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9th edition

Modeling the economic impact of MASH in the context of metabolic health

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Conflict of interest disclosure

- Member of advisory boards for Gilead, AbbVie, Abbott, Merck, Janssen, Roche, and VBI Vaccines.
- CDA/ CDAF has received research funding from Gilead, Assembly Biosciences, AbbVie, Boehringer Ingelheim, Intercept, Merck, Novartis, Pfizer, and Roche.
- This work was supported by an investigator-initiated research grant by Merck.





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Background:

- CDA MASH analyses were last published in 2017-2020.
- A number of clinical studies and publications came out after 2020.
- The US model was updated with the latest studies/data/ publications.
- The impact of GLP-1 & SGLT-2 treatments (in diabetic patients) was analyzed.
- The economic impact of potential therapies was assessed.

Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. *Hepatology* 2018; **67**(1): 123-33.

Estes C, Anstee QM, Arias-Loste MT, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016–2030. *Journal of Hepatology* 2018.

Alswat K, Aljumah AA, Sanai FM, et al. Nonalcoholic fatty liver disease burden - Saudi Arabia and United Arab Emirates, 2017-2030. *Saudi J Gastroenterol* 2018; **24**(4): 211-9.

Goossens N, Bellentani S, Cerny A, et al. Nonalcoholic fatty liver disease burden - Switzerland 2018-2030. *Swiss Med Wkly* 2019; **149**: w20152.

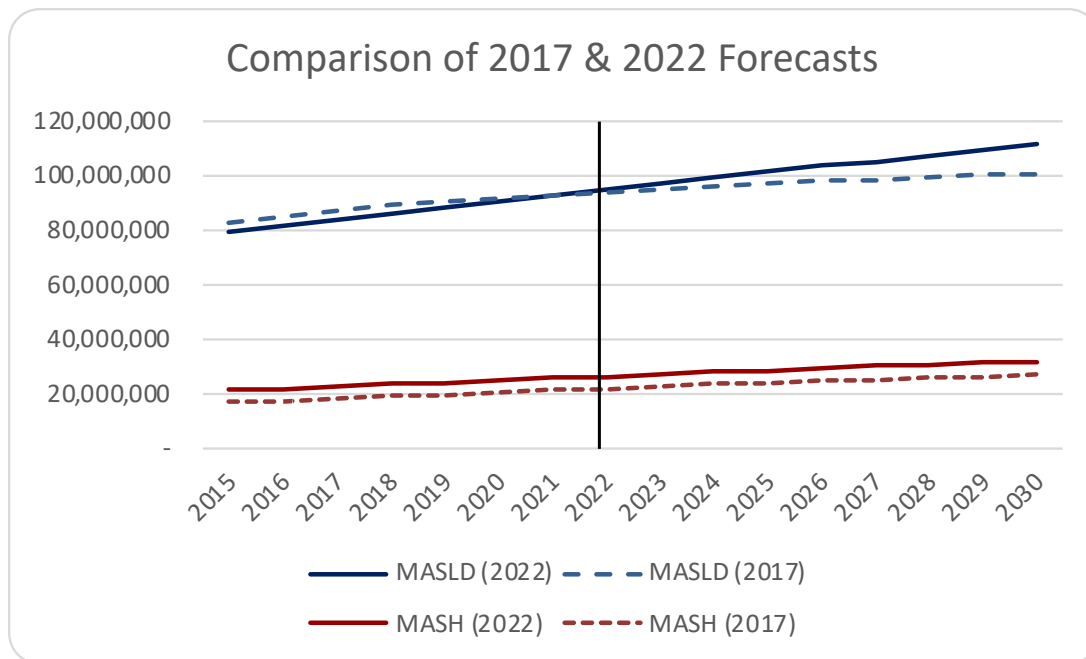
Estes C, Chan HLY, Chien RN, et al. Modelling NAFLD disease burden in four Asian regions-2019-2030. *Alimentary pharmacology & therapeutics* 2020; **51**(8): 801-11.

Swain MG, Ramji A, Patel K, et al. Burden of nonalcoholic fatty liver disease in Canada, 2019-2030: a modelling study. *CMAJ open* 2020; **8**(2): E429-E36.

Adams LA, Roberts SK, Strasser SI, et al. Nonalcoholic fatty liver disease burden: Australia, 2019-2030. *J Gastroenterol Hepatol* 2020; **35**(9): 1628-35.



The updated data did result in small changes in our MASLD and MASH forecasts



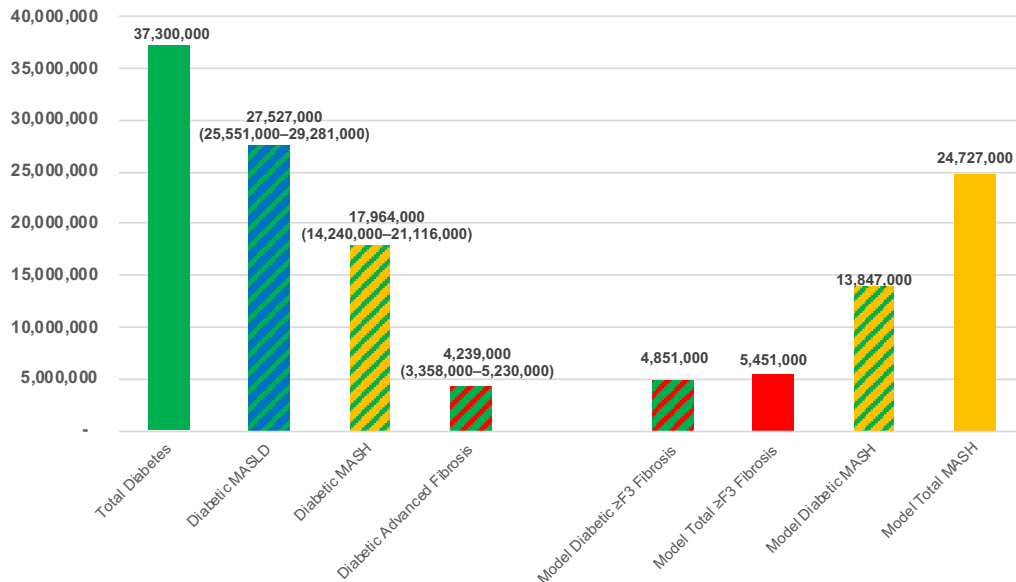
- Obesity continues to increase in the US – MASLD prevalence will group at a higher rate.
- The MASH forecasts are slightly higher than previous but similar growth rate.
- **Key Point – MASH prevalence has been increasing year after year.**
- In 2022, an estimated 26 million people had MASH in the US.
- In 2022, 2.5 million had cirrhosis.



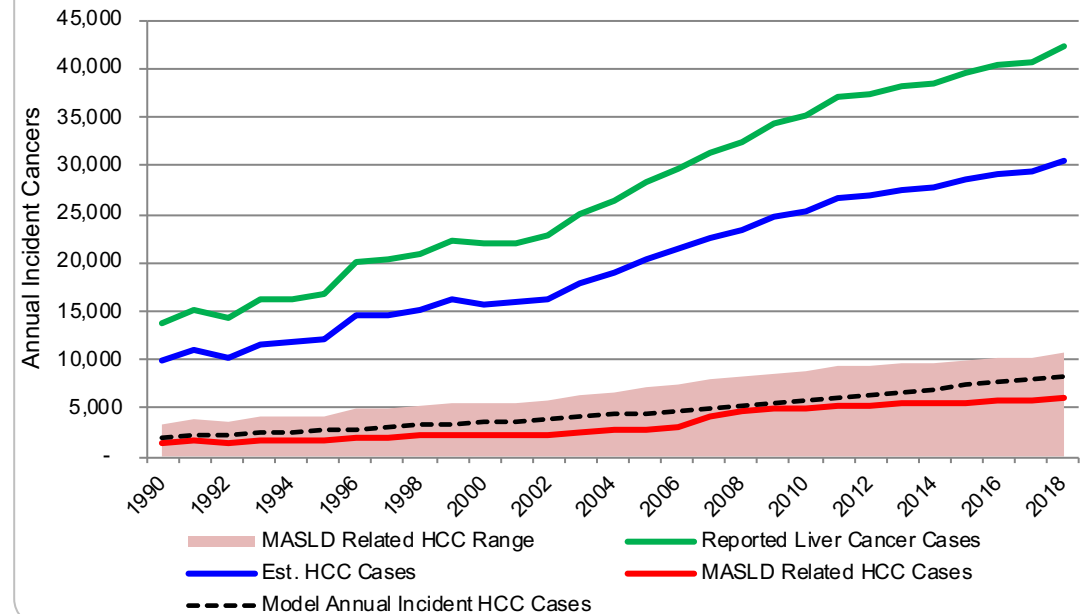
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However, we continue to have a good fit with empirical data

Diabetes among MASH and Advanced Fibrosis Populations, Reported Data and Model Outputs – 2020



Reported Cancer Data and Model Output



In the US, the model correctly forecasts the estimated number of diabetics with \geq F3 fibrosis & estimated number of HCC cases attributed to MASH

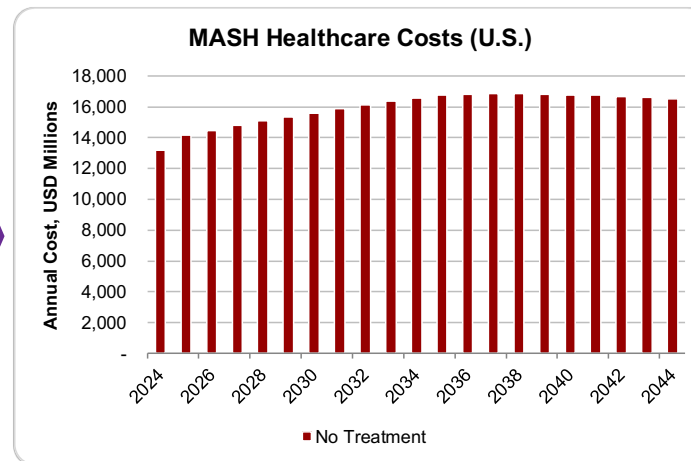
Sanyal AJ, et al. *The New England journal of medicine* 2021; 385(17): 1559-69, Younossi ZM, et al. *Lancet* 2019; 394(10215): 2184-96, CDC National Diabetes Statistics Report, Ciardullo S, et al. *Diabetes Care*. 2021;44(2):519-25, Younossi ZM, et al. *Clinical Liver Disease*. 2018;11(4):92-94, McPherson S, et al. *J Hepatol*. 2015;62(5):1148-55. SEER Cancer Statistics Review, 2022, Torner A, et al. *Hepatology*. 2017;65(3):885-92, Altekruse SF, et al. *Am J Gastroenterol*. 2014;109(4):542-53, Rahman RN, et al. *Hepatology*. 2012;56:241A, Younossi ZM, et al. *Hepatology*. 2015;62(6):1723-30, Barzi A, et al. *Cancers*. 2021;13(14).



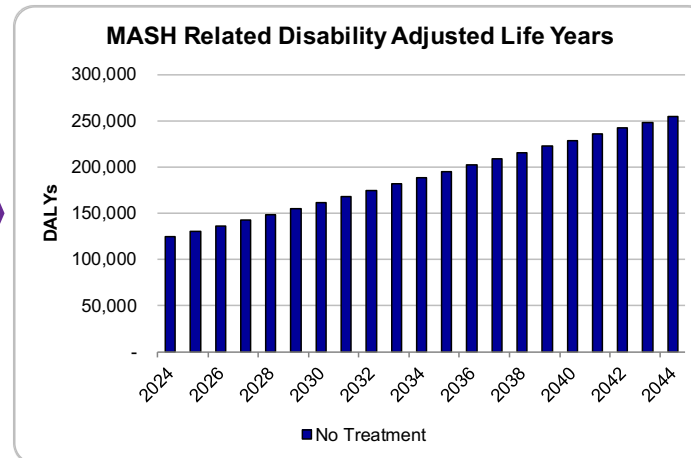
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With the current status quo, MASH will have a very large human and economic impact in the United States

MASH related healthcare costs will be more than \$16.8 billion per year (after 3% inflation rate)



MASH related disability adjusted life year will increase every year (>250,000 life years by 2044)



	Annual Cost (USD)	Source
F2	489	Younossi 2019
F3	602	Younossi 2019
Cirrhosis - F4	3,133	Chahal 2019
Decompensated Cirrhosis	37,098	Chahal 2019
HCC	59,175	Chahal 2019
Liver Transplant - First Year	234,921	Chahal 2019
Liver Transplant - Subs Years	51,164	Chahal 2019

Younossi ZM, et al. *Hepatology*. 2019;69(2):564-72.

Chahal HS, et al. *Open Forum Infect Dis*. 2019;6(1).



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Usage of GLP-1 and SGLT-2 can reduce steatohepatitis among MASH patients

	Population	% Treated with GLP-1		Country
Nargesi 2023	≥18-year-olds with T2DM with Medicare Part D or commercial insurance in 2018-2020	13.6%	11.5%	US
Farmer 2021	18–90-year-olds with T2DM in 2017-2019	4.3-4.9%	9.8-13.8 25.9%-45.5% as part of triple therapy by 2019	UK

- 42% of MASH patients have T2DM
- In the US, 6% ($13.6\% \times 42\%$) are on GLP1 or SGLT-2 therapies
- 70% of all patients stay on these therapies
- 50-60% will experience a reduction in steatohepatitis
- Assumed these therapies reduce F0-F1 progression by 38.5% ($70\% \times 55\%$)

Nargesi AA, Clark C, Aminorroaya A, Chen L, Liu M, Reddy A, et al. Persistence on Novel Cardioprotective Antihyperglycemic Therapies in the United States. *The American journal of cardiology*. 2023;196:89-98.

Farmer RE, Beard I, Raza SI, Gollop ND, Patel N, Tebbboth A, et al. Prescribing in Type 2 Diabetes Patients With and Without Cardiovascular Disease History: A Descriptive Analysis in the UK CPRD. *Clin Ther*. 2021;43(2):320-35



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Without demonstrating a reduction in fibrosis in \geq F2, the impact of GLP-1 & SGLT-2 treatments on MASH burden will be small

- 6% of all MASLD patients in the US were estimated to be on GLP-1 & SGLT-2 treatments (nearly all are diabetic patients who are reimbursed).
- It was assumed that treatment would increase to 18% by 2040 among all diagnosed MASH patients.

MASH burden will be driven by \geq F2 fibrosis progression.

Reversing steatohepatitis without stopping/reversing fibrosis progression in \geq F2 patients will have a minimal impact on disease burden prior to 2044.

	Total Cases Averted (2024-2044)
Decompensated Cirrhosis	4,125
HCC	985
Liver Related Deaths	2,180



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On the other hand, treatments that reduce (or reverse) fibrosis progression will have a much larger impact on MASLD disease burden under modest increase in diagnosis and treatment

	% Diagnosed (2025)	% Diagnosed (2040)	% Treated (2025)	% Treated (2040)	Lack of Progression
F2	5%	15%	5%	15%	70%
F3	10%	20%	15%	25%	70%
Cirr	15%	25%	25%	50%	70%



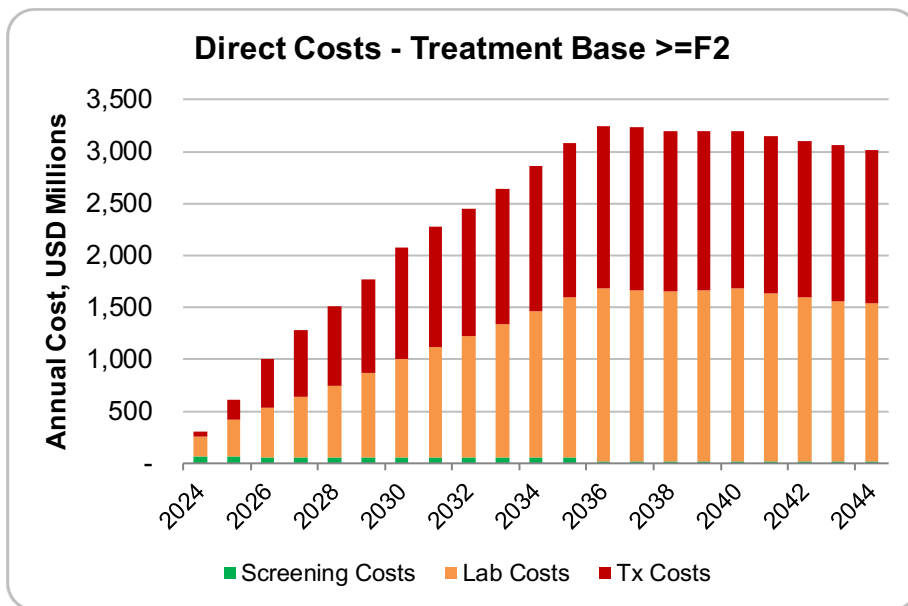
Total Cases Averted (2024-2044)	Treat ≥ F2	Treat ≥ F3	Treat Cirrhosis*
Decompensated Cirrhosis	286,700	281,100	253,300
HCC	30,300	29,400	26,500
Liver Related Deaths	186,500	183,500	163,400
DALY's Averted	373,500	367,300	327,500
Incremental Healthcare Costs Averted	\$23.9 Billon	\$23.4 Billon	\$20.5 Billon



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Due to the (likely) chronic nature of MASH treatment, the cost of annual diagnostic tests will be a key driver of total cost

- Screening for MASH could be as simple as a blood test and hepatic function panel (~\$15 per person using Medicare prices)
- However, liver staging needed for initiating treatment and annual follow up can cost \$500 annually (Medicare prices)



We need low-cost laboratory tests for the annual follow up.



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Conclusions:

- Our forecast of MASLD and MASH burden did not change significantly since our 2017 estimate.
- We estimate that an estimated 26 million people had MASH and 2.5 million had compensated or decompensated cirrhosis in the US in 2022.
- MASH related healthcare costs will be more than \$16.8 billion per year and MASH related disability adjusted life year will surpass 250,000 life years by 2044.
- Without demonstrating a reduction in fibrosis, the impact of GLP-1 & SGLT-2 treatments on MASH burden will be small.
- On the other hand, MASH treatment that can halt or reverse fibrosis progression can have a significant impact on disease burden, MASH related healthcare costs and DALYs.
- We need low-cost MASH diagnostics for the annual follow-up.



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