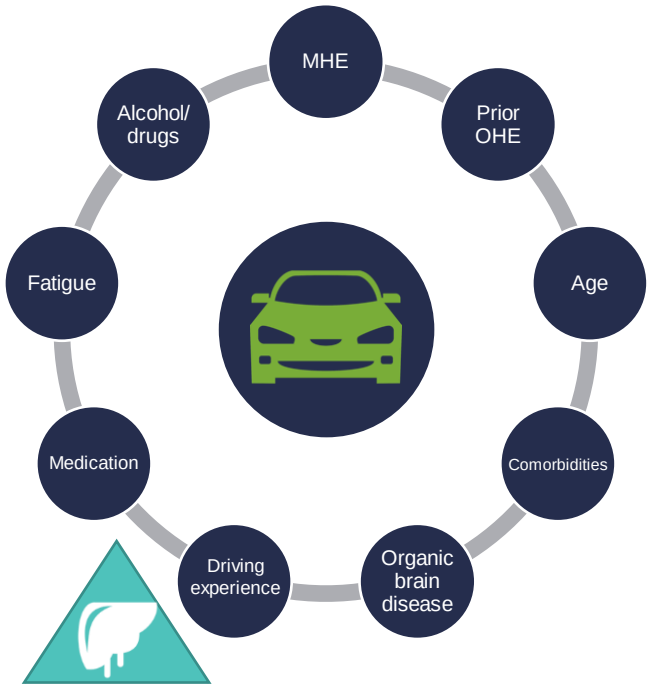

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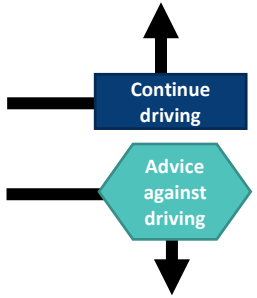

- Isolation
- Lower self-sufficiency
- Damage to patient-doctor relationship

Driving Assessment

- Short driving history should be taken at every visit
- On-road driving test
- Driving simulation
- Driving history
- Cognitive testing

CAUTION

- Physicians do not have legal authority to withdraw a patient's driver license
- Physicians may be obliged to report an unsafe driver to authorities

Bajaj JS, et al. *Am J Gastroenterol*. 2020;115:989-1002.

Contributing Factors, Consequences, and Management of Driving Impairment in HE

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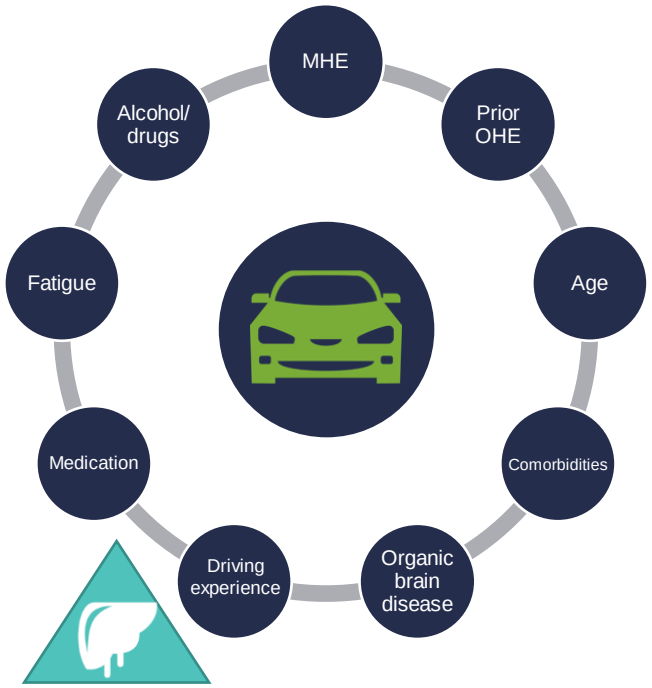

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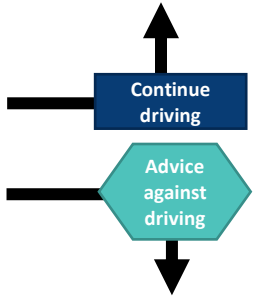

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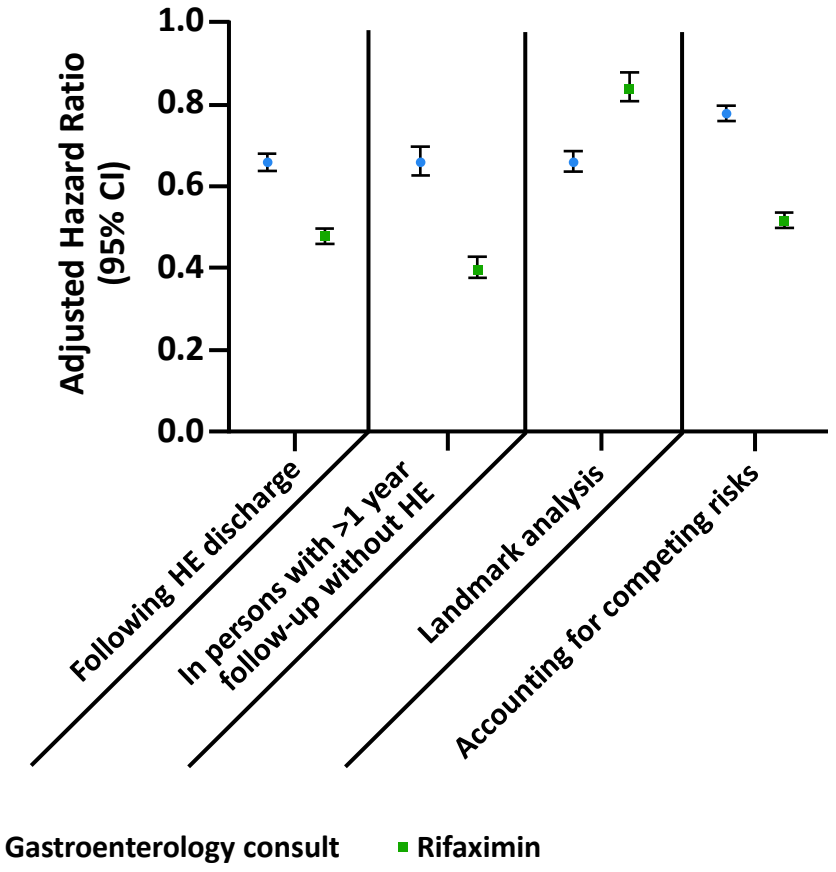
Management

- Advise patients not to drive ~3 months after the last overt HE episode
- No evidence to support a driving ban to all with CHE/MHE without prior overt HE, also take driving history into account
- Initiate or optimize HE treatment
- Avoid/withdraw/decrease sedative medications
- Optimize treatment of comorbid diseases
- Refer to authorities for formal testing for resuming driving privileges

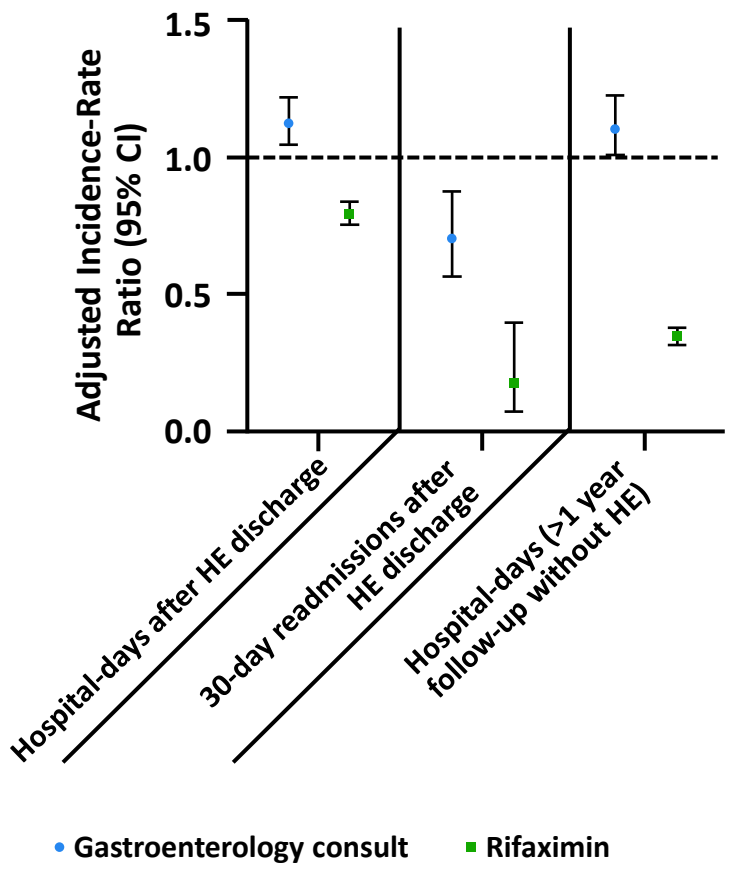
Bajaj JS, et al. *Am J Gastroenterol*. 2020;115:989-1002.

Impact of Combination Lactulose-Rifaximin and GI Consultation on Postdischarge Outcomes in Patients With HE

Effect on Mortality



Effect on Hospitalization-Risk



Tapper EB, et al. *Aliment Pharmacol Ther*. 2020;51:1397-1405.

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Case Study Evaluations

Case Patient 1: Henry

A 52-year-old man with a history of cirrhosis presents to the ED for severe, diffuse abdominal pain over the past 3 to 4 days. According to his wife, he has developed mental status changes accompanied by nausea and vomiting over the past 24 hours. He denies having a sore throat, chest pain, myalgia, or anosmia. Physical exam reveals shortness of breath and a temperature of 99.6°. Testing reveals elevated LFTs. The patient demonstrates a mild cough, but otherwise normal respiratory exam. His chest x-ray is unremarkable.

ED, emergency department; LFTs, liver function tests.

Case #1: Discussion Question

Which of the following tests would be of little prognostic value in the patient assessment?

A. Ammonia levels

B. Serum electrolytes

C. Blood cultures

D. PCR test for COVID-19

PCR, polymerase chain reaction.

Case #1: Discussion Question

What is your next course of action for this patient?

A. Provide supportive care for unconscious patients

B. Identify and address precipitating factors for HE

C. Initiate empirical HE treatment

D. Evaluate alternative causes of HE symptoms

E. All of the above

Case Patient 2: Gina

A 68-year-old woman with a history of cirrhosis and recurrent OHE presents with an acute episode of HE. The patient lives with her daughter and son-in-law, who report that she has been sleeping more than usual over the past two days. The patient is stuporous and lethargic, and her responses to questions are delayed. She doesn't appear to know what day it is or where she is.

The patient is currently being treated with lactulose. When asked about adherence to her maintenance therapy, her daughter responds that she is generally reluctant to change any eating-related behaviors and complains constantly about the GI side effects of the lactulose.

Case #2: Discussion Question

Once the current HE episode is resolved, what changes (if any) to the patient's prophylactic therapy would you recommend?

A. No change

B. Adjust the patient's dose of lactulose

C. Prescribe rifaximin as add-on therapy

D. Prescribe PEG as an alternative

Case #2: Discussion Question

Prior to leaving the hospital, the patient asks about restrictions on driving. How long would you advise the patient to wait before driving again?

A. 6 weeks

B. 2 months

C. 3 months

D. 6 months

Summary

- HE is a major complication of liver disease that represents a substantial healthcare burden in the hospital setting.
- HCPs should be aware that patients with cirrhosis and COVID-19 may present with signs of HE and are at heightened risk for poor health outcomes including death.
- Management goals include active treatment of acute episodes, prevention of recurrence, and evaluation for surgical intervention.
- Several agents have shown good efficacy when administered as acute treatment or secondary prophylaxis.
- Following an acute episode of HE, prophylaxis, patient education, and follow-up are essential to prevent recurrence and hospitalization, and improve health outcomes.

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Thank you!

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