

# Use of the LiverRisk Score for prediction of moderate to advanced liver fibrosis in United States adults

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## Introduction

- Resmetirom is the first conditionally-approved treatment in the United States (US) for noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH; formerly known as nonalcoholic steatohepatitis [NASH]), for use in adults with moderate to advanced liver fibrosis (consistent with stages F2 to F3).
- Recent practice guidelines indicate that patient selection for treatment with resmetirom may be based on evidence of fibrosis from noninvasive tests (NITs).[1-2]
  - In particular, liver stiffness measurement (LSM) of 8-15 kPa by vibration-controlled transient elastography (VCTE) (with exclusion of cirrhosis) is considered to approximate fibrosis stages F2-F3.[1]
- The LiverRisk Score (LRS) is calculated from blood-based biomarkers and demographics, developed for prediction in the general population of liver fibrosis and future liver-related outcomes.[3]

## Objectives

- To evaluate in US adults the performance of the LRS in classifying LSM  $\geq 8$  kPa and  $\geq 15$  kPa, compared to the Fibrosis-4 (FIB-4) Index.

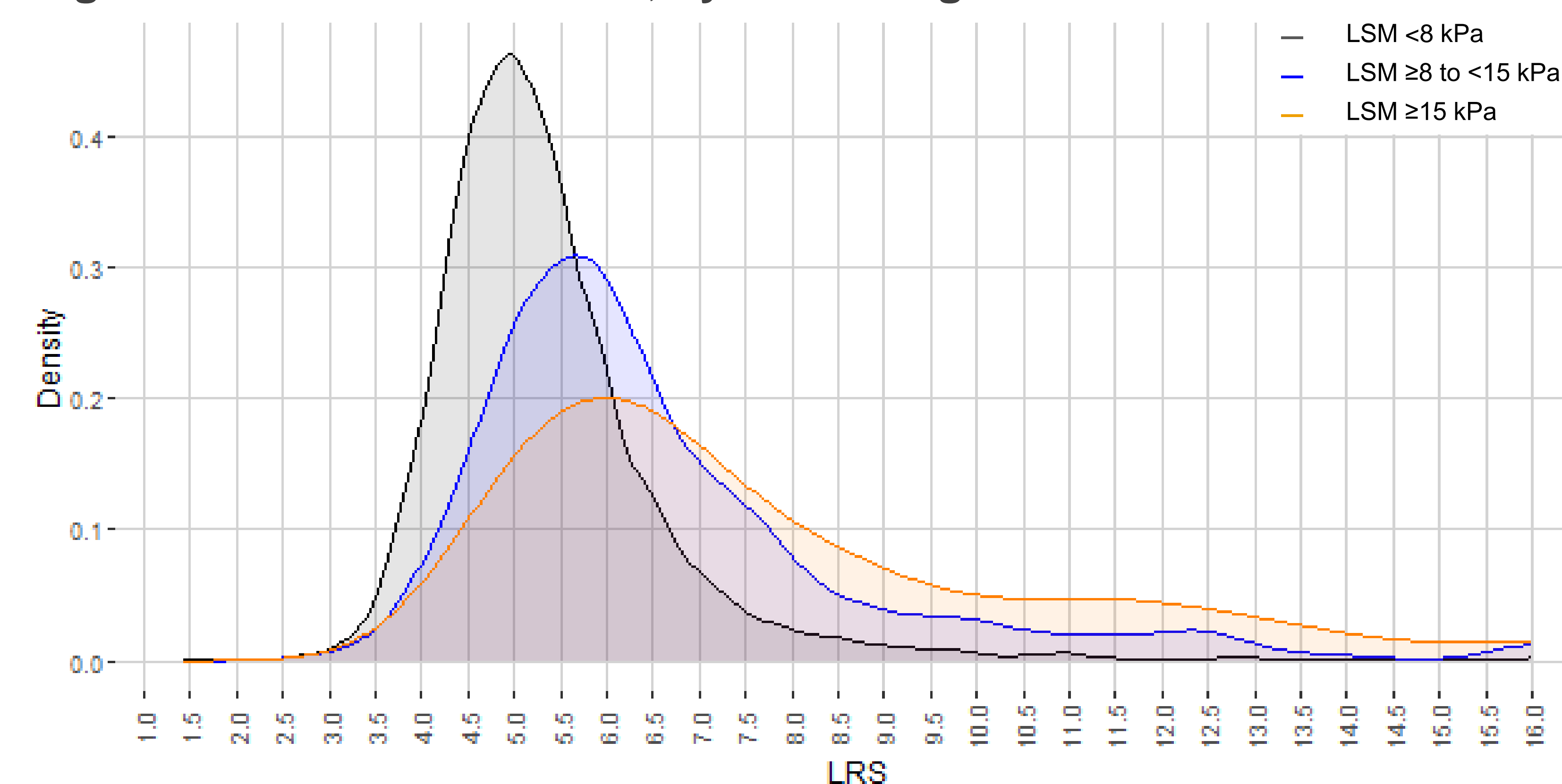
## Methods

- An observational analysis was conducted of the National Health and Nutrition Examination Survey (NHANES) 2017-2020 cycle.
- Participants were included if they:
  - were  $\geq 18$  years of age
  - had complete information to calculate the LRS, including: age, sex, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, total cholesterol, platelet count, and fasting plasma glucose (imputed from non-fasting serum glucose when missing)
  - had a median LSM (of 10 measurements) meeting quality criteria (“complete”)
- Discrimination of the LRS vs. FIB-4 for classifying LSM was evaluated as area under the curve (AUC), estimated by survey-weighted logistic regression of LSM  $\geq 8$  kPa /  $\geq 15$  kPa vs. the LRS or FIB-4 (as continuous measures).
  - ROC curves were generated using the “pROC” package in R v.4.43
  - 95% confidence intervals (CIs) for AUCs were calculated using 2000 bootstraps
  - Comparison of AUCs for the LRS vs. FIB-4 was conducted via DeLong test
- Analyses were conducted applying survey weights for the medical-examination sample of the 2017-2020 cycle, allowing for estimation of measures representative of the civilian, non-institutionalized adult US population.

## Results

- The unweighted study population included N = 7,076 participants (of 7,768 aged  $\geq 18$  years and with “complete” LSM), with mean (95% CI) age of 47.1 (46.0-48.3) years, female sex 50.4% (48.6%-52.2%), BMI  $\geq 30$  kg/m<sup>2</sup> 40.3% (37.7%-42.9%), and prevalence of LSM  $\geq 8$  kPa of 9.0% (7.7%-10.3%).
- The median (Q1-Q3) LRS increased with LSM (kPa) category: 5.04 (4.55-5.65) for LSM < 8, 5.93 (5.20-7.08) for LSM  $\geq 8$  to <15, and 6.28 (5.56-7.94) for LSM  $\geq 15$ .

Figure 1. Distribution of LRS, by LSM categories



## Discussion

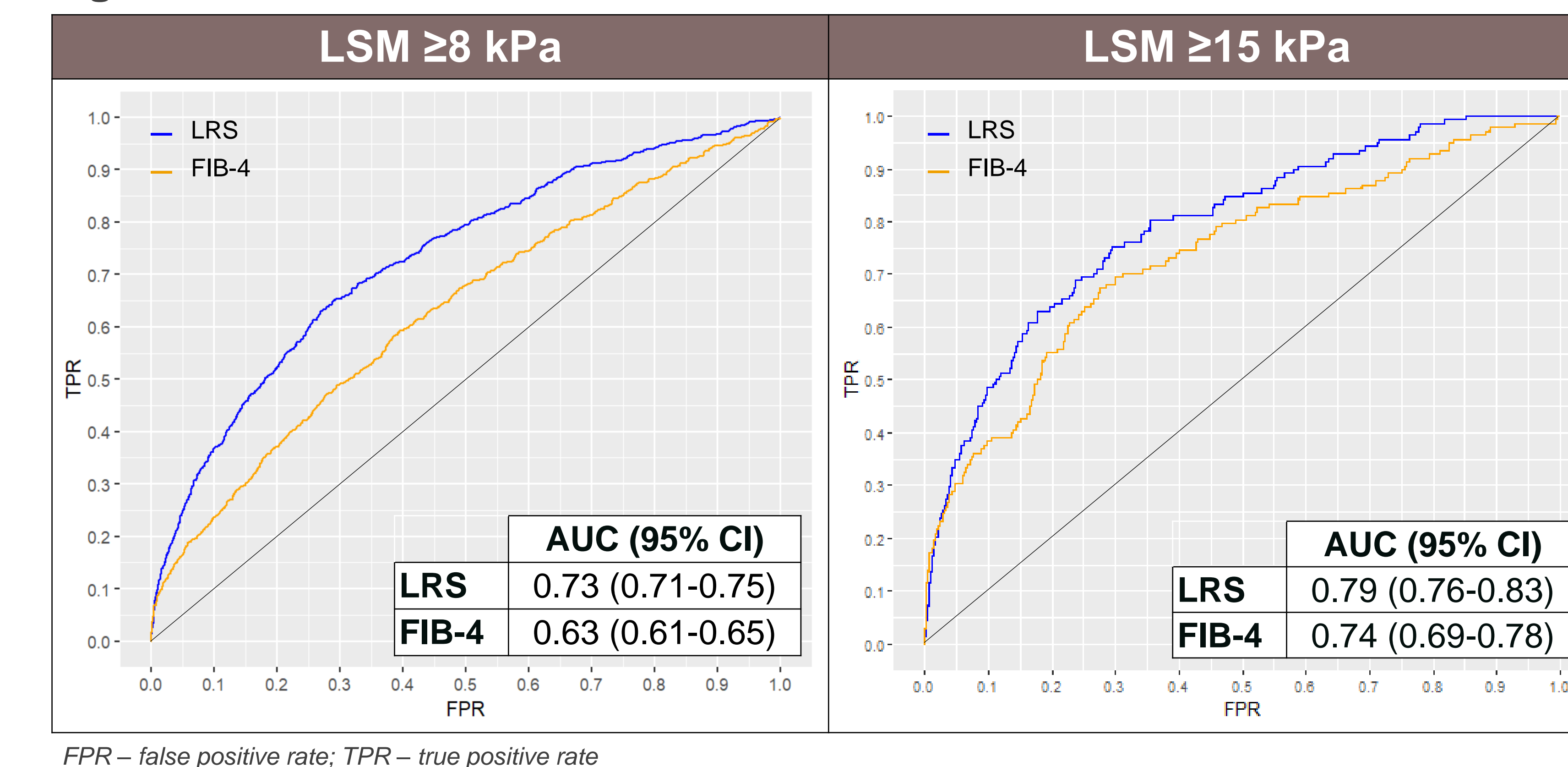
- This analysis reports insights on use of the LRS in general-population screening for chronic liver disease, building on existing research [4-6] by characterizing classification of LSM categories relating to resmetirom eligibility recommendations proposed in recent guidelines.[1]
- For fixed specificity in classification of LSM  $\geq 8$  kPa, sensitivity was generally improved for the LRS vs. FIB-4 (e.g., for specificity = 0.90, sensitivity = 0.37 vs. 0.24, indicating  $\geq 50\%$  additional cases identified).
- Certain limitations of the analysis should be noted, including:
  - Participants were excluded if missing necessary information for the analysis, which could introduce bias if information is not missing completely at random.
  - Incomplete measures of LSM (i.e., fasting <3 hours, <10 valid measures, IQR/median >30%) were excluded, and were more common for BMI  $\geq 30$  (9%) vs. BMI <30 (5%).

## References

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- For discrimination of LSM  $\geq 8$  kPa, the LRS demonstrated statistically significantly ( $p < 0.05$ ) superior AUC (95% CI) of 0.73 (0.71-0.75) vs. 0.63 (0.61-0.65) for FIB-4.
- For discrimination of LSM  $\geq 15$  kPa, LRS trended towards statistically significantly superior ( $p = 0.06$ ), with AUC (95% CI) of 0.79 (0.76-0.83) vs. 0.74 (0.69-0.78) for FIB-4.

Figure 2. ROC curves for discrimination of LSM  $\geq 8$  and  $\geq 15$  kPa



FPR – false positive rate; TPR – true positive rate

## Conclusions

- In US adults, the LRS demonstrated superior discrimination vs. FIB-4 for classification of LSM  $\geq 8$  kPa and  $\geq 15$  kPa.
- Further, results of this study contextualize values of the LRS in the US adult general population.
- Accordingly, findings may assist in interpretation of the LRS in clinical practice.

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