

ASSOCIATION OF CLINICAL AND DEMOGRAPHIC VARIABLES AND INCIDENT CIRRHOSIS BY FIB-4 SCORE IN A LARGE PRIMARY CARE COHORT

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BACKGROUND: The Fibrosis-4 (FIB-4) score is widely used to stratify risk of advanced fibrosis and is most appropriately used in low-prevalence primary care settings. The FIB-4 score can be reassessed within 3 years depending on the patient's metabolic risk factors. However, recent studies have suggested limitations in FIB-4 score accuracy even in nonspecialty settings. We aimed to identify the association of clinicodemographic variables and risk of incident cirrhosis by FIB-4 score in a large primary care cohort.

METHODS: We assembled a retrospective cohort of consecutive primary care patients defined as having ≥ 2 ambulatory visits ≥ 1 year apart from 2006 to 2022. The sample included patients with available ambulatory labs to calculate an index FIB-4 score and excluded patients with baseline chronic liver disease (steatotic liver disease, chronic viral hepatitis, autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, Wilson disease, hemochromatosis, cirrhosis, hepatocellular carcinoma), liver failure, or liver transplantation using ICD codes. Incident cirrhosis was defined as a new cirrhosis ICD code within 3 years of the index FIB-4 score. FIB-4 score risks were categorized as low (<1.3 for ages 35-65, <2 for ages >65), intermediate (1.3-2.67 for ages 35-65, 2-2.67 for ages >65), or high (>2.67). We identified predictors of cirrhosis by FIB-4 scores using multivariable logistic regression.

RESULTS: The sample, which included 242,970 adult primary care patients, had a median age of 53 (IQR 42, 65), was mostly female (55%), non-Hispanic White (63%), English-speaking (97%), and privately insured (85%) (Table 1). Median FIB-4 score was 1 (IQR 0.8, 1.4) and median follow-up time was 95.5 (IQR 65.3, 158.1) months. Most patients had low- (79%), followed by intermediate- (18%), and high-risk (3%) FIB-4 scores. Cirrhosis prevalence within 3 years of the index FIB-4 score was 0.2% ($n=541$). Median time from index FIB-4 score to incident cirrhosis was 34 months, 27 months, and 17 months for the low-, intermediate-, and high-risk FIB-4 score groups, respectively. Of those with incident cirrhosis, 32% ($n=171$), 24% ($n=132$), and 44% ($n=238$) had low-, intermediate-, and high-risk FIB-4 scores, respectively. The most salient predictors of cirrhosis were Medicaid for the low- (OR 3.63, $p<.001$) and intermediate-risk (OR 2.70, $p=.002$) groups and Hispanic/Latino ethnicity (OR 2.29, $p<.001$) for the high-risk group (Table 2).

CONCLUSION: In this large primary care cohort, cirrhosis was detected within 3 years of follow-up even among patients with low index FIB-4 scores. Sociodemographic variables, including Medicaid and Hispanic/Latino ethnicity, had a more significant role in predicting cirrhosis than other variables. Further evaluation of the role of sociodemographic factors is needed to improve risk stratification among primary care patients.

Table 1. Distribution of demographic and clinical characteristics, overall and by FIB-4 score risk group

	Total (N = 242970)	Low Risk FIB-4 Score (N = 191656)	Intermediate Risk FIB-4 Score (N = 43592)	High Risk FIB-4 Score (N = 7722)
Characteristic	Median (IQR)			
Age	53.0 (42.0, 65.0)	49.0 (40.0, 62.0)	60.0 (53.0, 65.0)	77.0 (66.0, 85.0)
	N (%)			
Sex				
Female	133946 (55.1)	109430 (57.1)	21128 (48.5)	3388 (43.9)
Male	109021 (44.9)	82223 (42.9)	22464 (51.5)	4334 (56.1)
Race or Ethnicity				
Non-Hispanic AIAN	569 (0.3)	452 (0.3)	94 (0.2)	23 (0.3)
Non-Hispanic Asian	24029 (10.6)	19423 (11.0)	3798 (9.2)	808 (10.9)
Non-Hispanic Black	12920 (5.7)	9776 (5.5)	2616 (6.4)	528 (7.1)
Hispanic/Latino	25923 (11.5)	21669 (12.2)	3605 (8.8)	649 (8.8)
Non-Hispanic NHOP	444 (0.2)	356 (0.2)	74 (0.2)	14 (0.2)
Non-Hispanic White	141352 (62.6)	108751 (61.4)	27724 (67.4)	4877 (65.9)
Non-Hispanic Other	20570 (9.1)	16833 (9.5)	3232 (7.9)	505 (6.8)
Language				
English	234511 (96.6)	185560 (96.9)	41835 (96.0)	7116 (92.2)
Spanish	4239 (1.7)	3211 (1.7)	782 (1.8)	246 (3.2)
Other	4124 (1.7)	2808 (1.5)	961 (2.2)	355 (4.6)
Insurance				
Private	206304 (85.4)	166174 (87.1)	35420 (81.8)	4710 (62.2)
Medi-Cal	6377 (2.6)	4409 (2.3)	1417 (3.3)	551 (7.3)
Medicare	19330 (8.0)	13331 (7.0)	4463 (10.3)	1536 (20.3)
Other	9613 (4.0)	6850 (3.6)	1985 (4.6)	778 (10.3)
Type 2 diabetes mellitus	20408 (8.4)	15481 (8.1)	3727 (8.5)	1200 (15.5)
Pre-diabetes	59519 (24.5)	46364 (24.2)	11105 (25.5)	2050 (26.5)
Hypertension	30381 (12.5)	22536 (11.8)	6226 (14.3)	1619 (21.0)
Dyslipidemia	72091 (29.7)	52731 (27.5)	15573 (35.7)	3787 (49.0)
BMI				
Overweight (BMI ≥ 25)	80425 (33.1)	63945 (33.4)	14115 (32.4)	2365 (30.6)
Obese (BMI ≥ 30)	51429 (21.2)	42868 (22.4)	7390 (17.0)	1171 (15.2)
	Median (IQR)			
Follow-up time, months	94.0 (65.1, 155.9)	100.9 (67.0, 166.6)	107.2 (66.4, 163.2)	95.5 (65.3, 158.1)
ALT	19.0 (14.0, 26.0)	19.0 (14.0, 26.0)	19.0 (14.0, 27.0)	19.0 (13.0, 30.0)
AST	21.0 (17.0, 25.0)	20.0 (17.0, 24.0)	24.0 (21.0, 30.0)	28.0 (22.0, 41.0)
Platelet count	243.0 (208.0, 282.0)	255.0 (223.0, 291.0)	198.0 (174.0, 226.0)	157.0 (128.0, 186.0)
Index FIB-4 score	1.0 (0.8, 1.4)	0.9 (0.7, 1.2)	1.7 (1.4, 2.1)	3.2 (2.9, 3.9)

Abbreviations: FIB-4, fibrosis-4; AIAN, American Indian and Alaskan Native; NHOP, Native Hawaiian or Pacific Islander; alanine aminotransferase, ALT; aspartate transferase, AST. Clinicodemographic variables were collected at the time of the patient's index FIB-4 measure. FIB-4 score risks were categorized as low (<1.3 for ages 35-65 or <2 for ages >65), intermediate (1.3-2.67 for ages 35-65 or 2-2.67 for ages >65), or high (>2.67). Kruskal-Wallis rank sum test and Pearson's chi-square test were used to compare clinicodemographic variables across FIB-4 risk groups. Comparisons of clinicodemographic variables across FIB-4 risk groups were all statistically significant ($p < .001$).

Denominators used for the total sample, low-risk, intermediate-risk, and high-risk groups are 242,970, 191,656, 43,592, and 7,722, respectively except for sex (242,967/191,653/43,592/7,722), race or ethnicity (225,807/177,260/41,143/7,404), language (242,874/191,579/43,578/7,717), and health insurance (241,624/190,764/43,285/7,575).

Table 2. Predictors of index cirrhosis, stratified by FIB-4 score risk group

Clinicodemographic Variables	Low Risk (N = 173529)		Intermediate Risk (N = 40053)		High Risk (N = 7167)	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.03 (1.02, 1.04)	< 0.001	0.99 (0.97, 1.01)	0.204	0.96 (0.95, 0.97)	< 0.001
Male	1.54 (1.12, 2.11)	0.008	1.07 (0.74, 1.54)	0.719	1.11 (0.83, 1.47)	0.487
Latino	1.52 (1.01, 2.28)	0.045	1.91 (1.21, 3.01)	0.005	2.29 (1.62, 3.23)	< 0.001
Insurance (ref: private)						
Medicaid	3.63 (2.14, 6.14)	< 0.001	2.70 (1.43, 5.10)	0.002	2.02 (1.29, 3.18)	0.002
Medicare	1.97 (1.26, 3.06)	0.003	1.77 (1.04, 3.00)	0.034	1.47 (1.01, 2.13)	0.042
Other	1.22 (0.58, 2.54)	0.602	0.88 (0.32, 2.42)	0.798	1.62 (0.98, 2.67)	0.058
Type II diabetes	1.91 (1.25, 2.91)	0.003	1.94 (1.15, 3.29)	0.014	2.04 (1.42, 2.94)	< 0.001
Pre-diabetes	0.69 (0.45, 1.06)	0.094	1.14 (0.75, 1.75)	0.540	0.70 (0.47, 1.04)	0.082
Hypertension	0.98 (0.65, 1.49)	0.932	0.95 (0.58, 1.54)	0.831	1.15 (0.82, 1.61)	0.418
Dyslipidemia	0.94 (0.66, 1.34)	0.750	0.72 (0.48, 1.08)	0.109	0.39 (0.28, 0.54)	< 0.001
BMI (ref: normal weight)						
Overweight	0.82 (0.55, 1.21)	0.321	1.19 (0.76, 1.85)	0.448	1.12 (0.80, 1.56)	0.510
Obese	1.37 (0.93, 2.00)	0.110	2.17 (1.39, 3.40)	< 0.001	1.69 (1.19, 2.40)	0.003

Abbreviations: FIB-4, fibrosis-4. Clinicodemographic variables were collected at the time of the patient's index FIB-4 measure. FIB-4 score risks were categorized as low (<1.3 for ages 35-65 or <2 for ages >65), intermediate (1.3-2.67 for ages 35-65 or 2-2.67 for ages >65), or high (>2.67). Statistically significant variables are highlighted.