Optimizing MASLD Diagnostic Protocols: A Microsimulation Analysis of Test Sensitivity Requirements

Please scan the above QR code or click the following link to download this poster https://ter.li/k19354

Osvaldo Ulises Garay MSc[1]*, Maria Karagianni PhD [1], Roland Fritz PhD[1], Brigitta Monz MD[2]

1 Roche Diagnostics International, Rotkreuz, Switzerland, 2 Roche Diagnostics GmbH, Mannheim, Germany

Poster no. MT33

Introduction

Evaluating the diagnostic performance of an intervention that occurs over time requires a shift from analyzing a single test to assessing the performance of the entire diagnostic protocol with repeated testing. This is especially pertinent for patients with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), for whom diagnostic strategies involve re-testing over years. Given MASLD's high incidence and slow progression, prioritizing test sensitivity could cause significant financial strain due to costs associated with false positives.

Objective

Our aim was to determine the minimal individual diagnostic protocol sensitivity needed to diagnose 90% of MASLD patients with significant or advanced fibrosis (F2-F3) before progression to cirrhosis (F4) or F2-F3-related mortality, across various scenarios.

Methods

We developed a microsimulation model tracking 10,000 MASLD individuals through fibrosis stages (F0-F4). Detection was defined as F2-F3 prior to reaching F4 or death at F2-F3. Model parameters, including age, stage distribution, progression/regression rates, and mortality, were derived from published literature. Our base case assumed full adherence and annual testing, while scenario analyses explored the impact of reducing adherence and testing frequencies. We assumed a fixed test specificity of 90%. Test correlation 'with disease' over time was incorporated to adjust the sequential sensitivity following the methods in Fanshawe 2024[1], starting from the moment an individual develops F2/F3.

Figure 1: model structure

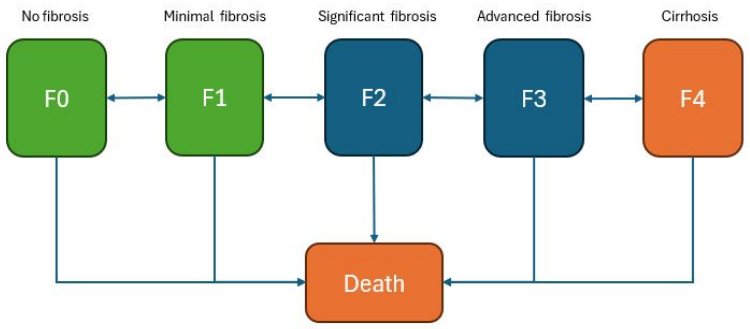


Table 1: Model parameters, source, base case and scenario analyses explored

Parameter	Value	Source
Mortality Hazard Ratios (HR)		
HR F0/2	1	[2] Sanyal 2021
HR F3vs F0/2	1.9	[2] Sanyal 2021
HR F4 vs F0/2	3.9	[2] Sanyal 2021
Fibrosis stage distribution		
F0	86.4%	[3] Estes 2018
F1	6.4%	[3] Estes 2018
F2	3.6%	[3] Estes 2018
F3	2.1%	[3] Estes 2018
F4	1.4%	[3] Estes 2018
Progression probabilities		
F0->F1	6.5%	[4] Le 2023
F1->F2	6.9%	[4] Le 2023
F2->F3	5.8%	[4] Le 2023
F3->F4	4.5%	[4] Le 2023
Regression probabilities		
F1->F0	2.5%	[4] Le 2023
F2->F1	4.6%	[4] Le 2023
F3->F2	6.0%	[4] Le 2023
F4->F3	0.0%	- Model assumption
Others		
Adherence to testing	52.0%	[5] Zhao 2018
Test frequency	Every year	- Model assumption
Death probability	(*)	[6] Eurostat Life Tables

Notes: *Age dependent, RR: Relative risk

Reference case & scenarios explored
Reference case:
Annual testing
No correlation between sequential tests
Adherence to recommendations of 100%
Starting age 50 years old
Scenarios:
Frequency every 2 years
Frequency every 3 years
Adherence 50%
Assumed correlation ρ+=0.25
Assumed correlation ρ+=0.5
Assumed correlation ρ+=0.75
Increase mortality, RR=1.5
Increase mortality, RR=2
Starting age 40
Starting age 60

Results

The simulated cohort had an average life expectancy of 81.4 years. Of these individuals, 5,601 developed F2-F3 fibrosis at some point in their lives, and 719 progressed to cirrhosis (F4).

Key findings:

- Our base-case screening model achieved a threshold of 90% case detection rate with a test sensitivity of 32% (Figure 2).
- The detection rate was highly dependent on screening adherence and frequency (Figure 3).
- The assumption of test correlation was the most significant factor influencing detection estimates (Figure 3).
- Results were robust against changes in starting age and mortality rates, which had minimal impact (Figure 3).

Figure 2: % of F2/F3 detected before F4 or Death for different assumed sensitivities of the diagnostic intervention

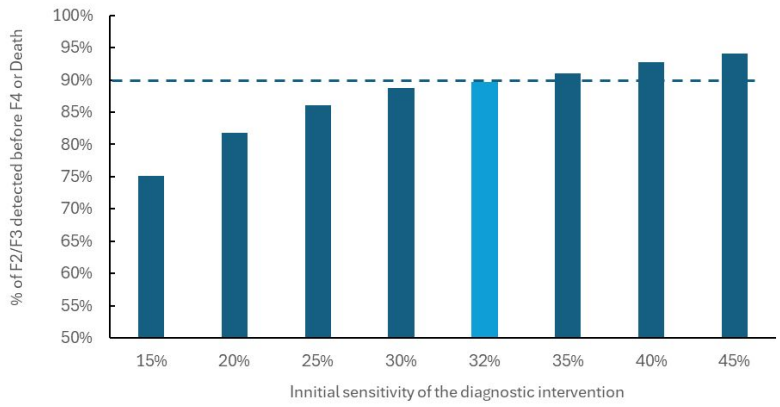
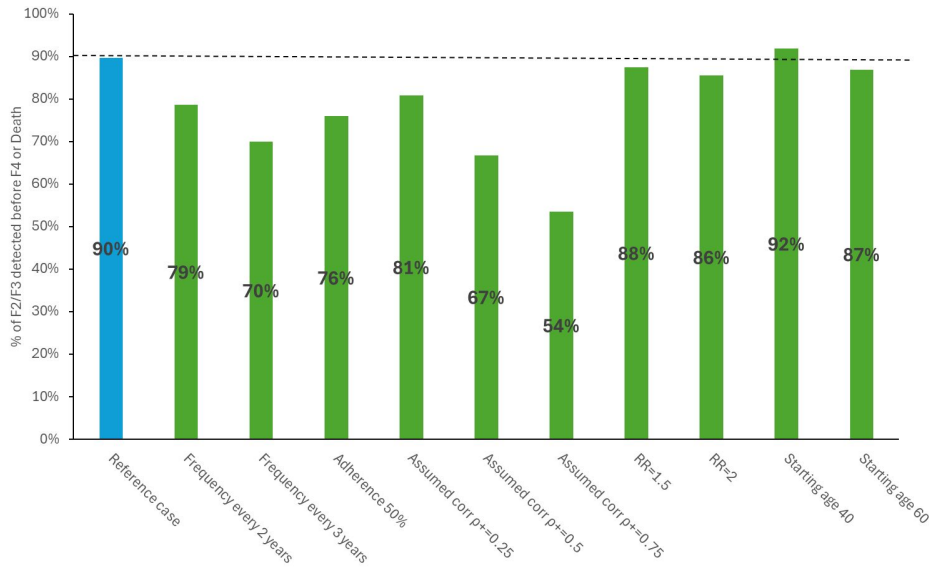


Figure 3: % of F2/F3 detected before F4 or Death. Base case and scenario analyses



Discussion & Conclusions

- Balancing diagnostic sensitivity and specificity within longitudinal monitoring protocols is complex.
- This model indicates that diagnostic protocols using tests with relatively low sensitivity can effectively identify a high proportion of MASLD patients.
- Assumptions on test results correlation impact results considerably. It would be important for future research to characterize this correlation to allow health economic evaluations to more accurately estimate the implications of the diagnostic performance.

Acknowledgements and Disclosures

All authors were involved in the study design, data interpretation, and preparation of this poster. This study was funded by Roche Diagnostics International Ltd. Rotkreuz, Switzerland.

References

1) Fanshawe, (2024) https://doi.org/10.1186/s41512-024-00175-3, 2) Sanyal, (2021) https://doi.org/10.1056/NEJMoa2029349, 3) Estes, (2018) https://doi.org/10.1016/j.jhep.2018.05.036, 4) Le, (2023) https://doi.org/10.1016/j.cgh.2022.07.033, 5) Zhao, (2018) https://doi.org/10.1111/liv.13561, 6) Eurostat, (n.d.) https://ec.europa.eu/eurostat/en/