Current multi-dimensional view of non-alcoholic steatohepatitis (NASH) / metabolic dysfunction-associated steatohepatitis (MASH) global epidemiological rates

Yestle Kim¹, Michael Charlton², Gauri Saal³ ¹Madrigal Pharmaceuticals, Inc., West Conshohocken, Pennsylvania, USA; ²Center for Liver Diseases, University of Chicago, Illinois, USA; ³Neulumic Consulting, Birmingham, UK

Background

- The rising epidemiological burden of MASH, associated with the increasing incidence of obesity, type 2 diabetes (T2D), and metabolic syndrome, is well recognized.^{1,2}
- There is, however, less clarity on the precise prevalence and incidence of MASH, potentially reflecting barriers to diagnosis and disparate diagnostic approaches (Table 1); ascertainment of incidence and prevalence of MASH is critical for clinical decision-making.
- This targeted literature review aims to capture a multi-dimensional view of MASH epidemiology by characterizing prevalence by population and diagnostic approaches.

Table 1. MASH diagnostic approaches	
Histologi c	Hepatocyte ballooning, lobular inflammation, and steatosis
NIT- based	 Aspartate aminotransferase (AST) to platelet ratio index (APRI) FibroScan AST (FAST) Liver fibrosis index (FIB) Liver stiffness measurement (LSM) Liver stiffness on magnetic resonance elastography (MEFIB) Magnetic resonance imaging aspartate aminotransferase (MAST) Magnetic resonance imaging/magnetic resonance elastography (N Nonalcoholic fatty liver disease (NAFLD) activity score (NAS) Proton density fat fraction (PDFF) Vibration-controlled transient elastography (VCTE)
Mixed	Biopsy and NIT

Methods

Targeted literature searches (2014–2024) covered US and global studies on MASH prevalence or incidence in adults lean, with or without obesity or T2D, respectively, as diagnosed with NITs or biopsy.

Results

Searches identified five systematic literature reviews/meta-analyses (overall covering studies from inception to 2023) and 11 primary observational studies; all pointing to a range of MASH prevalence rates in various general and patient populations (key studies are summarized).

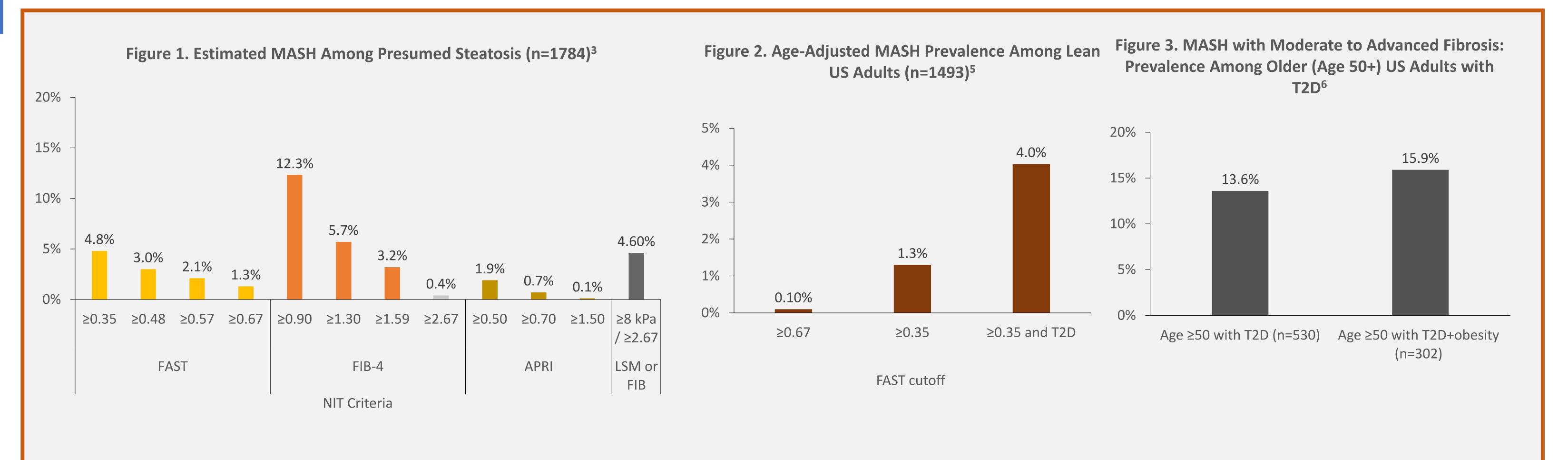
References

- 1. Godoy-Matos A et al. *Diabetology & Metabolic Syndrome* 2020;12:60.
- 2. Younossi Z et al. Gut. 2020; 69 (3): 564–68.
- 3. Fishman J et al. Journal of Health Economics and Outcomes Research. 2024;11 (1): 32–43.
- 4. Payne J et al.. *Hepatology Communications*. 2023; 7 (1): e0019.
- 5. Kalligeros M et al. Annals of Gastroenterology. 2023;36 (6): 670–77.
- 6. Mittal N et al. Alimentary Pharmacology & Therapeutics. 2024. https://doi.org/10.1111/apt.17997.
- 7. Harrison S et al.. Journal of Hepatology. 2021. 75 (2): 284–91.
- 8. Younossi Z et al. *Hepatology.* 2016. 64 (1): 73.
- 9. Younossi Z et al. *Clinical Gastroenterology and Hepatology* 0 (0). <u>https://doi.org/10.1016/j.cgh.2024.03.006</u>. 10.Cho E et al. Gut. 2023;72(11):2138-2148.
- 11.Estes C et al.*Hepatology.* 2018;67 (1): 123–33





- disease features (Figure 3).⁶
- Biopsy-based MASH prevalence estimates varied by population:



CONCLUSIONS

• Across three US National Health and Nutrition Examination Survey (NHANES) studies, MASH prevalence varied according to NIT and cutoff applied: In patients with steatosis identified by VCTE (2017–2020; n=6969) rates of MASH were 2–5% on FAST, 0.4-12% on FIB-4, 0.1–2% on APRI, 5% on FS-LSM (Figure 1).³ • The prevalence of MASH with fibrosis was 11.6% for patients with NAS ≥ 4 (2017-2018; n=9254).⁴ In a lean population with T2D (2017–2020; n=1628) MASH prevalence on FAST scores were between 0.1-1%, and 4% (Figure 2).⁵ In an older (age 50+) US clinical cohort of patients of normal weight with T2D, 13.6% had moderate to advanced fibrosis (>F2, including higher risk of disease progression; positive MEFIB score [MRE >3.3 kPa + Fib4 > 1.6], FAST score \geq 0.67 or a MAST score \geq 0.242), while **15.9%** of those with obesity (BMI \geq 30 kg/m2) and T2D, had these

37–61% among US⁷ and global meta-analytic patient populations⁸ with steatosis; 66% in T2D⁹ with an indication for a biopsy compared with 5% in a voluntarily biopsied individuals from a meta-analytic general global populations¹⁰ Based on Markov modelling, country-specific MASH prevalence estimates in general populations point to the highest MASH prevalence in the US (5.3%), relatively consistent across European countries and the UK (between 4.4-3.6%), and lowest in Japan and China (3.0-2.4%).¹¹

> • The literature base of epidemiological data are discrepant, and MASH epidemiology estimates vary widely depending on diagnostic approaches, diagnostic parameters, and the populations studied. • With the recent availability of a novel treatment for NASH with moderate to advanced fibrosis, capturing the epidemiological burden of the disease through a multidimensional approach may provide useful input for clinical decision-making.

