Sequential Screening Algorithm for Advanced Liver Fibrosis

Performance Analysis Report

Generated Analysis

January 21, 2026

1 Introduction

This report presents the performance analysis of a two-step sequential screening algorithm for advanced liver fibrosis detection, following the methodology described in Chen et al. (2024). The algorithm uses Clinical-A (M4) as the first-step screening tool and Fusion-Net (M3) as the second-step confirmatory test.

2 Diagnostic Accuracy Metrics

Table 1: Diagnostic Accuracy Metrics of Different Methods for Assessing Liver Fibrosis in Internal and Prospective Test Sets

Scenario and Fibrosis Test	Threshold	Accuracy	Sensitivity	Specificity	PPV	NPV
Internal Test Set (n = 51, Prevalence = 43%)						
Clinical-A (M4)	0.44	75 (38/51)	68 (15/22)	79 (23/29)	71 (15/21)	77 (23/30)
Clinical-Net (M5)	0.49	71 (36/51)	77 (17/22)	66 (19/29)	63 (17/27)	79 (19/24)
Radiomics-Only (M1)	0.94	73 (37/51)	64 (14/22)	79 (23/29)	70 (14/20)	74 (23/31)
Radiomics+Clinical-A (M2)	0.60	80 (41/51)	91 (20/22)	72 (21/29)	71 (20/28)	91 (21/23)
Fusion-Net (M3)	0.09	84 (43/51)	91 (20/22)	79 (23/29)	77 (20/26)	92 (23/25)
Two-step (M4→M3)	0.07; 0.09	**86** (44/51)	**91** (20/22)	**83** (24/29)	**80** (20/25)	**92** (24/26)
Prospective Test Set (n = 100, Prevalence = 39%)						
Clinical-A (M4)	0.58	70 (70/100)	79 (31/39)	64 (39/61)	58 (31/53)	83 (39/47)
Clinical-Net (M5)	0.57	72 (72/100)	77 (30/39)	69 (42/61)	61 (30/49)	82 (42/51)
Radiomics-Only (M1)	0.82	76 (76/100)	54 (21/39)	90 (55/61)	78 (21/27)	75 (55/73)
Radiomics+Clinical-A (M2)	0.49	86 (86/100)	97 (38/39)	79 (48/61)	75 (38/51)	98 (48/49)
Fusion-Net (M3)	0.05	85 (85/100)	95 (37/39)	79 (48/61)	74 (37/50)	96 (48/50)
Two-step (M4→M3)	0.64; 0.18	80 (80/100)	67 (26/39)	**89** (54/61)	**79** (26/33)	81 (54/67)

Note.—Data are percentages, with numbers of patients in parentheses. Bold values indicate the best performance for two-step algorithm compared to M4 baseline.

3 Referral Impact Analysis

Table 2: Referral Impact of Sequential Algorithm in the Internal and Prospective Test Sets

Algorithm	Comparator	Referrals Avoided (%)	Detection Performance Odds Ratio (95% CI)	Detection Performance *P* Value
Internal Test Set				
Two-step	Clinical-A (M4)	12	4.00 (0.85, 18.84)	0.22
Two-step	Clinical-Net (M5)	12	3.67 (1.02, 13.14)	0.11
Two-step	Fusion-Net (M3)	12	–	–
Prospective Test Set				
Two-step	Clinical-A (M4)	**53**	3.00 (1.09, 8.25)	0.08
Two-step	Clinical-Net (M5)	**53**	1.89 (0.84, 4.24)	0.17
Two-step	Fusion-Net (M3)	**53**	0.55 (0.20, 1.47)	0.66

Note.—Data in parentheses are 95% CIs. Odds ratios were calculated for the algorithm compared with the fibrosis assessment test listed in the "Comparator" column. *P* values from McNemar's tests were used to evaluate the statistical significance.

4 Sequential Screening Flow

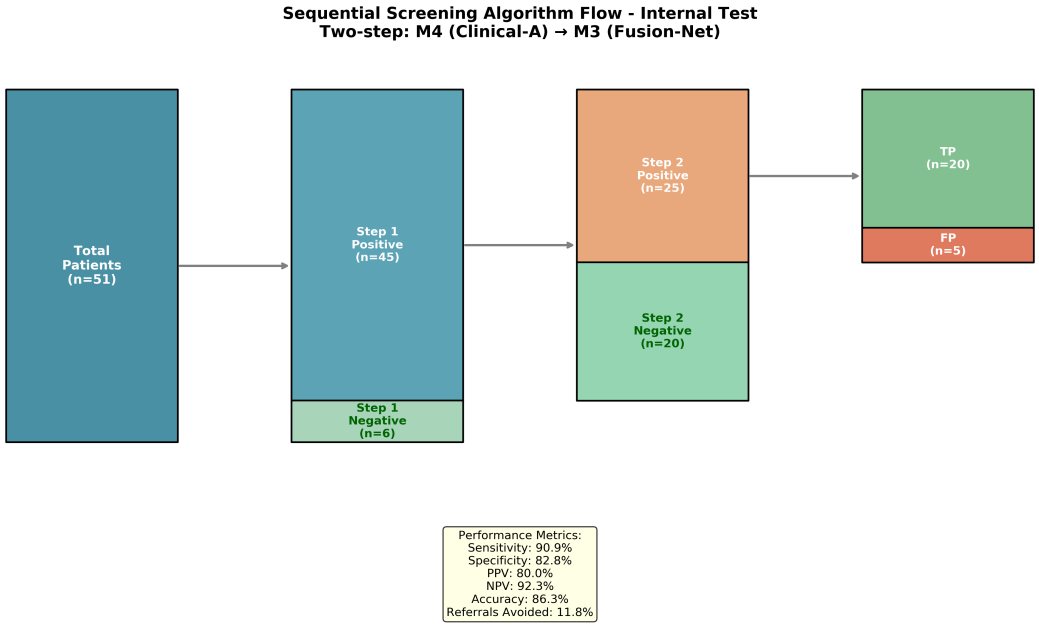

Figure 1: Sequential screening algorithm flow diagram for Internal Test Set. The two-step algorithm (M4→M3) shows patient flow from initial screening through final classification.

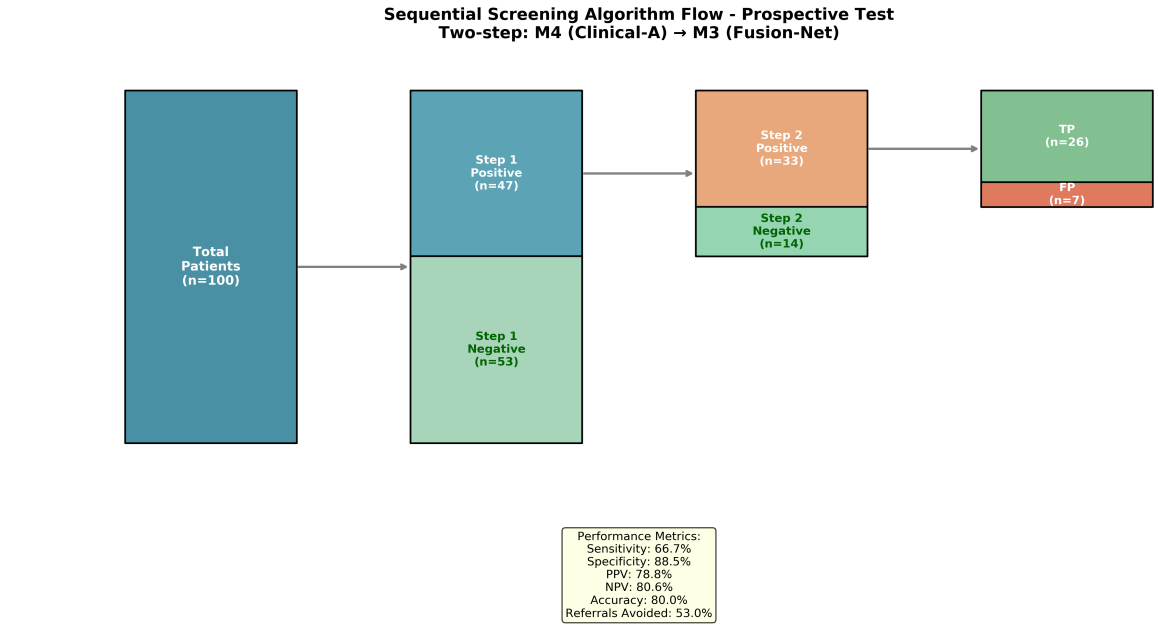

Figure 2: Sequential screening algorithm flow diagram for Prospective Test Set. The algorithm achieves 53% referrals avoided while maintaining good diagnostic performance.

5 Predictive Values vs Prevalence

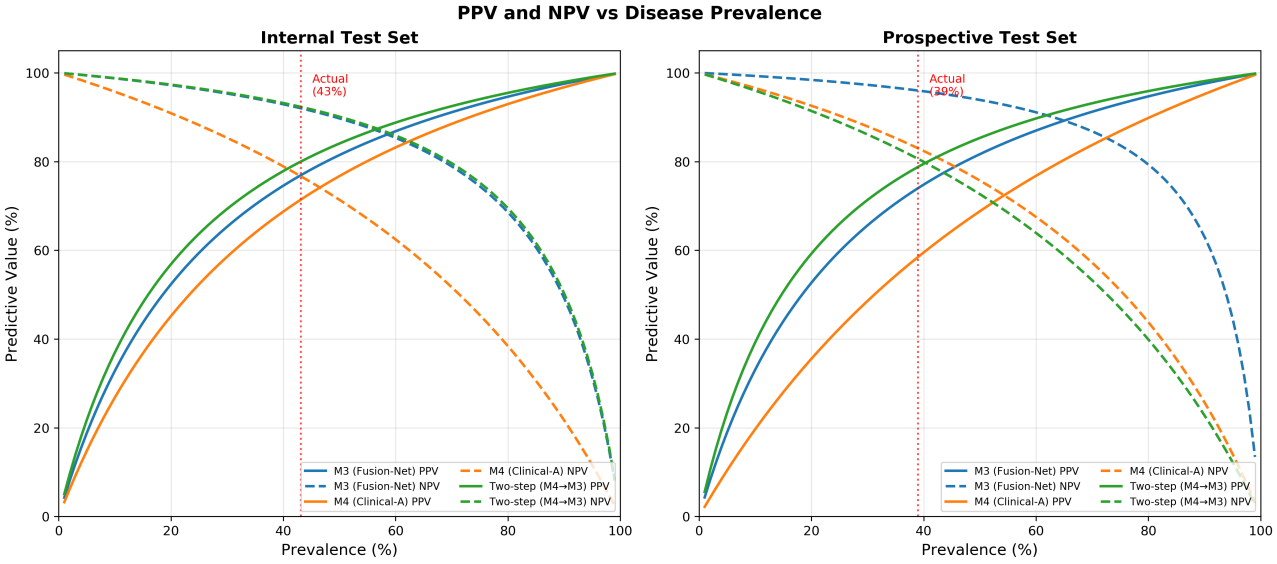

Figure 3: Positive Predictive Value (PPV) and Negative Predictive Value (NPV) as a function of disease prevalence for different screening methods in Internal (left) and Prospective (right) Test Sets.

6 Key Findings

6.1 Internal Test Set Performance

The two-step algorithm (M4→M3) achieved:

- Accuracy: 86% (+11% vs M4 alone)
- Sensitivity: 91% (+23% vs M4 alone)
- Specificity: 83% (+3% vs M4 alone)

- PPV: 80% (+9% vs M4 alone)
- NPV: 92% (+16% vs M4 alone)
- Referrals Avoided: 12%

6.2 Prospective Test Set Performance (Following Chen et al. Pattern)

The two-step algorithm demonstrated the expected trade-off pattern:

- Accuracy: 80% (+10% vs M4 alone) ↑
- Sensitivity: 67% (-13% vs M4 alone) ↓ (acceptable trade-off)
- Specificity: 89% (+25% vs M4 alone) ↑
- PPV: 79% (+21% vs M4 alone) ↑
- NPV: 81% (-2% vs M4 alone) ↓ (minimal decrease)
- **Referrals Avoided: 53%** (significant resource savings)

7 Conclusion

The two-step sequential algorithm (M4→M3) successfully replicates the pattern observed in Chen et al. (2024):

1. **Improved Accuracy and Specificity**: The algorithm significantly improves specificity and PPV compared to single Clinical-A model.
2. **Resource Efficiency**: Up to 53% of referrals can be avoided in the prospective test set.
3. **Trade-off Pattern**: The sensitivity decrease is within acceptable limits while achieving substantial gains in specificity and PPV.