The Changing Landscape of Liver Care

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Program Director, Transplant Hepatology Fellowship
The Ohio State University Wexner Medical Center
September 14, 2019

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To Now… Hepatology MDs

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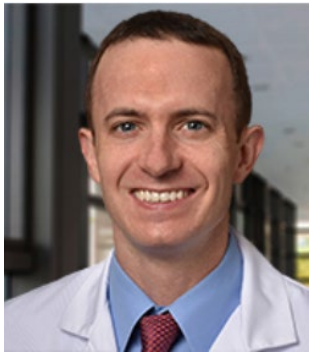

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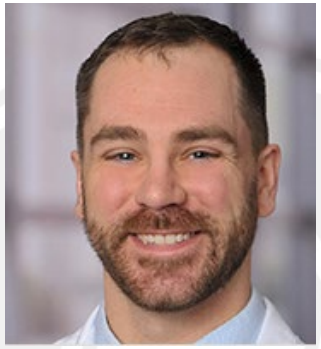

Michael Wellner, MD

To Now… Hepatology CNPs

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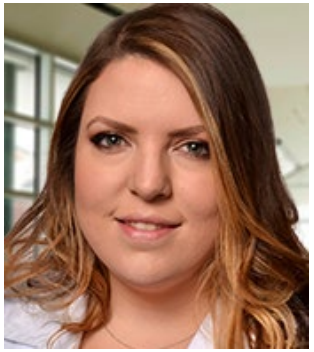

Nicole Gray, CNP

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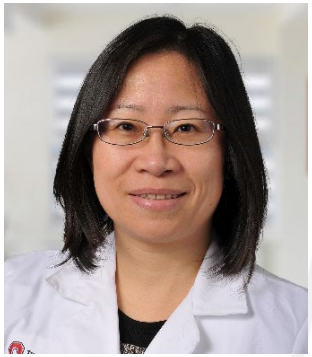
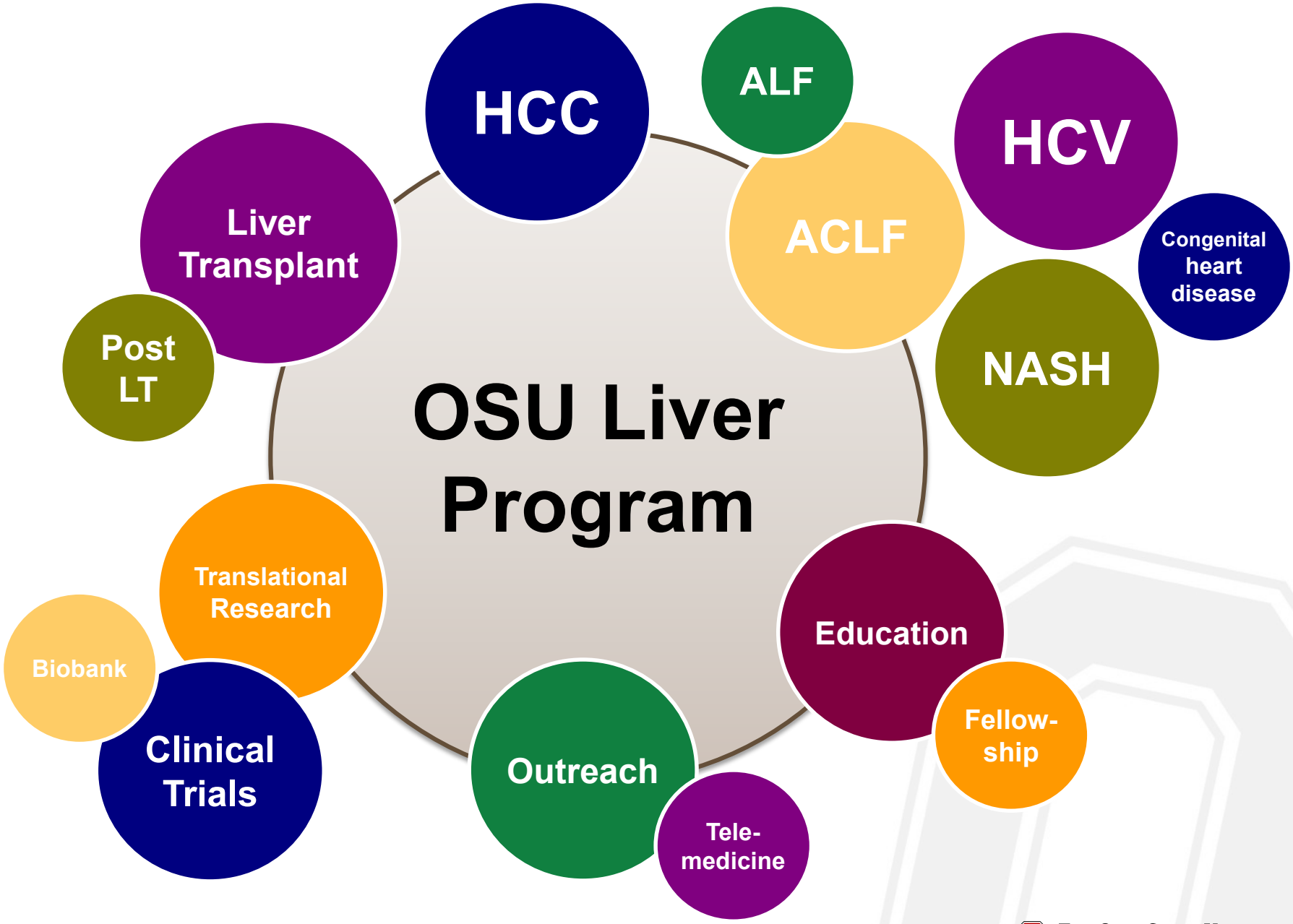
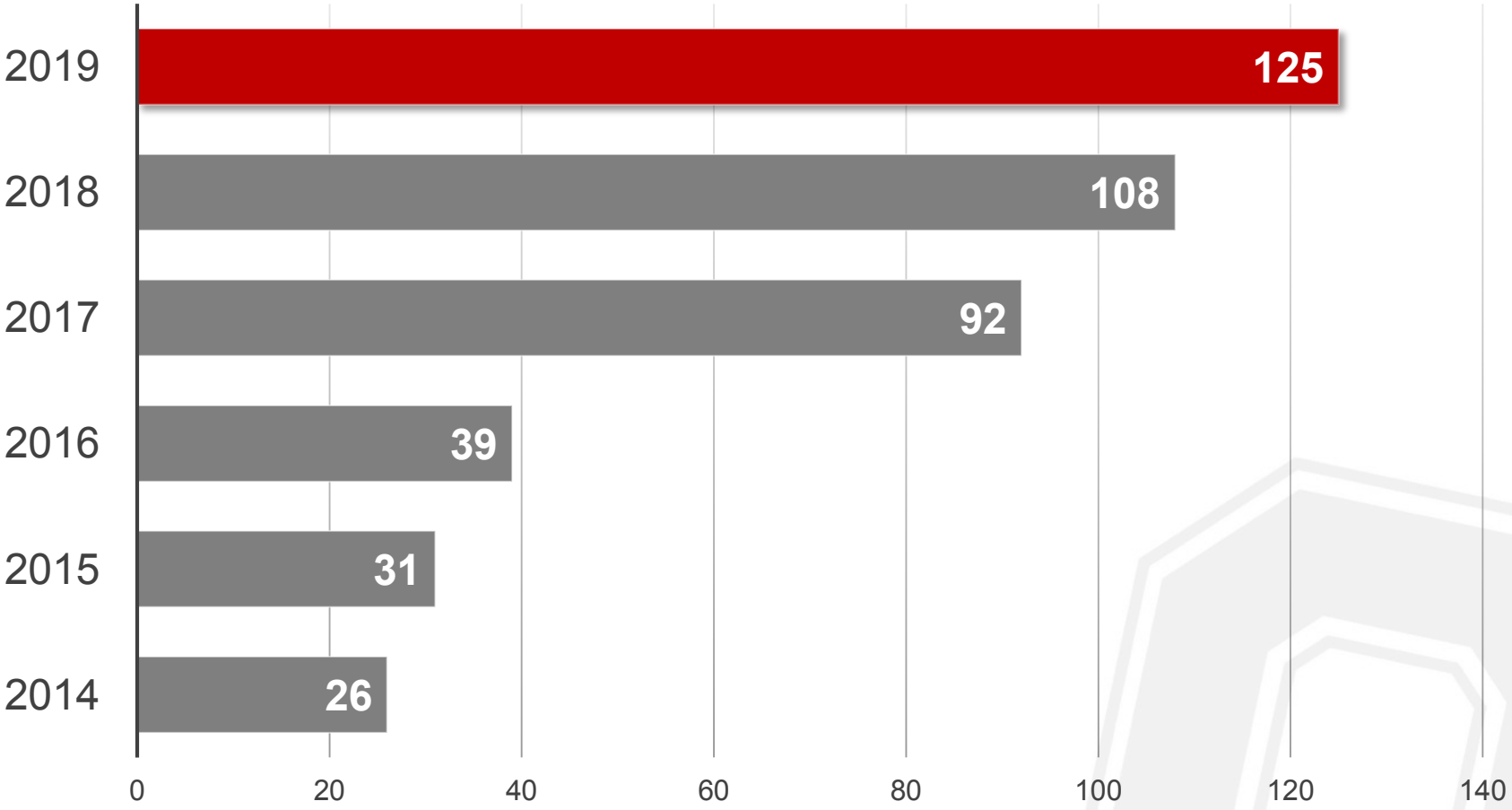


Sherry Ma, CNP


HCC
ALF
HCV
Liver Transplant
ACLF
Congenital heart disease
Post LT
NASH
OSU Liver Program
Translational Research
Biobank
Education
Fellow-ship
Clinical Trials
Outreach
Tele-medicine

Liver Transplants Performed



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Patient Outcomes: 1 Year Patient Survival

Released July 2019 (patients transplanted 1/1/2016 – 6/30/2018)

	EXPECTED	OBSERVED	NATIONAL
HEART	91.93%	**87.44%**	91.46%
LUNG	89.61%	**87.36%**	89.55%
BEST IN OHIO → LIVER	93.61%	**93.21%**	93.04%
KIDNEY	98.13%	**97.96%**	97.68%
KIDNEY/ PANCREAS	97.99%	**97.83%**	97.45%

Center Volume

National Recognition

#9 by Volume is U.S. (Jan – July 2019)

		All Organs	Kidney	Liver	Pancreas	Kidney / Pancreas	Heart	Lung	Heart / Lung	Intestine
	All Centers	22,834	13,406	5,121	90	500	2,078	1,556	28	42
1	CAUC-TX1 UCLA Medical Center	431	242	89	1	1	38	59	0	1
2	FLJM-TX1 Jackson Memorial Hospital	430	286	93	6	13	16	9	0	7
3	CASF-TX1 Univ of CA San Francisco Med Ctr	365	215	89	1	9	15	36	0	0
4	OHCC-TX1 Cleveland Clinic Foundation	357	128	92	7	5	37	76	0	7
5	FLTG-TX1 Tampa General Hospital	342	207	83	0	6	22	23	1	0
6	AZMC-TX1 Mayo Clinic Hospital	336	222	78	0	11	25	0	0	0
7	TNVU-TX1 Vanderbilt Univ Med Ctr	328	148	88	1	3	69	19	0	0
8	NCDU-TX1 Duke University Hospital	326	121	79	1	2	50	69	1	2
9	**OHOU-TX1 Ohio State Univ Med Ctr**	**323**	**182**	**84**	**1**	**10**	**17**	**29**	**0**	**0**
10	CACS-TX1 Cedars-Sinai Med Center	323	173	62	0	4	77	7	0	0
11	COUC-TX1 University of Colorado Hospital/HSC	319	174	84	0	6	26	29	0	0
12	MOBH-TX1 Barnes-Jewish Hospital	315	163	64	0	4	23	61	0	0
13	PAUP-TX1 The Hosp of the Univ of PA	313	137	79	1	9	28	55	2	0
14	WIUW-TX1 Univ of Wisconsin Hosp and Clinics	309	157	63	9	22	27	31	0	0
15	TXMH-TX1 Houston Methodist Hospital	308	155	90	3	6	24	29	1	0
16	NYCP-TX1 New York-Presbyterian/Columbia	296	126	52	0	5	61	51	1	0
17	LAOF-TX1 Ochsner Foundation Hospital	293	132	119	1	5	19	17	0	0
18	GAEM-TX1 Emory University Hospital	273	161	76	1	3	19	13	0	0
19	FLSL-TX1 Mayo Clinic Florida	265	102	103	1	11	19	28	1	0
20	ALUA-TX1 Univ of Alabama Hospital	260	159	72	0	5	15	6	3	0
21	SCMU-TX1 Medical Univ of SC	258	170	48	0	18	16	6	0	0
22	TXHS-TX1 Methodist Specialty & Transplant Hosp	257	210	27	0	0	20	0	0	0
23	MNUM-TX1 Univ. of Minnesota Medical Center	251	112	59	4	19	31	26	0	0
24	MDJH-TX1 Johns Hopkins Hospital	250	145	61	1	3	20	20	0	0
25	PAPT-TX1 Univ of Pittsburgh Med Ctr	248	109	66	1	2	24	45	0	1

Past Population: Hepatitis C

- Baby Boomers (Born in 1945–1965) account for 76.5% of HCV in the US
- Almost 35% of undiagnosed baby boomers with HCV are estimated to currently have advanced fibrosis (F3-F4; bridging fibrosis to cirrhosis)

Smith BD et al. *MMWR Recomm Rep.* 2012;61:1-32. 2. Pyenson B et al. Milliman report, 2009. Available at www.milliman.com/expertise/healthcare/publications/rr/consequences-hepatitis-c-virus-RR05-15-09.php . McGarry LJ et al. *Hepatology.* 2012;55:1344-1355.

Evolution of Care

HEPATOLOGY

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Liver Biology/Pathobiology

Hepatic gene expression during treatment with peginterferon and ribavirin: Identifying molecular pathways for treatment response†

Jordan J. Feld, Santosh Nanda, Ying Huang, Weiping Chen, Maggie Cam, Susan N. Pusek, Lisa M. Schweigler, Dickens Theodore, Steven L. Zacks, T. Jake Liang ✉, Michael W. Fried

First published: 10 October 2007 Full publication history

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Towards the Elimination of Hepatitis C in the United States

Sammy Saab, Long Le, Satvir Saggi, Vinay Sundaram, Myron Tong

Accepted manuscript online: 27 November 2017 Full publication history

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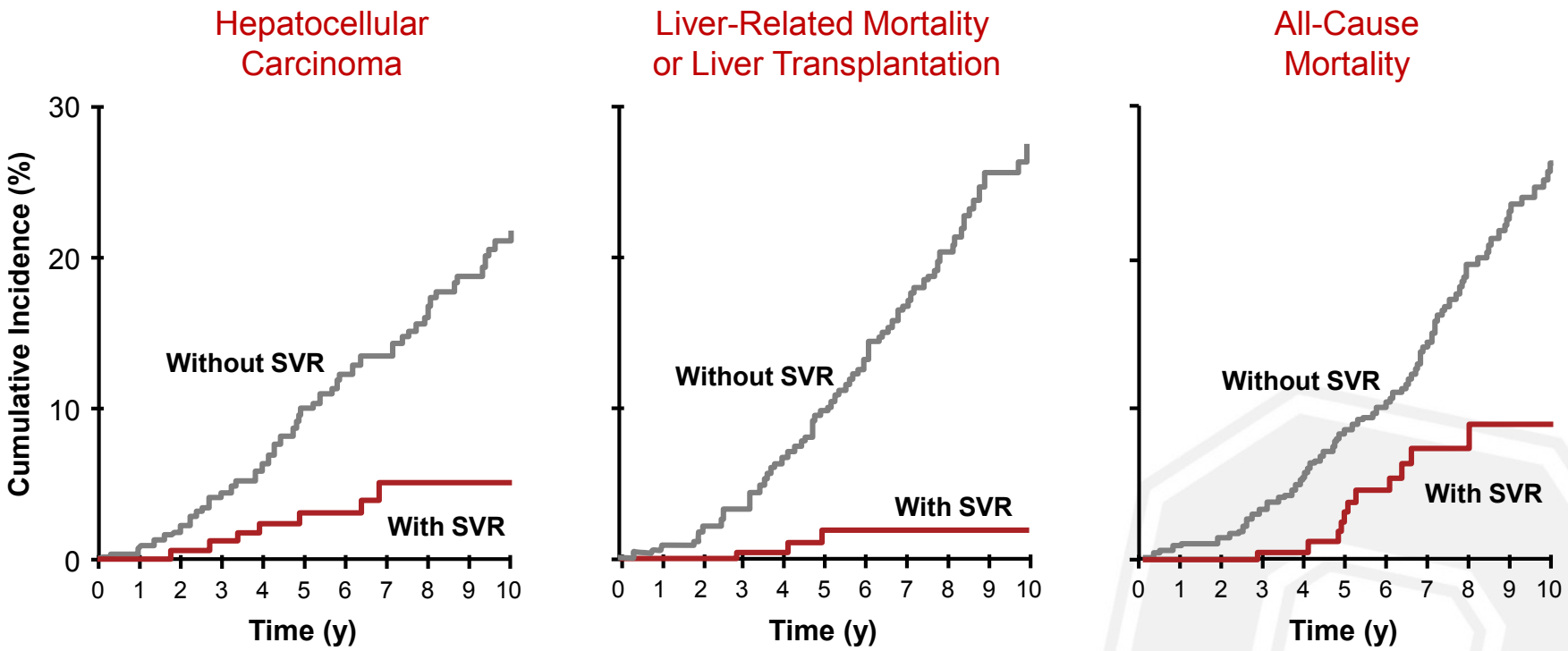
HCV: Current Treatment

- Treatment options:
  - Oral regimens
  - 8-12 week treatment course
  - High SVR rates
  - Rare side effects
  - Pangenotypic
- Screen for Hepatitis B PRIOR to treatment for HCV
- DO NOT treat decompensated cirrhotics listed for OLT
  - HCV PCR + donor offers
  - Treat HCV post-transplant

SVR Associated with a Reduction in HCC, Liver-Related Mortality, Transplantation, and All-Cause Mortality



Van der Meer AJ, et al. *JAMA*. 2012;308:2584-2593

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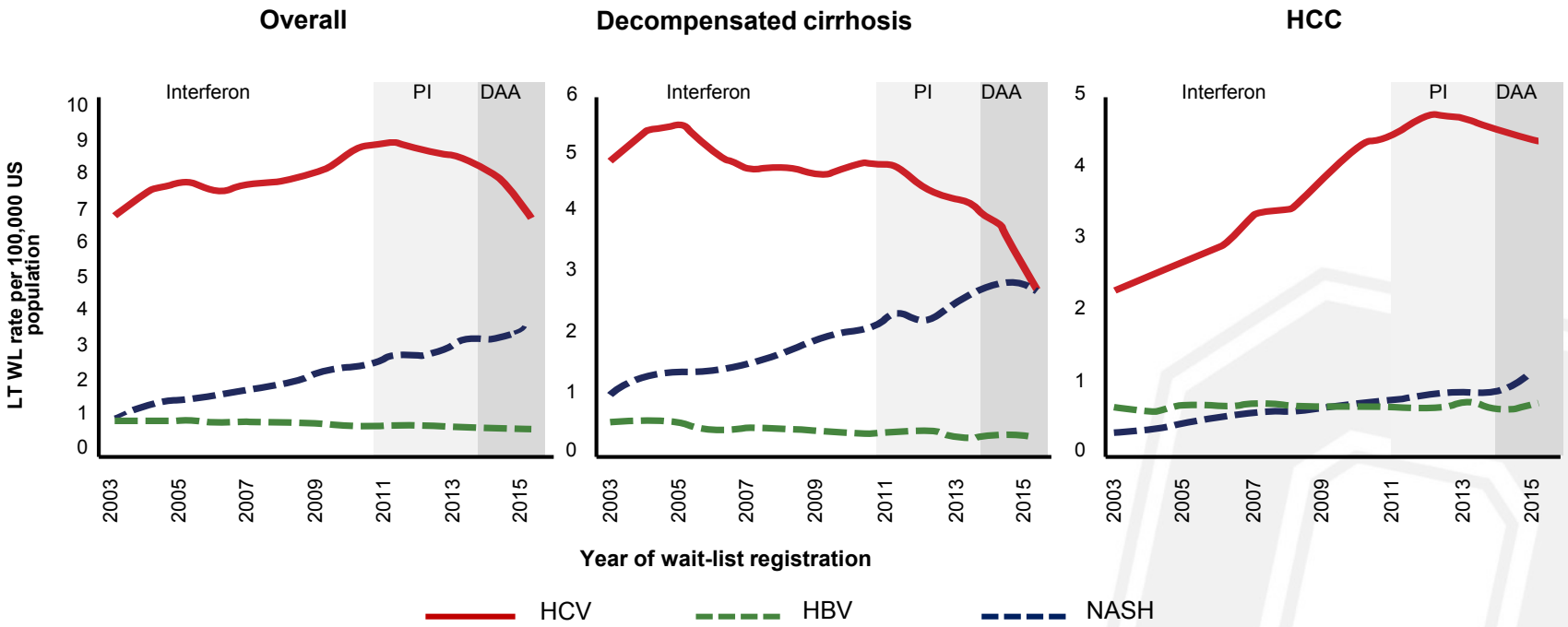
Reduction in Liver Transplant Waitlist

Cohort study of 47,591 adults wait-listed for liver transplant (LT WL) using the Scientific Registry of Transplant Recipients database from 2003–2015

Annual Standardized Incidence Rates (ASIR) of LT Wait-Listing per 100,000 US Population



The rate of liver transplant wait-listing for HCV secondary to decompensated cirrhosis has decreased by 32% in the era of DAA therapy as compared to the IFN era and is now equal to that of NASH

 Flemming JA, et al. Hepatology, Vol.65, NO.3, 2017.

Current Population: Non-alcoholic Fatty Liver Disease (NAFLD)

Dallas Heart Study (2,200 adults)

Assessed NAFLD with liver imaging

General prevalence of fatty liver 31%
(range 24% - 45%)

Most individuals (79%) with fatty liver do not exhibit aminotransferase elevations

NHANES III (15, 700 adults)

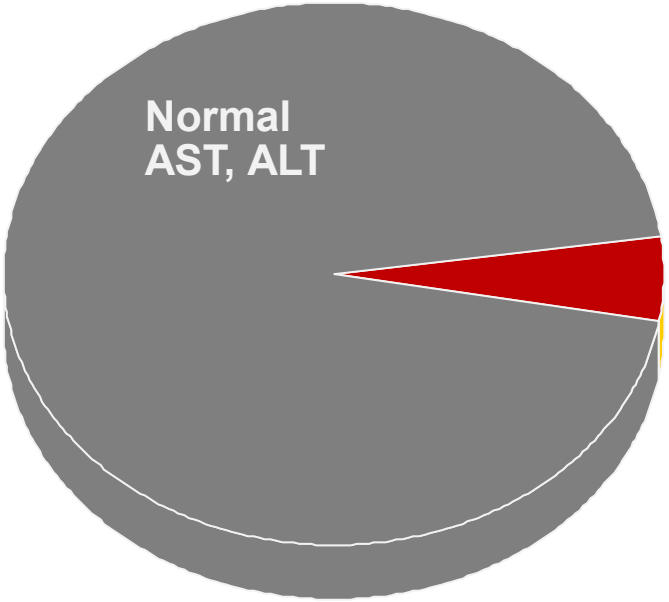
Assessed NAFLD with aminotransferases

General prevalence of NAFLD 5.5%

NAFLD prevalence 5.5-31%

3-10 x more prevalent than Hepatitis C

NAFLD: Risk Factors



5.5%

Unexplained Hepatitis

↑ BMI

Waist circumference

Triglycerides

Insulin

↓ HDL cholesterol

Metabolic Syndrome

Clark, Brancati, Diehl. Am J Gastro 2003; 98:960

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Wexner Medical Center

NAFLD Natural History

Liver-related morbidity and mortality

NAFL NASH Cirrhosis

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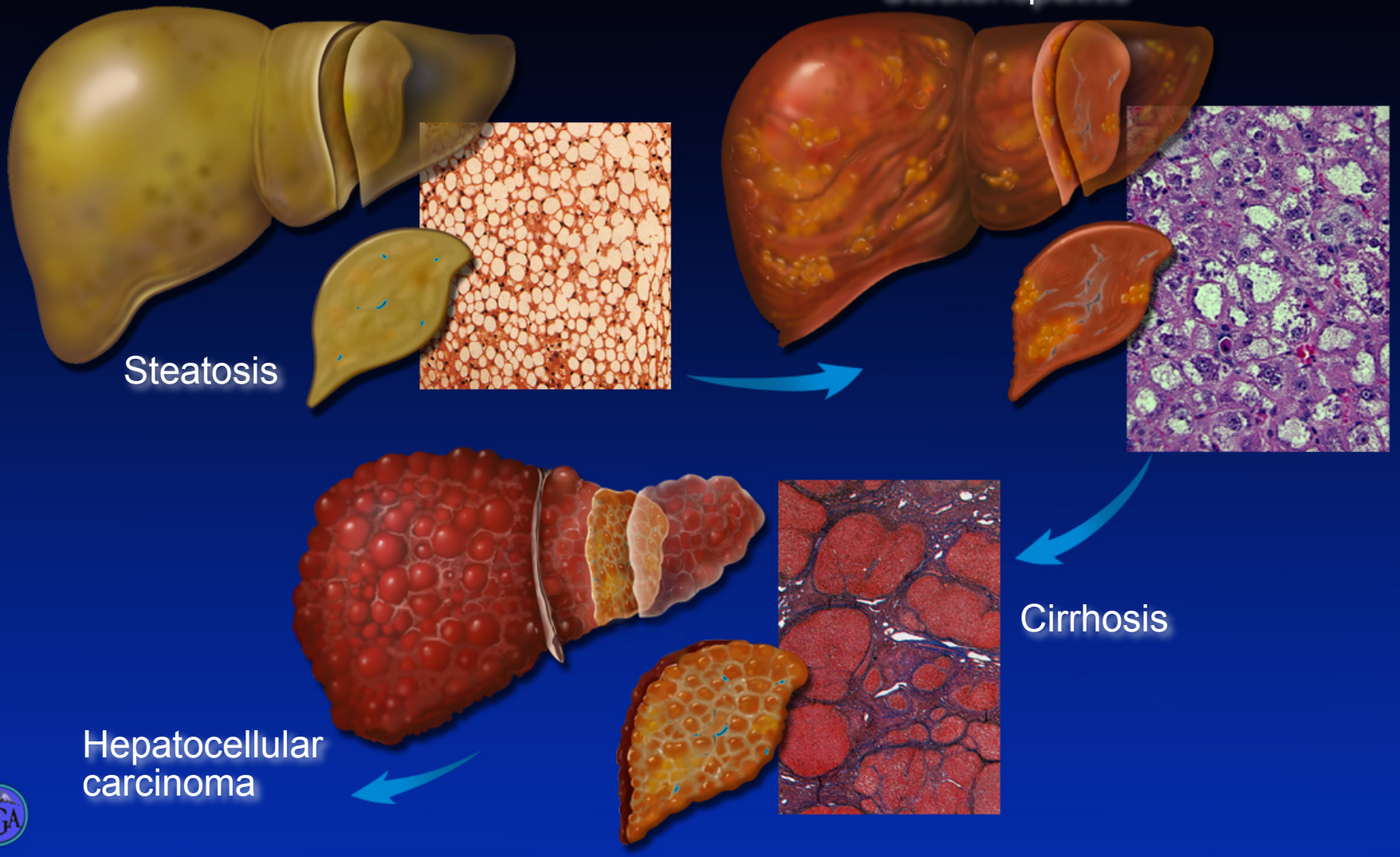
NAFLD

Spectrum of Hepatic Pathology

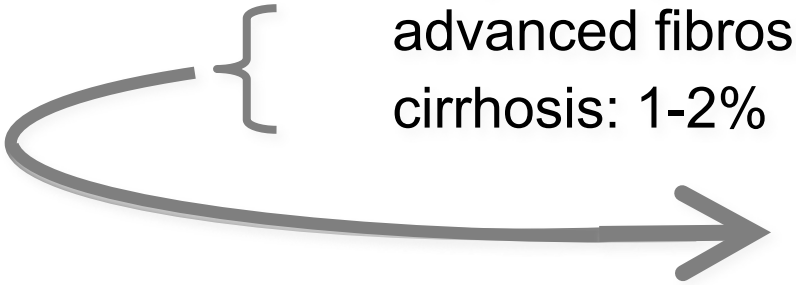


NAFLD in High-Risk Populations: Morbidly Obese Gastric Bypass Patients

Liver disease often unsuspected pre-operatively

Intraoperative liver biopsy typically shows NAFLD

- Steatosis: 30-90%
- Steatohepatitis: 33-42%
- Fibrosis:
  - idiopathic portal fibrosis: 33%
  - advanced fibrosis: 12%
  - cirrhosis: 1-2%



Advanced fibrosis 13-14%

NAFLD in High-Risk Populations: Type 2 Diabetes Mellitus

Prevalence of NAFLD is high

-ultrasound detects fatty liver in 50%

NASH unusually common

-NAFL: 12%

-NASH: 87%

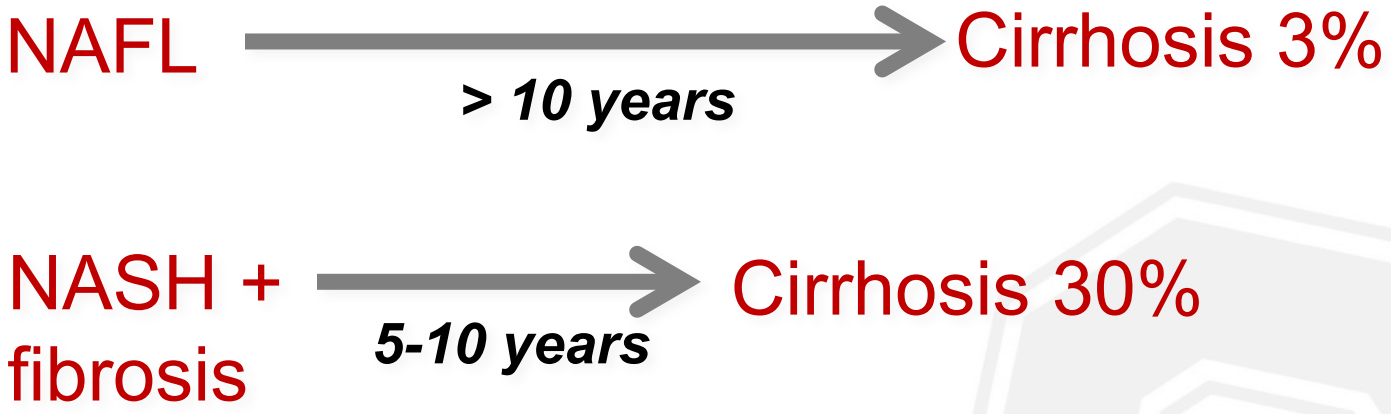
Fibrosis or cirrhosis documented in 20%

Standardized mortality rate for death from liver disease > than that for coronary disease

Gupter et al. J Gastro Hepatol 2004;19:854-859
Tolman et al. Ann Intern Med 2004; 141:946-956

Prognostic Implications of NASH + Fibrosis

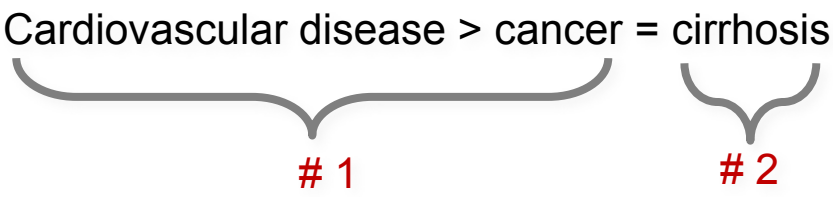
More consistent and rapid progression to cirrhosis than NAFL



Matteoni et al. Gastroenterology 1999; 116:1413

Prognostic Implications of NASH + Fibrosis

- More consistent and rapid progression to cirrhosis than NAFL
- Rate of liver related mortality about 10% within 10 years
- **Liver disease is a major cause of mortality**



Matteoni et al. Gastroenterology 1999; 116:1413

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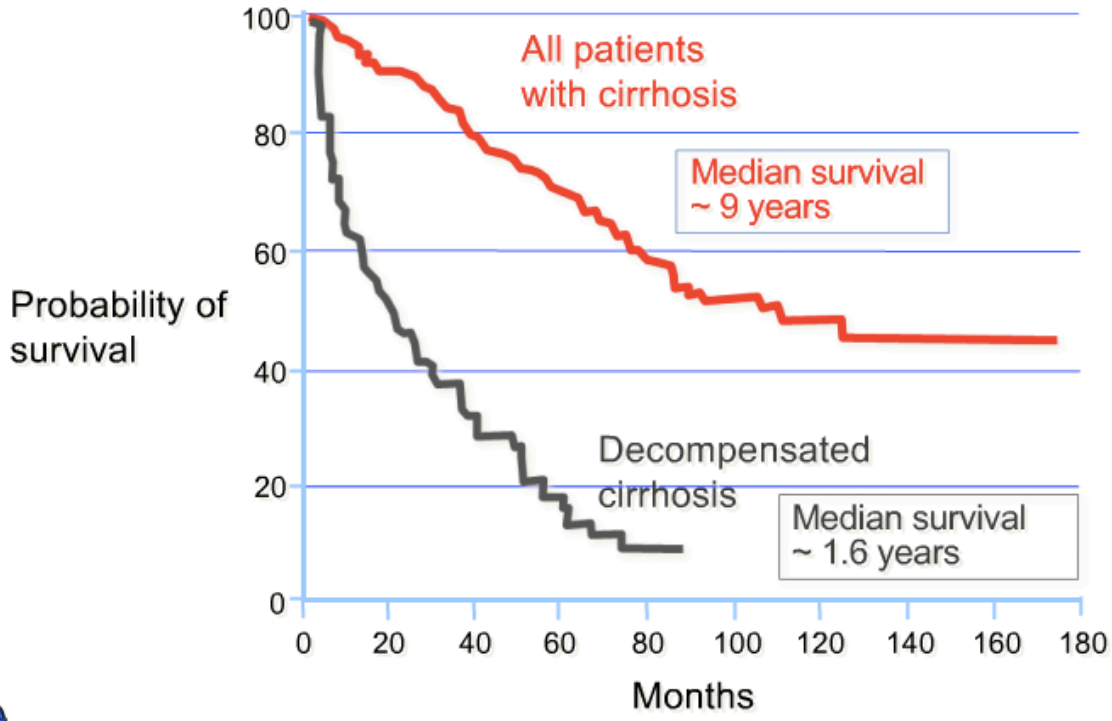
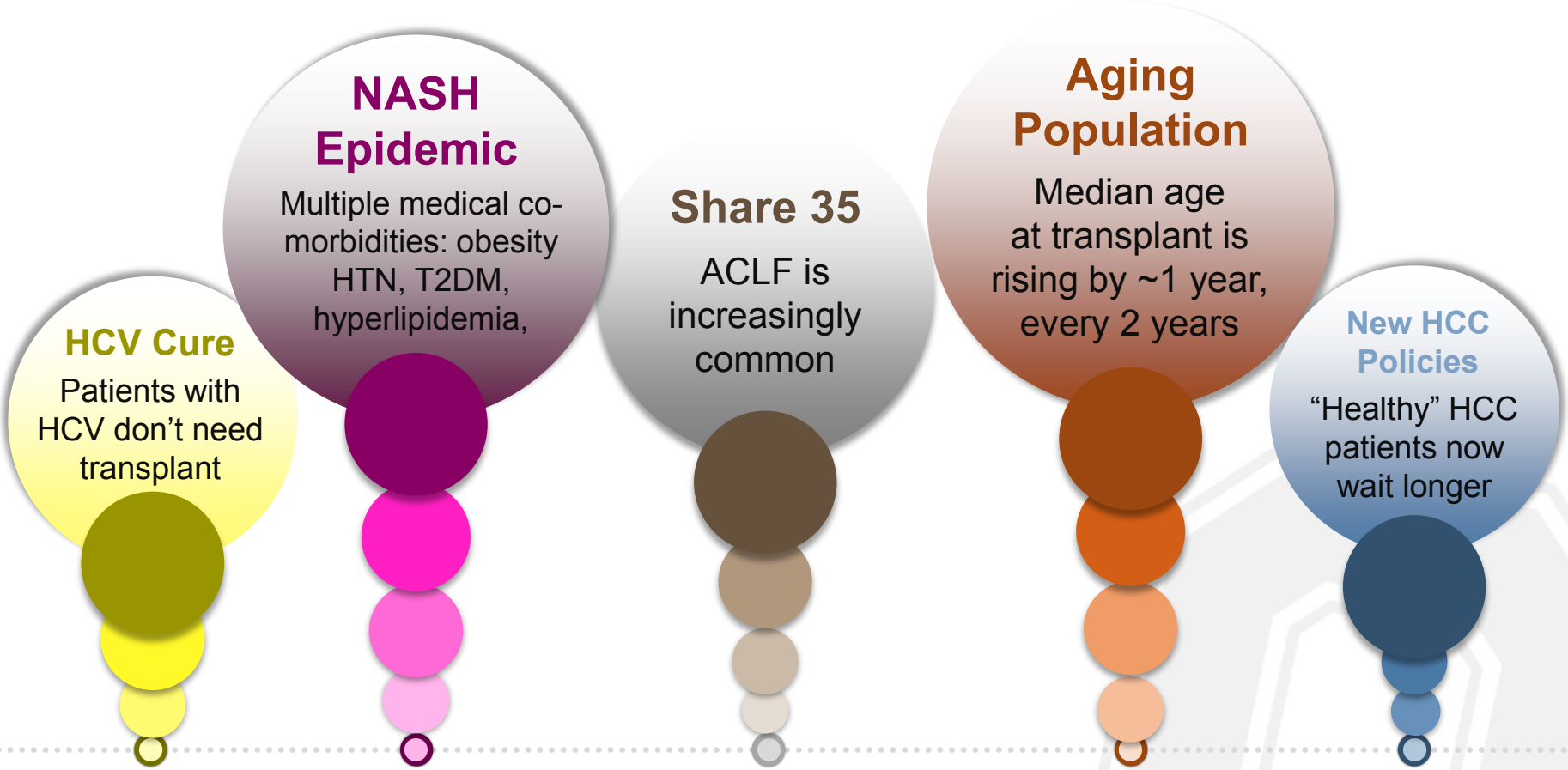
Decompensated Cirrhosis

Decompensation Shortens Survival



Gines et. al., Hepatology 1987;7:122

Major Changes in Liver Transplant



Major Changes in Liver Transplant

Acute on Chronic Liver Failure (ACLF)

- Acute decompensation (defined as worsening coagulopathy and jaundice) in a patient with chronic liver disease
- Often precipitated by infection
- Multi-organ system dysfunction
- Associated with poor prognosis

WGO consensus statement Jalan et al. Gastroenterology 2014;147(1):4-10

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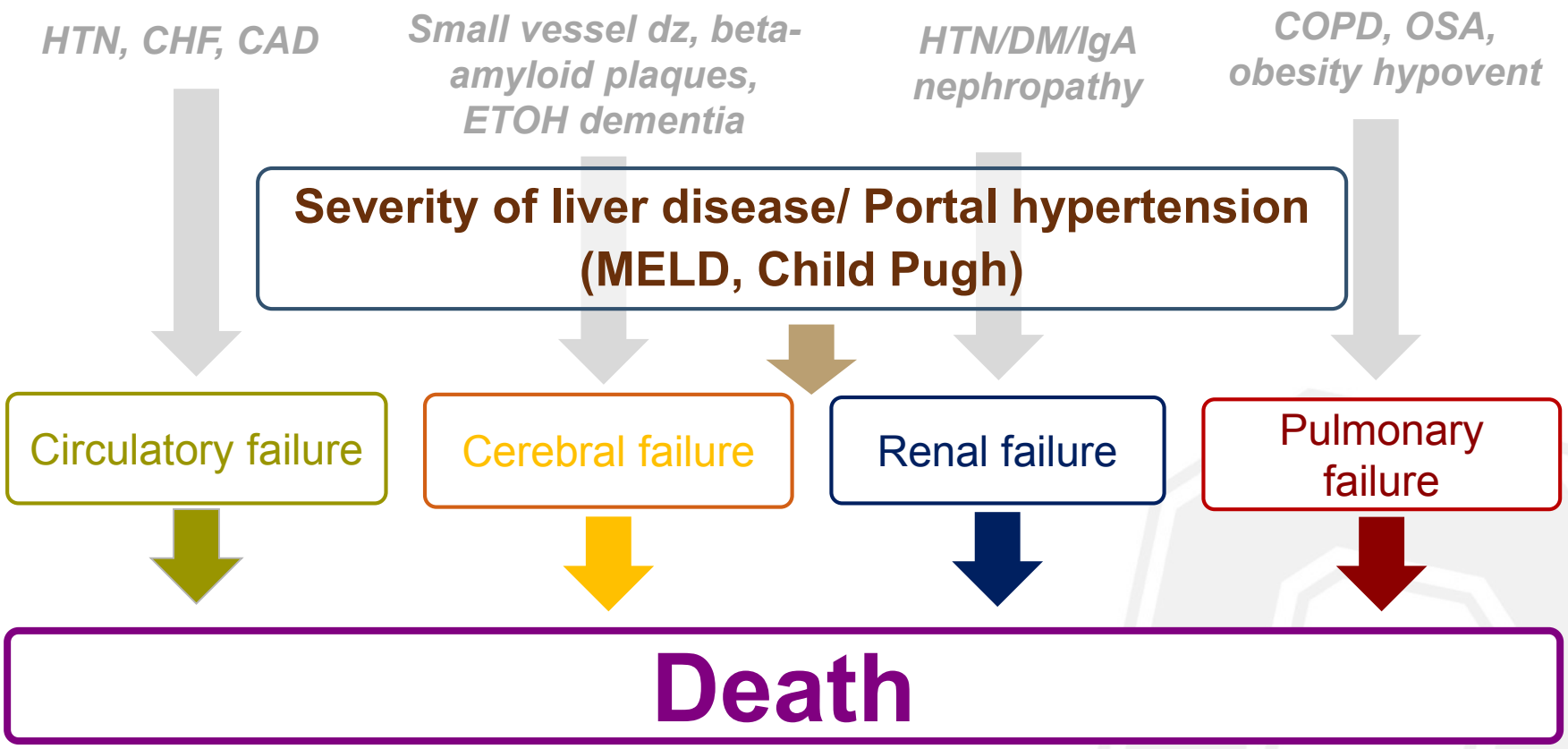
Severity and Prognosis of ACLF



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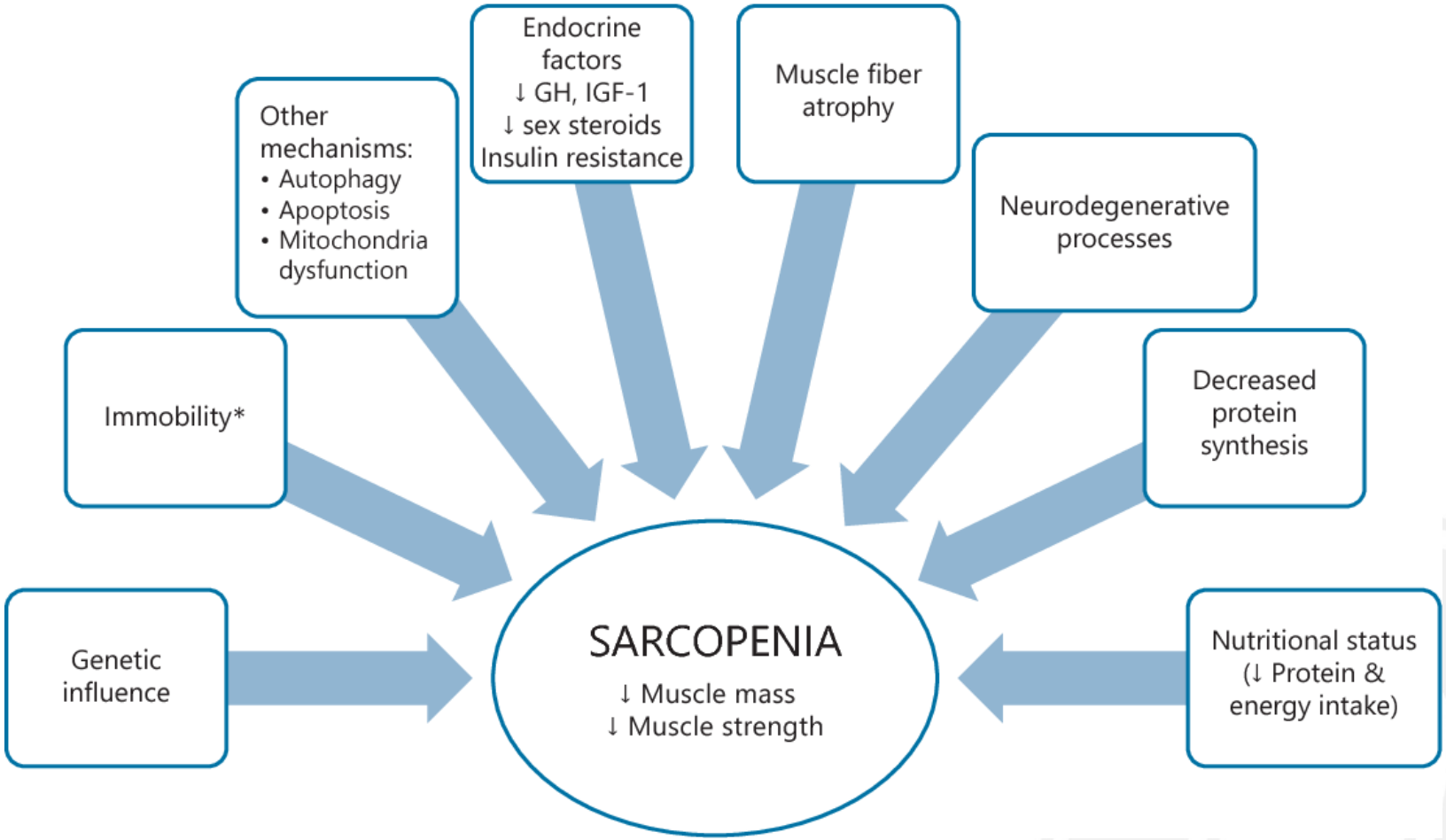
Sarcopenia



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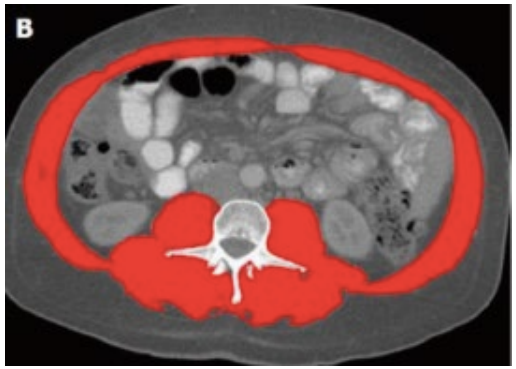
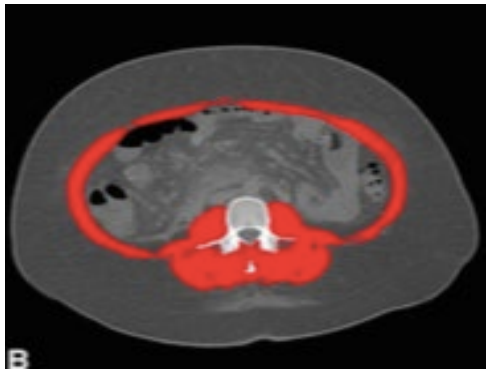
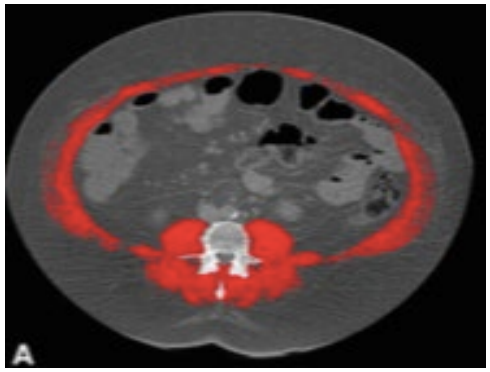
Sarcopenia by Skeletal Muscle Index



BMI 28 cirrhotic
Non-sarcopenic



BMI 47 cirrhotic
Non-sarcopenic



BMI 47 cirrhotic
Sarcopenic

Montano-Loza, WJG 2014

SMI cut-offs to define sarcopenia that predict mortality: 47 cm^2/m^2 for men; 42 cm^2/m^2 for women

 Carey/Lai, Liver Transpl 2017

Sarcopenia

A Multicenter Study to Define Sarcopenia in Patients With End-Stage Liver Disease

Elizabeth J. Carey,[1*] Jennifer C. Lai,[2*] Connie W. Wang,[3] Srinivasan Dasarathy,[5] Iryna Lobach,[4] Aldo J. Montano-Loza,[6] and Michael A. Dunn[7] for the Fitness, Life Enhancement, and Exercise in Liver Transplantation Consortium

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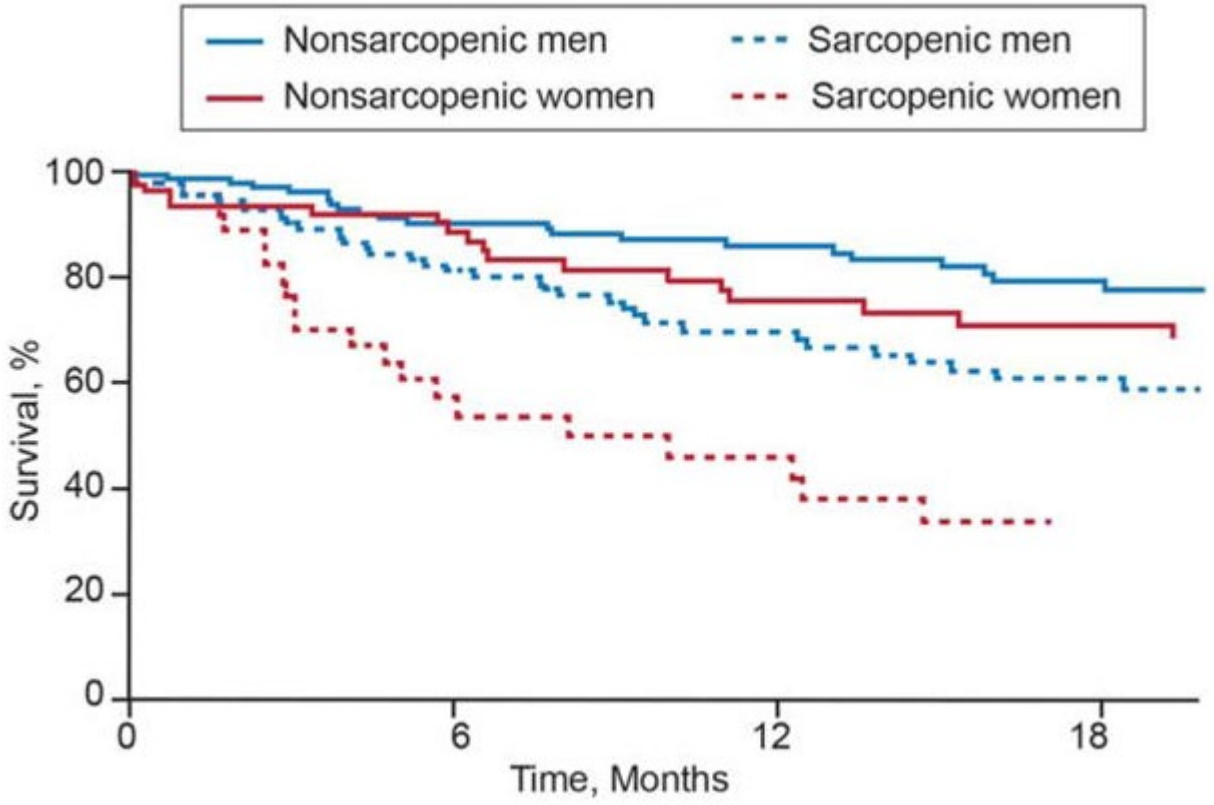
Sarcopenia


Nonsarcopenic men
Sarcopenic men
Nonsarcopenic women
Sarcopenic women
100
80
60
40
20
0
Survival, %
0
6
12
18
Time, Months

Co-morbidities Matter in Cirrhosis

- Diabetes increases risk of death in patients with ESLD
- Older age is associated with increased waitlist mortality
- Older age is associated with increased risk of post-transplant mortality
- CHF, COPD, and DM are predictive of mortality after liver transplant
- Sarcopenia is common in patients with ESLD
  - Preventable, reversible
  - Associated with increased risk of encephalopathy and mortality

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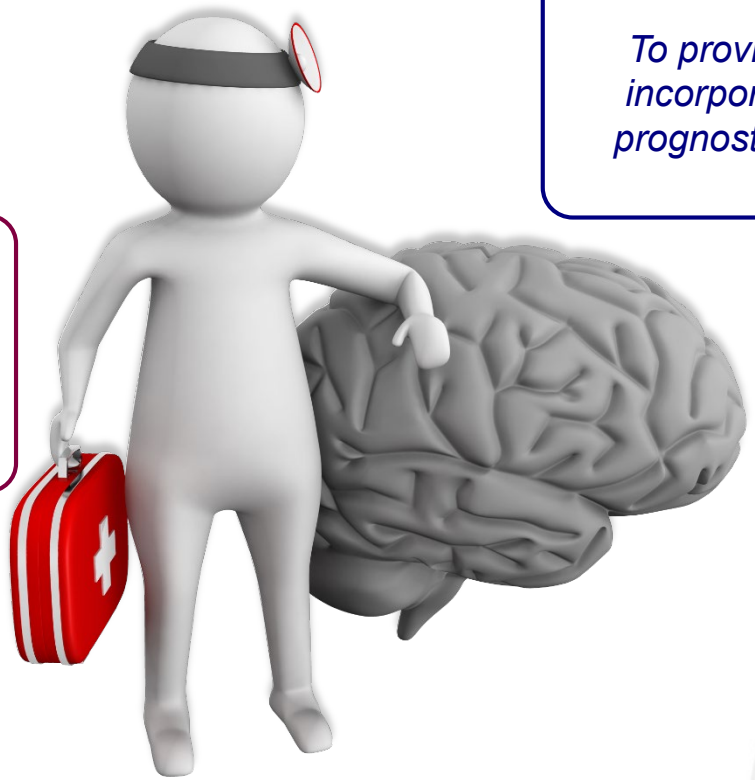
For the Increasingly Complex Patient, We Need…

Tools

To provide us with information that incorporates all systems to help us prognosticate and engage in shared decision-making



Frameworks

For dynamic, personalized decision-making for patients with multi-organ dysfunction

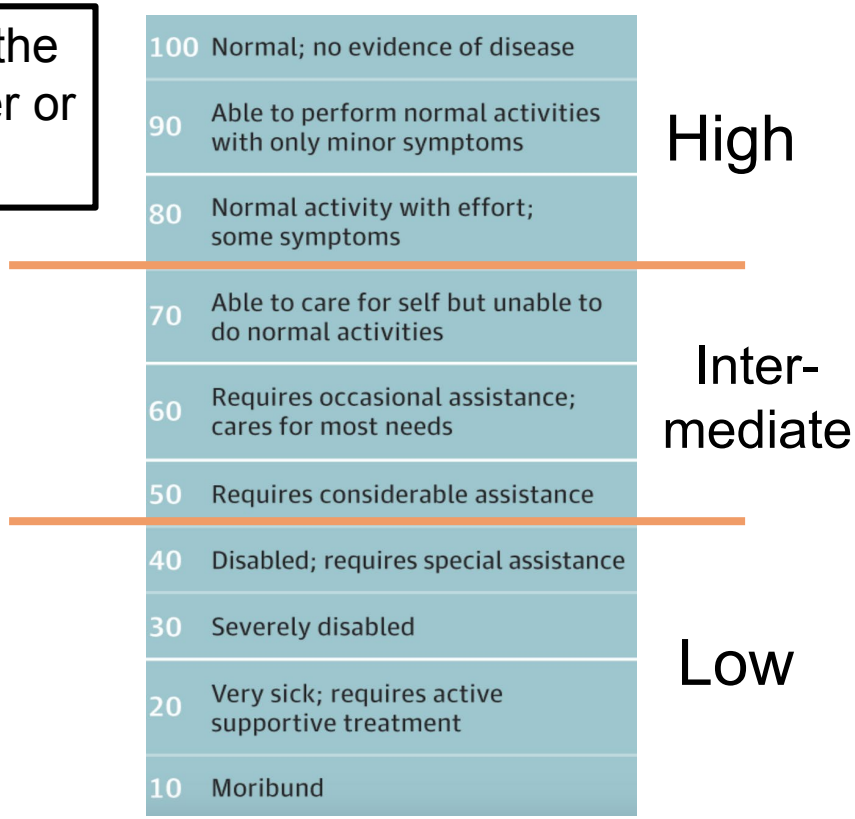
“Frailty”

- From the geriatrician’s toolbox
- “A distinct biologic syndrome of decreasing physiologic reserve and increasing vulnerability to health stressors”
- “Aggregate expression of risk resulting from age- and disease-related subthreshold decrements of multiple physiologic systems”

Fried L. J Gerontol A Biol Sci Med Sci 2004.

Karnofsky Performance Status

Assessed by the clinical provider or patient



- Predicts 3-month mortality after hospitalization (better than MELD + age alone)
- Predicts 30-day mortality after liver transplantation

Karnofsky, Cancer 1948. Tandon, Hepatology 2016. Dolgin, Clin Transpl 2016.

Frailty Assessment

HEPATOLOGY

AASLD

HEPATOLOGY, VOL. 66, NO. 2, 2017

Development of a Novel Frailty Index to Predict Mortality in Patients With End-Stage Liver Disease

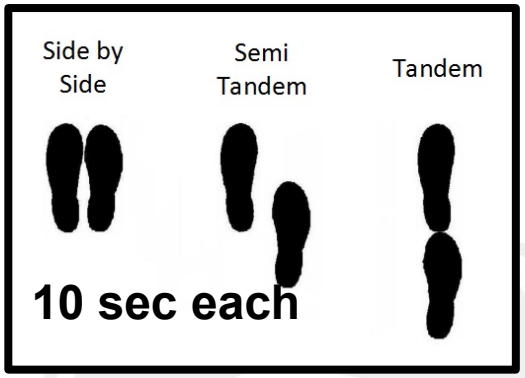
Jennifer C. Lai,[1] Kenneth E. Covinsky,[2] Jennifer L. Dodge,[3] W. John Boscardin,[2,4] Dorry L. Segev,[5] John P. Roberts,[3] and Sandy Feng[3]

The Liver Frailty Index
liverfrailtyindex.ucsf.edu

FrAILT

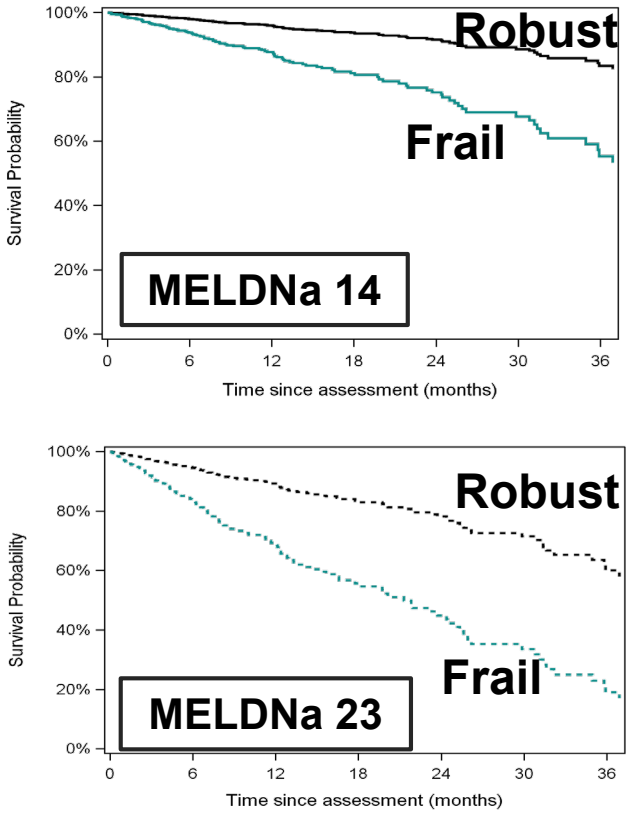
90 s

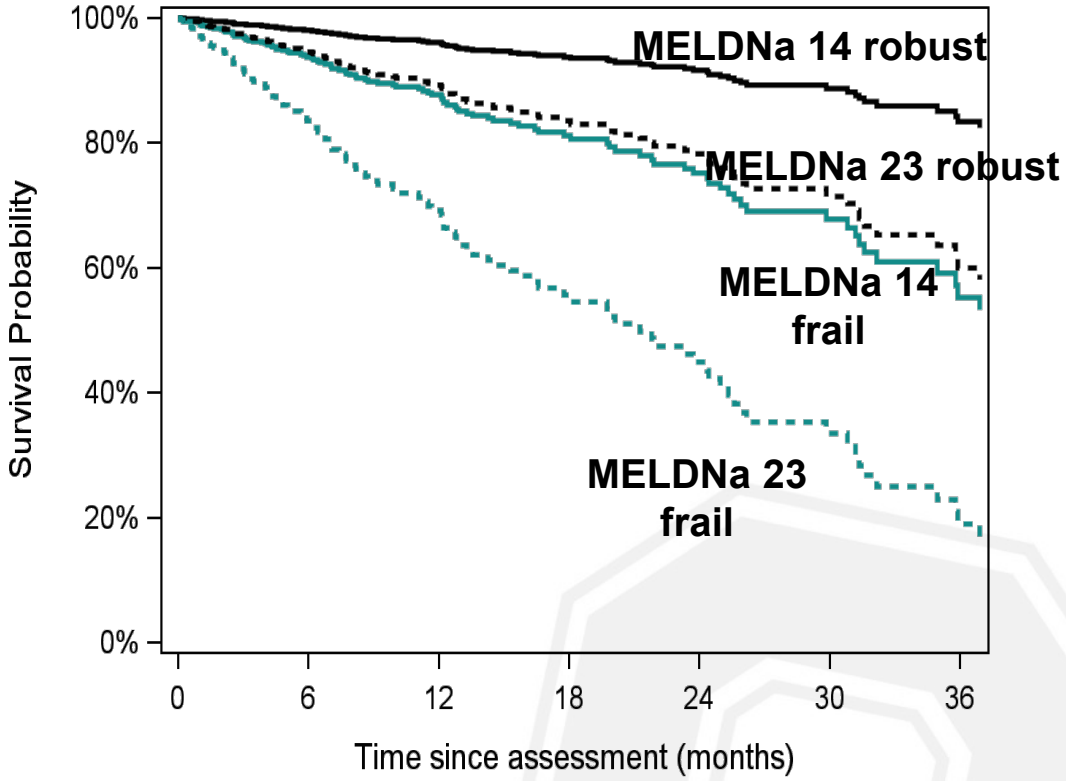
Grip + **Chair stands** + **Balance**



Lai JC, Hepatology 2017.

LFI Predicts Mortality Better Than MELD-Na Alone





* Robust / Frailty defined as the 20% / 80%ile Liver Frailty Index values.

Final Thoughts

- A framework for medical decision-making that accounts for frailty can facilitate more individualized decisions
- Tools for medical decision-making need to move beyond organ-specific assessments and incorporate the aggregate effects of multi-morbidity and aging
- “Frailty” tools such as the KPS, ADL, Liver Frailty Index, and skeletal muscle index should be incorporated into routine assessments

Acknowledgements

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- Anthony Michaels, MD, Division of Gastroenterology, Hepatology and Nutrition, The Ohio State University
- Nicole O'Bleness Gray, CNP, Division of Gastroenterology, Hepatology and Nutrition, The Ohio State University
- Amber Swayne, RN, Hepatology Referral Coordinator, Division of Gastroenterology, Hepatology and Nutrition, The Ohio State University

Thank You