Budget Impact Analysis Of Various Diagnostic Tests For Metabolic Dysfunction-Associated Steatohepatitis (MASH) In Japan

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Aim

To evaluate the budgetary implications of diagnosing MASH using non-invasive tests (NITs) alone compared to a diagnostic strategy combining NITs with liver biopsy

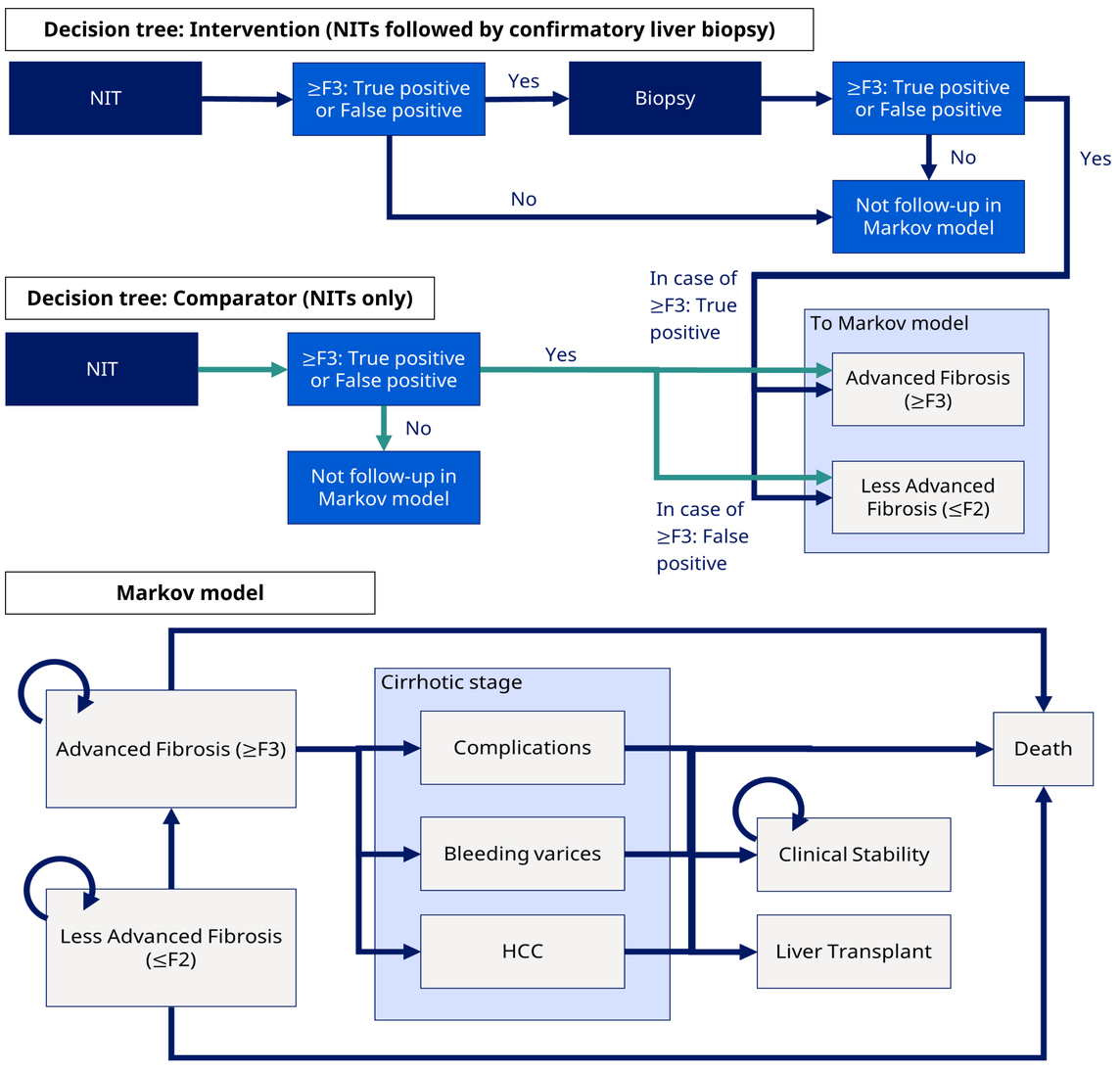
Introduction

- In Japan, liver biopsy is regarded as the standard for diagnosing and staging MASH but has limitations like high cost and invasiveness. Due to these, NITs such as transient elastography, Fibrosis-4 (FIB-4) index, and serum are gaining preference [1] as more efficient and safer alternative with sufficient accuracy.
- In Japan, Type IV Collagen 7S (T4C7S), a serum biomarker, is broadly adopted and reimbursed by the national health insurance.
- Budget impact analyses (BIA) are typically conducted over short time horizons (1–5 years) [2]. However, this limited timeframe may be suboptimal for diagnostic strategies, overlooking potential long-term cost changes [3].

Methods

- An Excel-based BIA model was developed to describe the diagnosis costs of MASH using a decision tree and subsequent management costs of patients using a lifetime Markov model (Figure 1). A previously published model was used as the basis of conceptualizing the model for the current study [4].
- The model was used to compare the budget impact of diagnosis of MASH in patients with metabolic dysfunction-associated steatotic liver disease (MASLD) using NITs alone compared to NITs in combination with confirmatory liver biopsy from a Japanese payer perspective. Their tests are conducted in first year.

Figure 1: Patient diagnostic and management flow (decision tree) and Markov model used for the budget impact analysis



F2, fibrosis stage F2; F3, fibrosis stage F3; HCC, Hepatocellular Carcinoma;; NIT, non-invasive tests

- The target population for the present analysis was estimated based on Japan's total population in 2023, as reported by the Statistics Bureau of Japan [5]. The analysis was restricted to individuals aged 18 to 65 years [6]. The incidence of MASLD within this population was assumed to be 3.4% [7]. Among these, 22.5% of patients were estimated to progress from MASLD to MASH [1]. Finally, it was assumed that all prevalent MASH cases—approximately 540,000 individuals—would be incorporated into the model.
- The base case analyzed the budget impact using a 2-step approach of diagnosis using the NIT combination first to ascertain the positive from the negative cases and then only the positives undergoing liver biopsy. This was compared to the NIT combination alone arm of the model.
- A scenario explored the use of test combinations assuming that these were done simultaneously. The analysis compared an NIT combination alone with the same combination along with liver biopsy to assess the budget impact (Scenario of "Alternative liver biopsy setup").
- Sensitivity and specificity values were used to evaluate the ability of each diagnostic test to stratify patients into low- and high-risk categories for advanced fibrosis (Table 1).The diagnostic performance parameters for the tests were sourced from Shima et al. 2020 [8]. To stay conservative, liver biopsy was assumed to have 100% sensitivity and specificity.
- Annual transition probabilities between Markov health states were derived from Rustgi et al. 2022 [9].
- Cost parameters were estimated from national insurance price listing and Sakata et al. 2011 [10, 11].
- In this BIA, three cost estimation approaches were employed to address the limitations of short time horizons, while also accounting for the lifetime costs incurred by patients following diagnosis. Approach 1 involved calculating lifetime costs using a Markov model, which were then annualized to assess potential long-term cost savings. Recognizing that BIA typically utilizes shorter time horizons, Approach 2 and Approach 3 were conducted to estimate costs over 1-year and 3-year periods, respectively, using the same modeling framework.
  - Approach 1: Lifetime costs calculated as diagnosis cost (Decision Tree) + management cost (Markov model), then annualized for analysis.
  - Approach 2: 1-year costs estimated using Decision Tree + Markov model.
  - Approach 3: 3-year costs estimated using Decision Tree + Markov model.
- Management costs incorporated into the Markov model were assigned only to patients identified as true positives or false positives. Patients classified as "negative" were excluded from cost calculations, as they did not receive any MASH specific medical care.

Results

Approach 1

Base case: The base case results over a 1-year time horizon using an annualized average of the lifetime costs approach using a 2-step diagnosis approach showed that the net budget impact was JPY 8.19 billion (USD 55.35 million) favoring NITs as the cost saving diagnostic approach (Figure 2, Base case).
Alternative liver biopsy setup: when liver biopsy is conducted for all cases simultaneously with NITs, the magnitude of cost saving in favour of comparator (NITs only) increased from USD55.36 million to USD 277.12 million. (Figure 2, Alternative scenario).

One-way sensitivity analysis results of base case and scenario case
One-way sensitivity analysis of base case and scenario case showed that the unit cost of liver biopsy and the sensitivity of the NITs were the parameters most affecting the results (Figure 3).

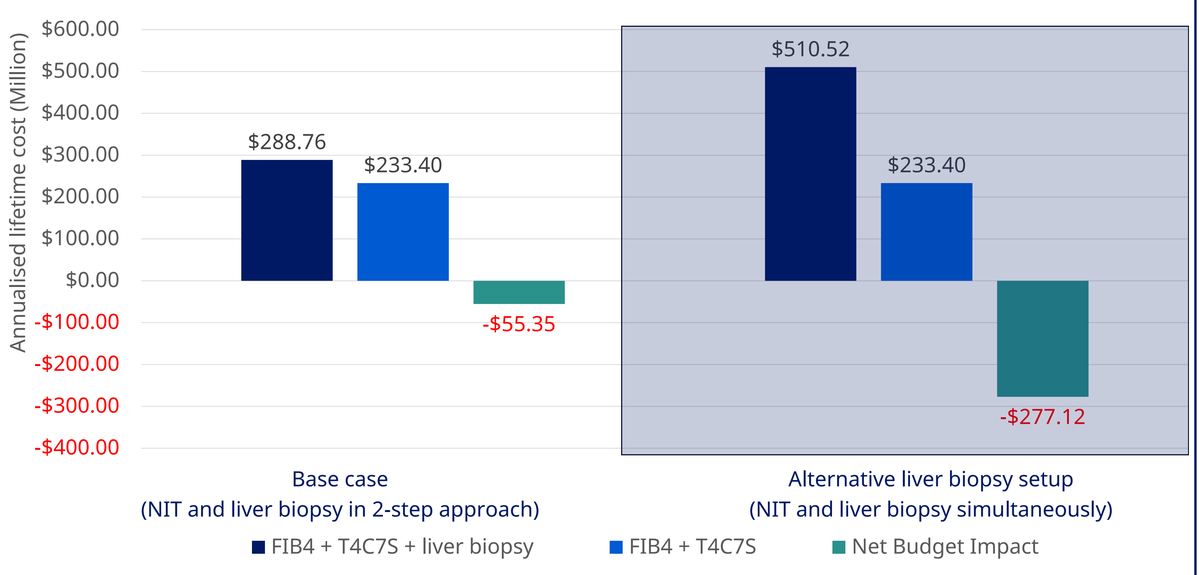
Table 1: Assumptions for Test performance and diagnostic accuracy of various diagnostic tests

Test Characteristics	Sensitivity	Specificity
Intervention		
FIB4 + T4C7S + liver biopsy	100%	100%
Comparator		
FIB4 + T4C7S	84.2% (95% CI: 67.36% to 100%)	84.6% (95% CI: 67.68% to 100%)

Test Characteristics	True Positives	False Positives	True Negatives	False Negatives
Base case				
Intervention				
1st step: FIB4 + T4C7S (NITs)	32.52%	6.10%	51.93%	9.45%
2nd step: Biopsy (after above NITs)	32.52%	0.00%	58.03%	9.45%
Comparator				
FIB4 + T4C7S (NITs)	32.52%	6.10%	51.93%	9.45%
Scenario				
Intervention				
FIB4 + T4C7S + biopsy	38.62%	0.00%	61.38%	0.00%
Comparator				
FIB4 + T4C7S (NITs)	32.52%	6.10%	51.93%	9.45%

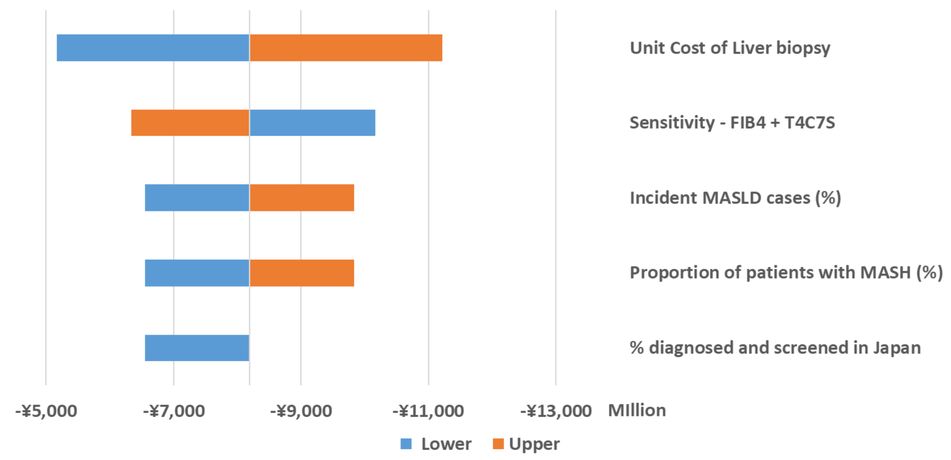
FIB-4, Fibrosis-4; NIT, non-invasive tests; T4C7S, Type IV Collagen 7S.

Figure 2: Total budget impacts per year of base case and scenario analysis (Approach 1)



FIB-4, Fibrosis-4; NIT, non-invasive tests; T4C7S, Type IV Collagen 7S. The currency conversion rate applied in the model was set at 1 USD = 148 JPY, reflecting the prevailing exchange rate at the time of analysis.

Figure 3: Tornado diagram for the base case analysis (Approach 1)
FIB4 + T4C7S + liver biopsy vs FIB4 + T4C7S



FIB-4, Fibrosis-4; NIT, non-invasive tests; MASLD, Metabolic dysfunction-associated steatotic liver disease; T4C7S, Type IV Collagen 7S. One-way sensitivity analysis using ±20% of the parameter value were also done.

Approach 2 and 3

Base case: For approach 2 (1-year time horizon using 1-year lifetime costs), the net budget impact was JPY 14.51 billion (USD 98.03 million) favoring NITs as the cost saving diagnostic approach. For approach 3 (3-year time horizon using 3-year lifetime costs), the net budget impact was JPY 1.79 billion (USD 12.13 million).
Alternative liver biopsy setup: For approach 2, changing the diagnosis setup to a simultaneous manner, the net budget impact increased in cost savings favoring NITs JPY 39.16 billion (USD 264.59 million). For 3-year time horizon, the net budget impact was JPY 51.06 billion (USD 344.98 million).

Discussion

- The analysis does not consider the individual diagnostic accuracy of the NIT tests in each combination in a sequential testing pattern. The sequence is limited to a 2-step approach assuming that only the test positives from the NITs undergo liver biopsy. This may have led to a slight overestimation of costs as in the real world setting not all patients might be undergoing all the tests in a combination. This is especially true for patients regarded as low-risk who might not be undergoing the full array of tests.
- Markov model did not assume any MASH specific treatments. Recent arrival of new treatments that modify MASH disease progression would warrant further studies.

Conclusion

NITs without liver biopsy can be considered to be an economically efficient MASH diagnosis strategy because of the lower overall costs associated with their use.

Conflict of interest

Y.S. received lecture fees from Kowa Company, Ltd., Novo Nordisk Pharma Ltd., Taisho Pharmaceutical Co., Ltd., and MSD Co., Ltd.

S.M. is an employee of Novo Nordisk Pharma Ltd. A.C. and H.M. are are employees of IQVIA Solutions Japan G.K.; IQVIA Solutions Japan G.K. received consulting fees from Novo Nordisk Pharma Ltd. for this project.

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References: (**1**) Kobayshi et al. Sci Rep 2022: 12(1); 18174; (**2**) Sullivan et al. Value Health 2014: 17(1); 5-14; (**3**) Henderson et al. 2025: available from https://www.ohe.org/publications/challenges-and-solutions-for-budget-impact-analysis-of-gene-therapies/; (**4**) Surivastava et al. BMC Gastronenterol 2019: 19(1); 122; (**5**) Statistics Bureau of Japan 2023: available from https://www.stat.go.jp/english/data/jinsui/2023np/index.html#a15k01-a; (**6**) Japan Census Data 2020: available from https://www.e-stat.go.jp/en/stat-search/file-download?statInfId=000032142404&fileKind=0; (**7**) Younossi et al. Hepatology 2016: 64 (1); 73-84; (**8**) Shima et al. Journal of gastroenterology 2020: 55; 100-112; (**9**) Rustgi et al. Journal of medical economics 2022: 25(1); 347-355; (**10**) Shirobon.net. 2024: available from: https://shirobon.net/.; (**11**) Sakata et al. J Hepatobiliary Pancreat Sci 2011: 18(2); 184-9.