Impact of Different Non-Invasive Tests on Estimated Prevalence of Presumed Nonalcoholic Steatohepatitis Among US Adults, NHANES 2017-2020

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BACKGROUND

- Non-invasive tests (NITs) are used for staging risk in nonalcoholic steatohepatitis (NASH)[1]
  - These include biomarker-based measures such as the Fibrosis-4 index (FIB-4)[2] and AST-to-Platelet Ratio Index (APRI),[2] and more recently, the FibroScan+AST (FAST)[3] score (which uses liver stiffness and steatosis measurements obtained via vibration-controlled transient elastography imaging)
- While NITs are primarily used for staging risk, they have also been considered for identification of presumed NASH in observational research[3-4]
  - However, existing research does not address how different NITs may impact the estimated prevalence

OBJECTIVES

- To estimate the prevalence of presumed NASH among US adults as well as assess the variation in prevalence arising from use of different NITs

METHODS

- A cross-sectional analysis was conducted using the 2017-March 2020 National Health and Nutrition Examination Survey (NHANES) cycle
  - The analysis was weighted to provide nationally-representative estimates for US adults
- NASH was identified using a multi-stepped approach by which participants were restricted to those with steatosis then to those without common alternative causes of liver disease
- Presumed NASH was distinguished based on FIB-4, APRI, and FAST score cut-offs[3-4] across 16 scenarios to assess the impact on prevalence estimates
- Prevalence estimates were compared to estimates obtained using a screening algorithm recently proposed in clinical practice (American Association of Clinical Endocrinology [AACE] *Cirrhosis Prevention in NAFLD* algorithm[5]) and eligibility criteria from the resmetirom Phase 3 MAESTRO-NASH trial (ClinicalTrials.gov identifier, NCT03900429)[6], which recommend initial screening based on metabolic risk factors and conditions associated with nonalcoholic fatty liver disease (NAFLD)/NASH as well as steatosis measures (if available)
  - An additional scenario was modeled to explore variation in the MAESTRO-NASH eligibility criteria, requiring ≥3 risk factors for significant liver fibrosis, but restricting to a liver stiffness measurement (LSM) ≥11 kPa or FAST ≥0.50 rather than LSM ≥8.5 kPa and CAP ≥280 dB/m

RESULTS

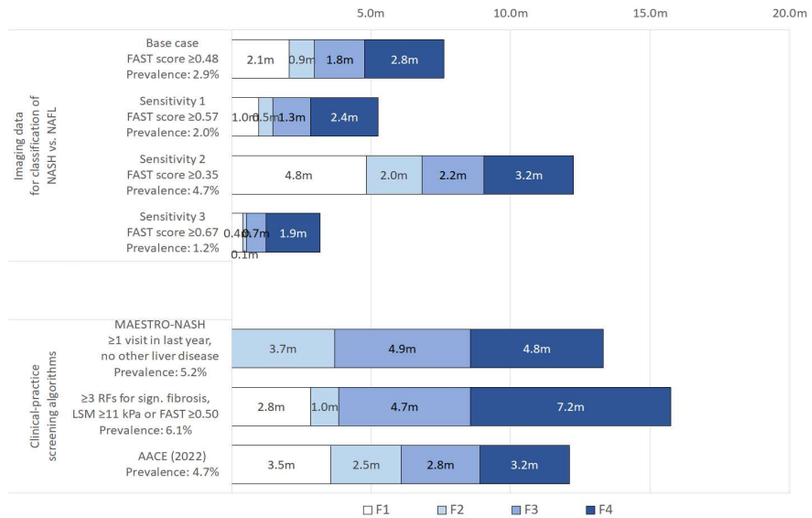
- Among NHANES participants with complete data for the analysis (N = 6,789), prevalence of presumed NASH identified using FAST score was estimated to range from 1.2%-4.7% (FAST score ≥0.67 and ≥0.35,respectively)
  - These compared to estimated prevalence of 4.7% (SE: 0.5%) when applying the AACE screening algorithm and 5.2% (SE: 0.6%) to 6.5% (SE: 0.7%) across the scenarios when applying the MAESTRO-NASH eligibility criteria
- Use of non-imaging NITs resulted in a wide range of prevalence estimates from 1.1%-1.6% for APRI ≥0.70, 7.8%-11.2% for FIB-4 ≥1.59, and 28.5%-39.2% for FIB-4 ≥0.90
- Liver fibrosis stage distributions differed when imaging versus non-imaging NITs were used (26%-36% vs 47%-95%, respectively, for F2-F3 fibrosis)

Table 1. Estimated prevalence of presumed NASH among US adults, and liver fibrosis stages

		Presumed NASH		Estimated liver fibrosis stage (%)			
Scenario	Steatosis	NASH	Weighted % (SE)	Fibrosis staging	F0-F1	F2-F3	F4
Base case	CAP ≥302	FAST ≥0.48	2.9% (0.2%)	LSM: 8.2/9.7/13.6	27%	36%	37%
Sensitivity 1		FAST ≥0.57	2.0% (0.2%)		19%*	35%	46%
Sensitivity 2		FAST ≥0.35	4.7% (0.4%)		39%	34%	26%
Sensitivity 3		FAST ≥0.67	1.2% (0.2%)		13%*	26%*	61%
Sensitivity 4	VAI >1.25	APRI ≥0.70	0.9% (0.1%)	FIB-4: 0.95/2.67/3.25	11%*	65%	25%*
Sensitivity 5				FIB-4: 1.30/2.67/3.25	25%*	50%	25%*
Sensitivity 6		FIB-4 ≥0.90	26.7% (1.6%)	FIB-4: 0.95/2.67/3.25	9%	89%	1%
Sensitivity 7				FIB-4: 1.30/2.67/3.25	52%	47%	1%
Sensitivity 8		FIB-4 ≥1.59	7.2% (0.7%)	FIB-4: 0.95/2.67/3.25	0%*	95%	5%
Sensitivity 9				FIB-4: 1.30/2.67/3.25	0%*	95%	5%
Sensitivity 10	TyG >8.38	APRI ≥0.70	1.1% (0.1%)	FIB-4: 0.95/2.67/3.25	9%*	67%	25%
Sensitivity 11				FIB-4: 1.30/2.67/3.25	24%*	52%	25%
Sensitivity 12		FIB-4 ≥0.90	28.5% (1.5%)	FIB-4: 0.95/2.67/3.25	9%	90%	1%
Sensitivity 13				FIB-4: 1.30/2.67/3.25	51%	47%	1%
Sensitivity 14		FIB-4 ≥1.59	7.8% (0.6%)	FIB-4: 0.95/2.67/3.25	0%*	95%	5%
Sensitivity 15				FIB-4: 1.30/2.67/3.25	0%*	95%	5%

NHANES guidelines recommend sample size of ≥30 for reporting proportions, means, and variances. Asterisks denote where sample size was <30.

Figure 1. Presumed NASH estimated population counts among US adults



CONCLUSIONS

- **Prevalence of presumed NASH estimated using FAST score aligned with historical biopsy-based estimates**
- **Analyses using non-imaging NITs (FIB-4, APRI) yielded wide ranges of prevalence estimates, suggesting these measures should be supplemented with additional information for identification of presumed NASH**

REFERENCES

1. Chalasani N, et al. *Hepatology*. 2018;67(1):328-357.
2. Curry MP, Afdhal NH. UpToDate. Accessed April 8, 2022.
3. Newsome PN, et al. *Lancet Gastroenterol Hepatol*. 2020;5(4):362-373.
4. Lee JS, et al. *Front Med (Lausanne)*. 2022;9:869190.
5. Cusi K, et al. *Endocr Pract*. 2022;28(5):528-562.
6. Loomba R, et al. *Hepatology*. 2022;76(S1):S92-593.

DISCLOSURES

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JF is employed by and owns stock/stock options in Madrigal Pharmaceuticals.