THE FORUM
For Collaborative Research℠

Liver Forum 15

September 6, 2023

Institut Pasteur

Veronica Miller, PhD
Director

Berkeley Public Health

Session II: Steatotic Liver Diseases: Review of New Nomenclature from Multi-Stakeholders Perspectives

Moderators:

Veronica Miller, *Forum for Collaborative Research*

Jörn Schattenberg, *University Medical Center Mainz*

Journal Pre-proof

A multi-society Delphi consensus statement on new fatty liver disease nomenclature

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Panel Discussion

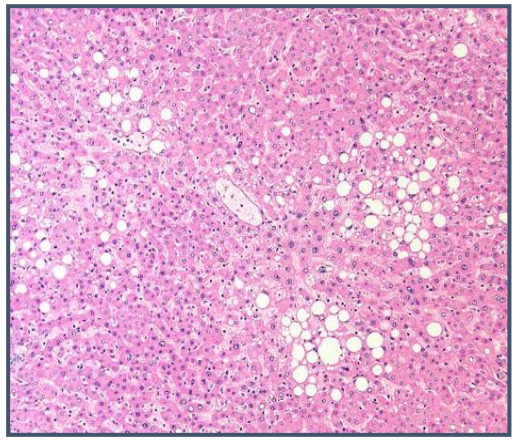
Panelists:

- Arun Sanyal, Virginia Commonwealth University
- Meena Bansal, Mount Sinai Hospital, NY
- Sven Francque*, University of Antwerp, Belgium
- George Makar*, US Food and Drug Administration (FDA)
- Joachim Musaus, European Medicines Agency (EMA)
- Don Chalfin, Patient
- Henry Chang*, Fatty Liver Foundation
- Michelle Long, NovoNordisk
- Judith Ertle, Boehringer Ingelheim

General Discussion

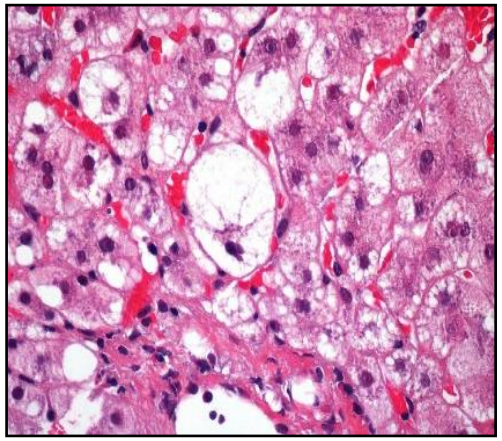
From NAFLD and NASH to MASLD- are we leaving people behind?

NAFL



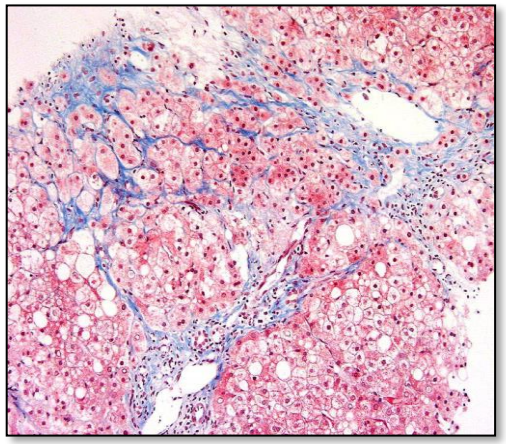
Metabolic dysfunction Associated steatosis (MAS)

NASH



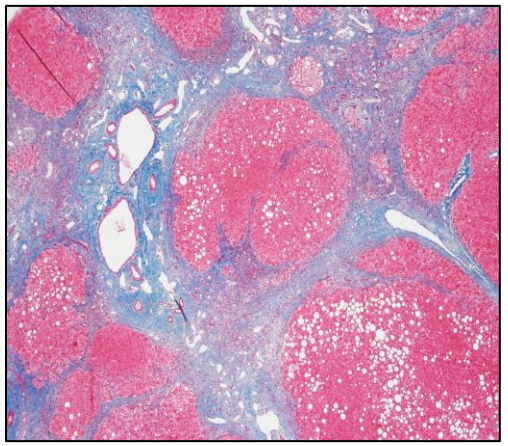
MASH

NASH with fibrosis



MASH with fibrosis

NASH Cirrhosis



MASH Cirrhosis

Arun J. Sanyal M.D.

Z Reno Vlahcevic Professor of Medicine, Physiology and Molecular Pathology

Virginia Commonwealth University School of Medicine

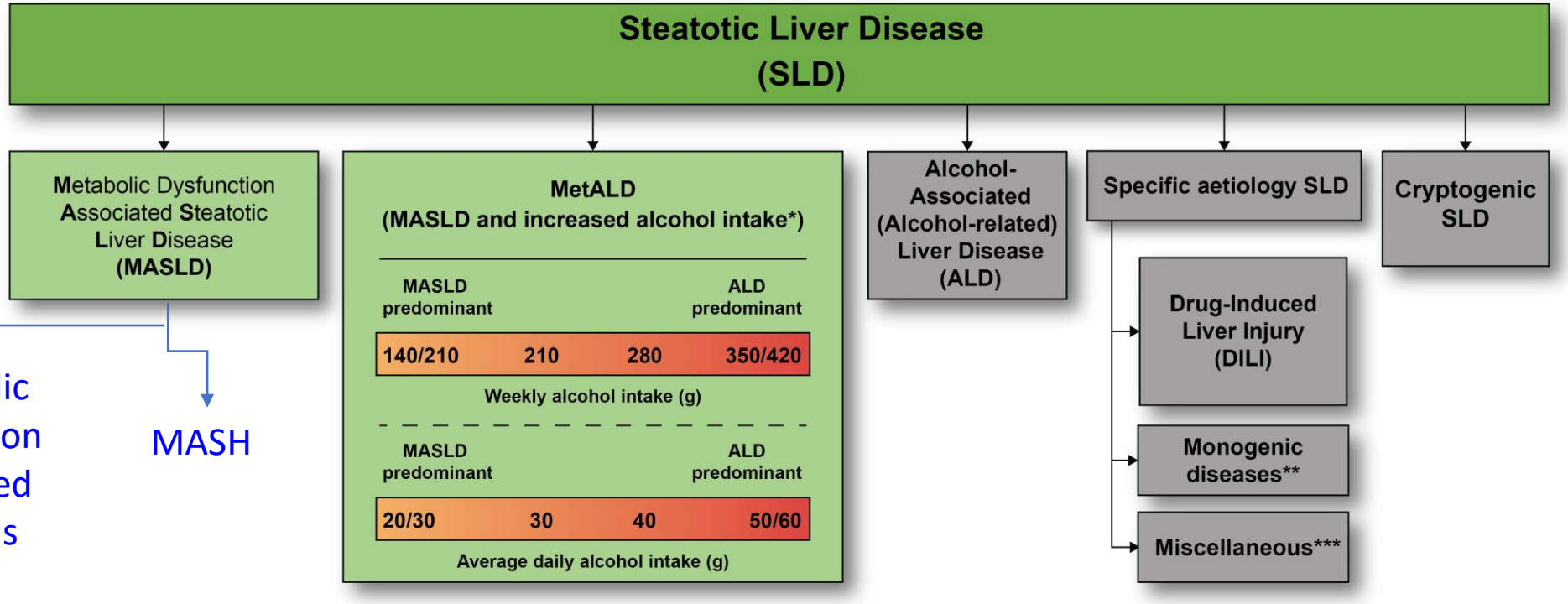
Disclosures

[Arun J. Sanyal]

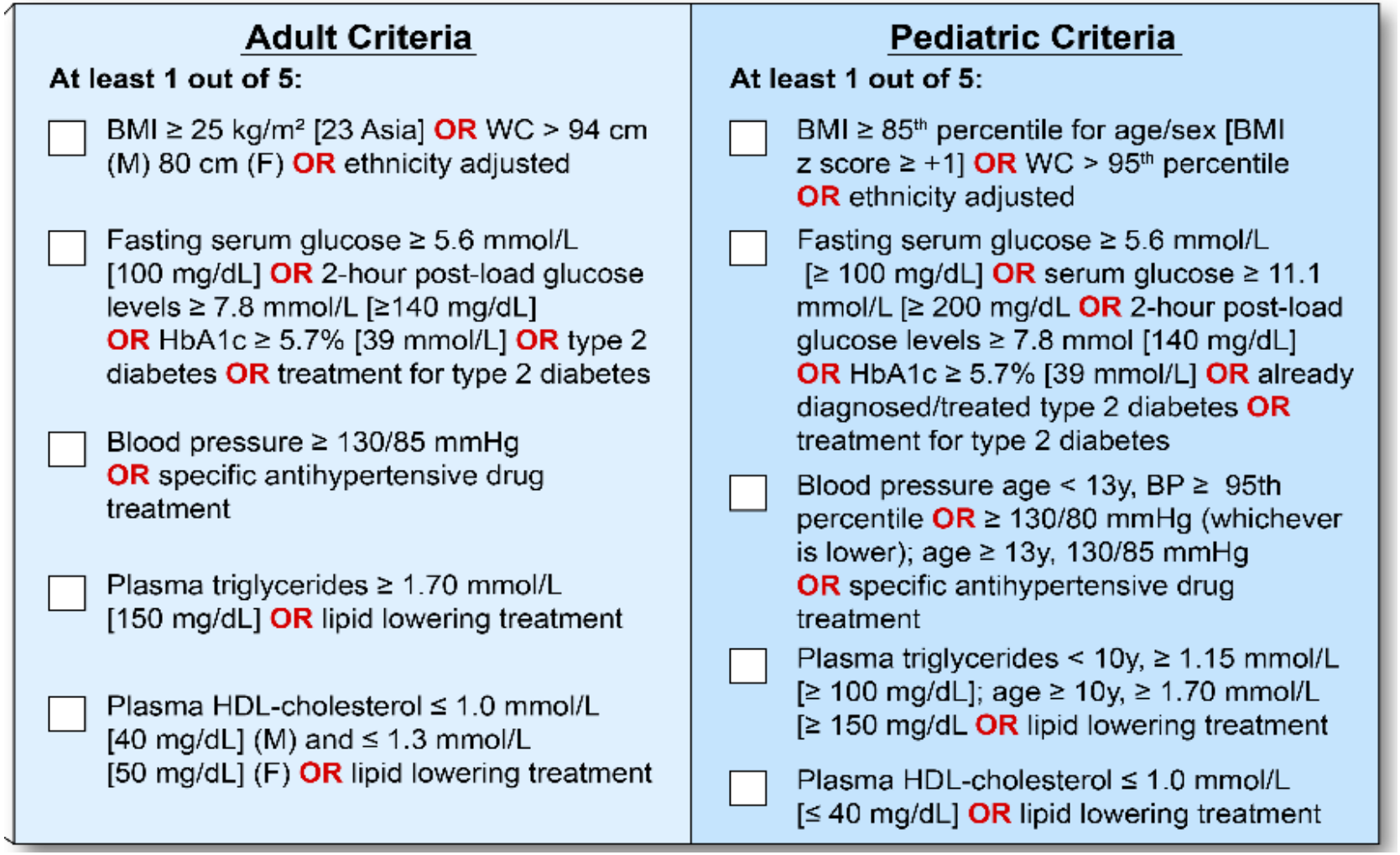
I disclose the following financial relationship(s) with a commercial interest:

- Ownership interests: Durect, Tiziana, Genfit, Exhalenz
- Consultant: Gilead, Intercept, Novartis, Novo Nordisk, Inventiva, Merck, Pfizer, Boehringer Ingelhiem, Bristol Myers Squibb, Eli Lilly, Genentech, Amgen, Alnylam, Regeneron, Thera Technologies, Madrigal, Salix, Malinckrodt, Gatehouse, Rivus, Siemens, Lipocine, 89 Bio, Astra Zeneca, Akero, Foresite, Mitopower, Takeda, Ursobio, Histoindex, Path AI,
- Grant support to school: Gilead, Intercept, Novartis, Novo Nordisk, Inventiva, Eli Lilly, Genentech, Boehringer Ingelhiem, Bristol Myers Squibb

Consensus nomenclature



*Weekly intake 140-350g female, 210-420g male (average daily 20-50g female, 30-60g male)
**e.g. Lysosomal Acid Lipase Deficiency (LALD), Wilson disease, hypobetalipoproteinemia, inborn errors of metabolism
***e.g. Hepatitis C virus (HCV), malnutrition, celiac disease



Aligned with **Alberti et al Circulation 2009**

Rinella et al, Hepatology 2023

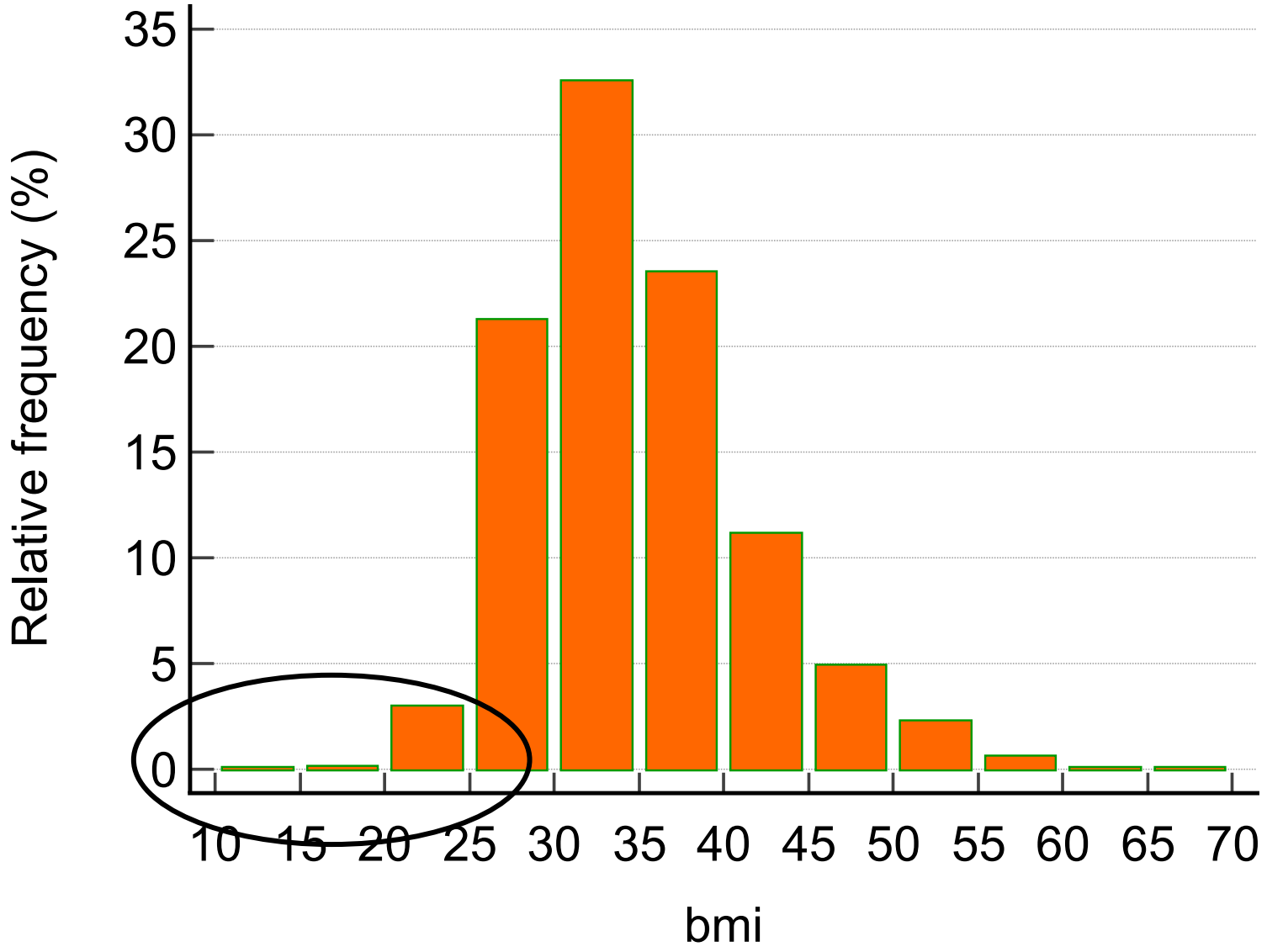
Analysis of NIMBLE circulating workstream stage 1 study population

- Aim:
  - To determine the distribution of metabolic risk parameters within the cohort
  - To determine how many patients were reclassified to be cryptogenic steatotic liver disease
  - To determine this histological spectrum of those reclassified as cryptogenic steatosis liver disease

NIMBLE stage 1 CWS study cohort derived from NASH CRN

		Stage 0 N= 222	Stage 1 N=114	Stage 2 N= 262	Stage 3 N= 277	Stage 4 N=198
Age (yrs)	Mean (SD)	47.8 (12.2)	48.1 (13.8)	51.7 (11.5)	54.4 (11.2)	56.2 (9.8)
Males	n (%)	99 (44.6%)	52 (45.6%)	102 (38.9%)	91 (32.9%)	60 (30.3%)
Caucasian	n (%)	158 (71.2%)	68 (59.6%)	199 (76.2%)	217 (78.9%)	169 (86.2%)
T2DM	n (%)	45 (20.3%)	41 (36.0%)	113 (43.1%)	162 (58.5%)	129 (65.2%)
BMI (kg/m2)	Mean (SD)	32.8 (6.6)	33.3 (6.1)	34.5 (6.3)	36.1 (6.6)	36.4 (7.3)
HbA1C (%)	Mean (SD)	5.8 (1.1)	6.0 (1.2)	6.4 (1.1)	6.7 (1.2)	6.7 (1.4)
AST (IU/l) ALT (IU/l) Alk phos (IU/l)	Mean (SD) Mean (SD) Mean (SD)	27.8 (13.3) 38.5 (25.4) 86.6 (30.5)	31.9 (17.7) 45.0 (34.6) 80.6 (28.2)	50.3 (29.3) 65.5 (43.1) 87.0 (28.0)	58.3 (39.8) 68.1 (47.8) 93.0 (33.2)	51.9 (28.9) 49.1 (34.5) 114.5 (53.2)
Bilirubin (mg/dl)	Mean (SD)	0.5 (0.3)	0.6 (0.5)	0.5 (0.3)	0.5 (0.4)	0.8 (0.8)
INR	Mean (SD)	1.0 (0.1)	1.0 (0.2)	1.0 (0.1)	1.1 (0.1)	2.8 (4.3)
LDL-Cholesterol (mg/dl)	Mean (SD)	117.5 (36.5)	105.9 (36.6)	112.0 (39.2)	106.1 (38.1)	100.7 (35.3)
NASH	n (%)	27 (12.2%)	91 (79.8%)	262 (100%)	277 (100%)	178 (89.9%)
NAS	Mean (SD)	2.5 (0.6)	2.5 (0.6)	4.8 (1.5)	5.2 (1.6)	4.2 (1.6)

Distribution of BMI

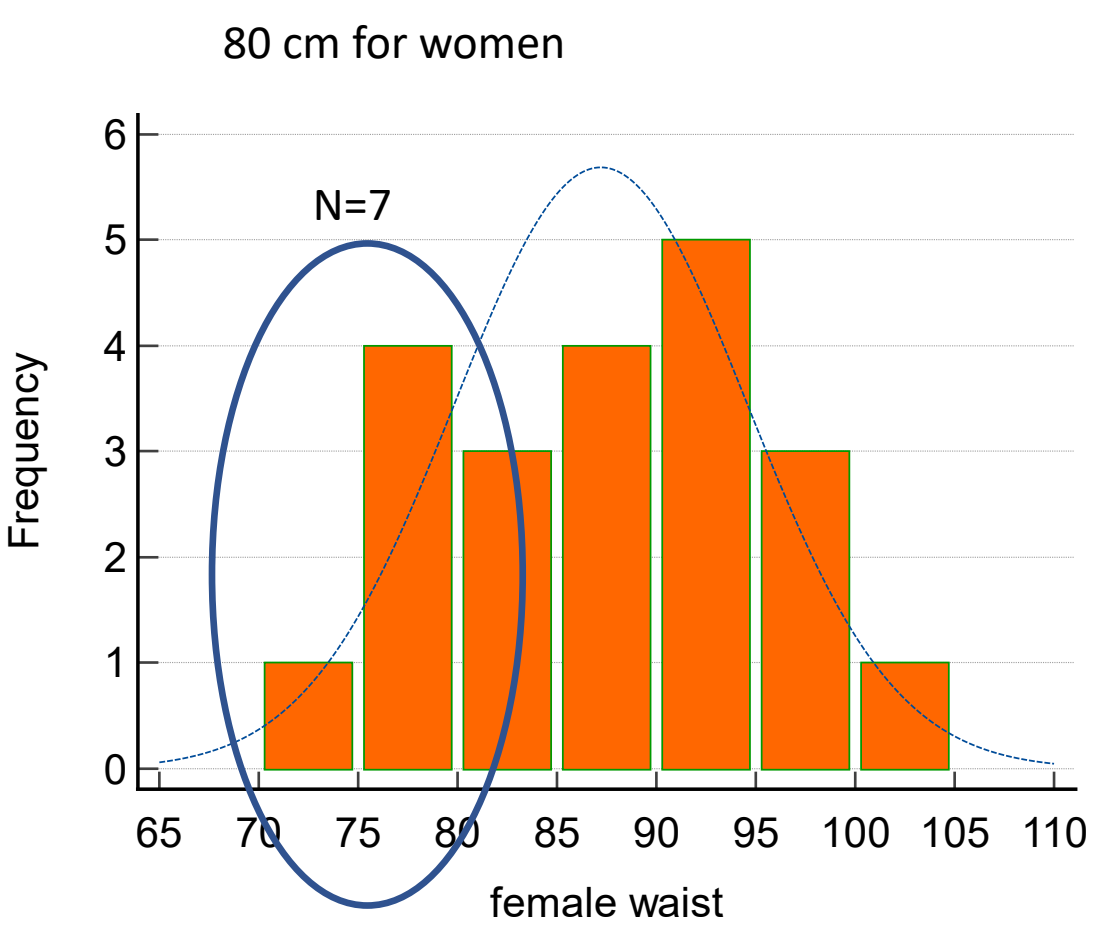


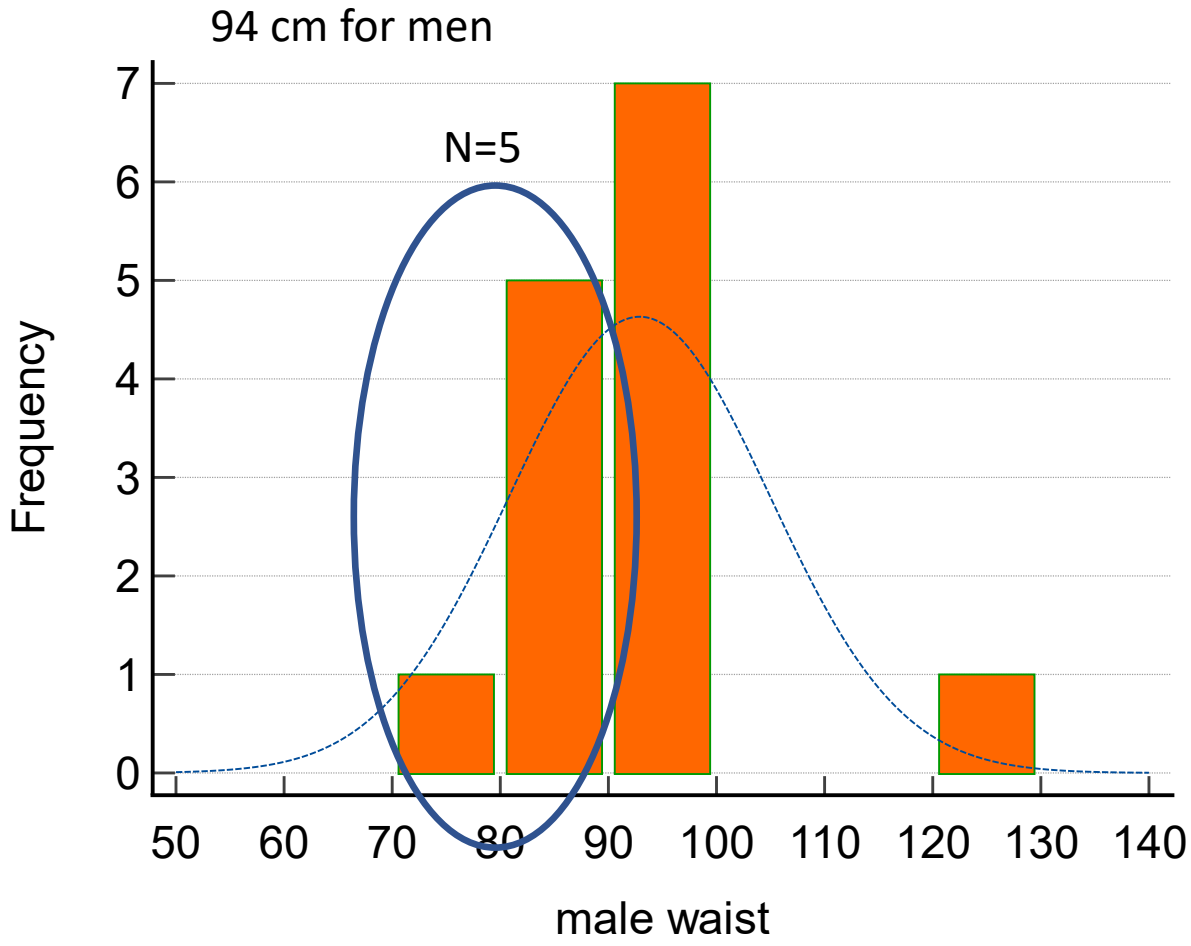
Total n= 1073

with BMI < 25= 36

3.3%

Now applying waist circumference cutoffs





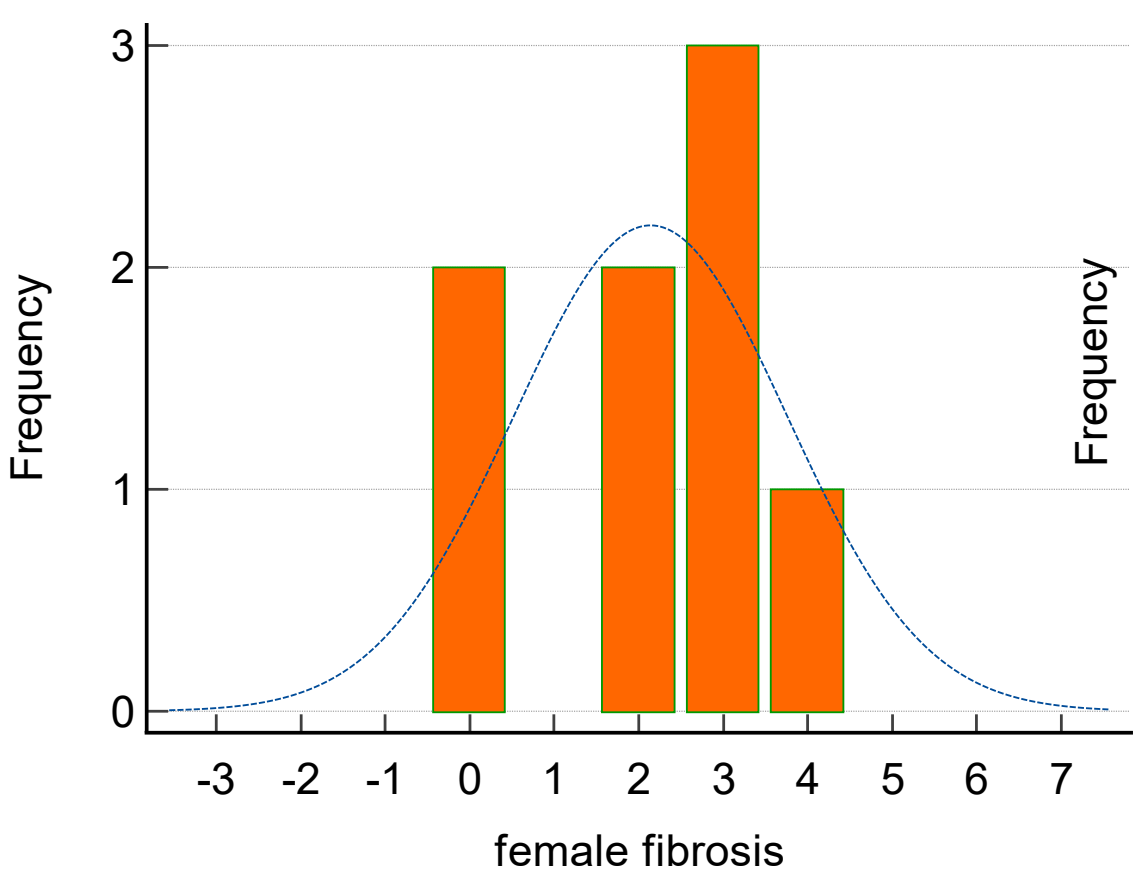
Now applying hypertension and T2DM

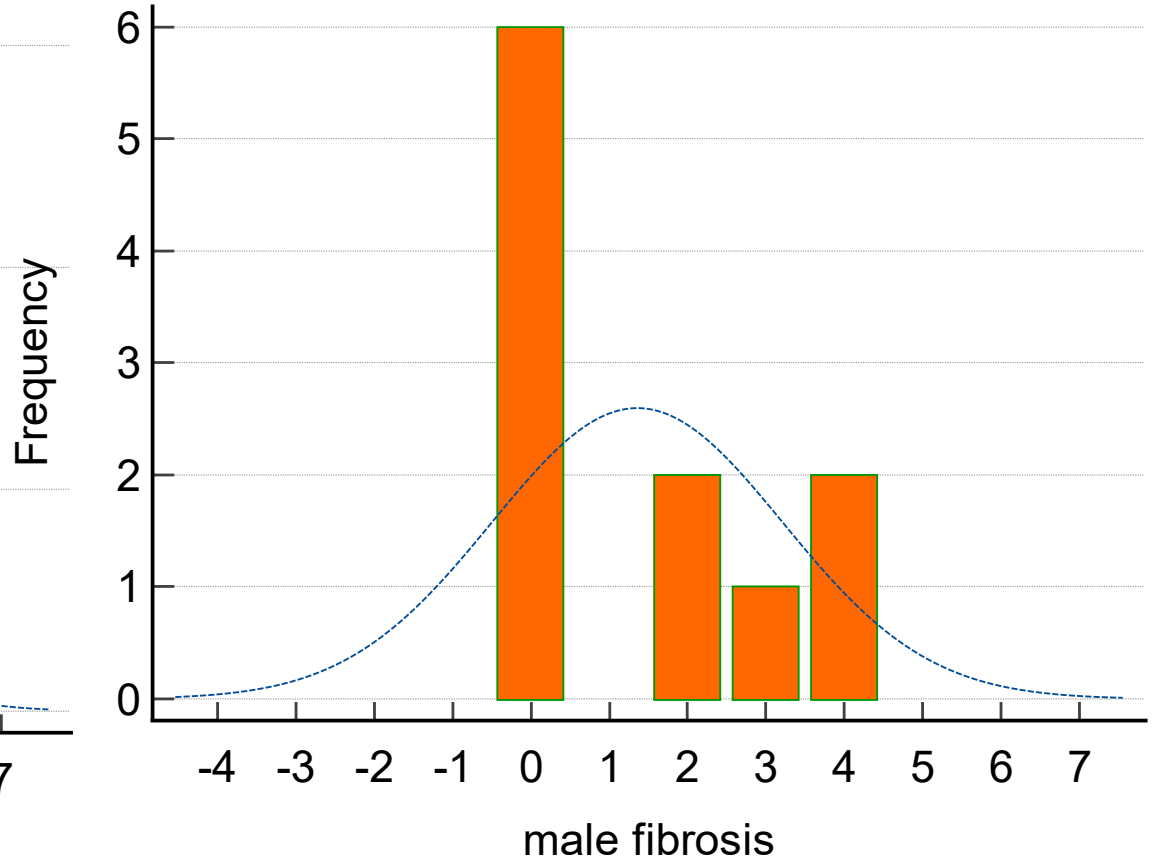
- Females:
  - 4/7 had hypertension
  - 0/7 had T2DM

- Males:
  - 2/8 had hypertension
  - 0/8 had T2 DM

9/1073 (< 1%) were reclassified as cryptogenic steatotic liver disease

Fibrosis distribution of cryptogenic steatotic liver disease





summary

- Very few patients are left behind by current nomenclature
- Of those reclassified as cryptogenic cirrhosis, some have advanced fibrosis or cirrhosis

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No More NAFLD

The NAFLD nomenclature is changing.

How do we facilitate change?

AASLD Efforts to Facilitate Implementation

- **Development of Steatotic Liver Disease (SLD) Task Force**
  - **SLD Global Partnerships, Advocacy, Awareness (GAA)**

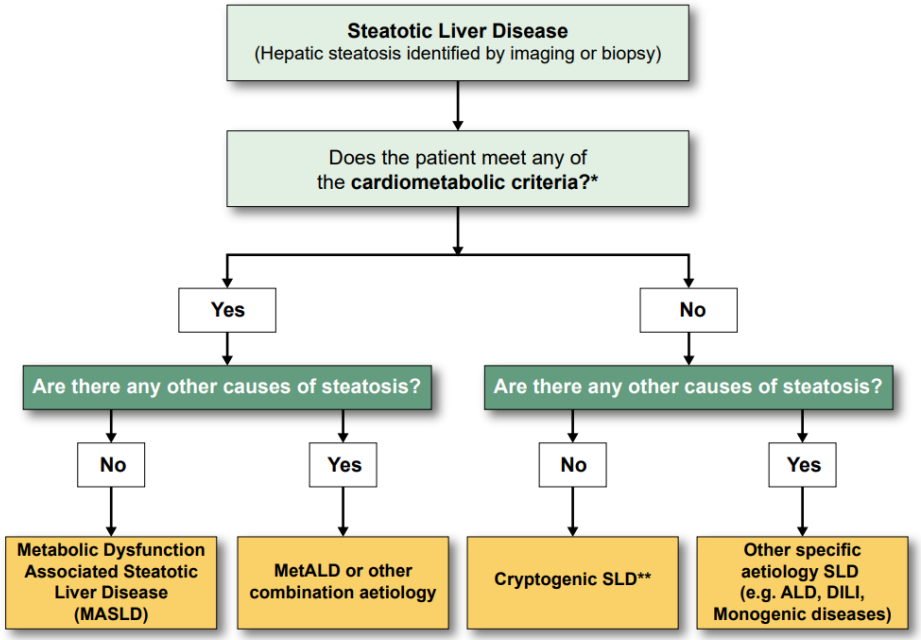
    Co-Chairs: Mary E. Rinella, MD, FAASLD and Naim Alkhouri, MD
  - **SLD Education, Guidelines, and Best Practices (EGBP)**

    Co-chairs: Meena B. Bansal, MD FAASLD and Bilal Hameed, MD
  - Convened In-Person June 23rd
  - Biweekly meeting to track initiatives and progress

- **TLM 2023: Nomenclature Implementation Symposium**
- **Saturday November 11th 8:30-10AM**
- **Topics to be included**
  - Global uptake and lessons learned
  - Impact on Biomarker Development and Qualification
  - Integration of nomenclature change into publications and timeline
  - Approach to diagnosis codes, billing, and timeline for inclusion into ICD 12.0
  - FDA perspective
  - Panel discussion including patient perspective

Provider Support

- Creation of Decision Support Tool
- Dissemination of name change via social media
- Offered opportunity for accepted TLM 2023 abstracts to align with new nomenclature change
- Creation of Nomenclature Change Deck to be shared



Community Conversations/Stakeholder Meetings

- **Community Conversations**
  - Launched August 4, 2023
  - Open forum to discuss challenges, barriers, and successes of nomenclature adoption

- **Stakeholder meetings**
  - To be scheduled with Industry, Regulatory Bodies, Patient Advocacy Organizations