



PARIS MASH MEETING

10th edition

**Organized by
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**September 5 & 6 2024
Institut Pasteur, Paris**

Impact of GLP-1 use for obesity and T2DM on MASH trends

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Disclosures:

I have nothing to declare

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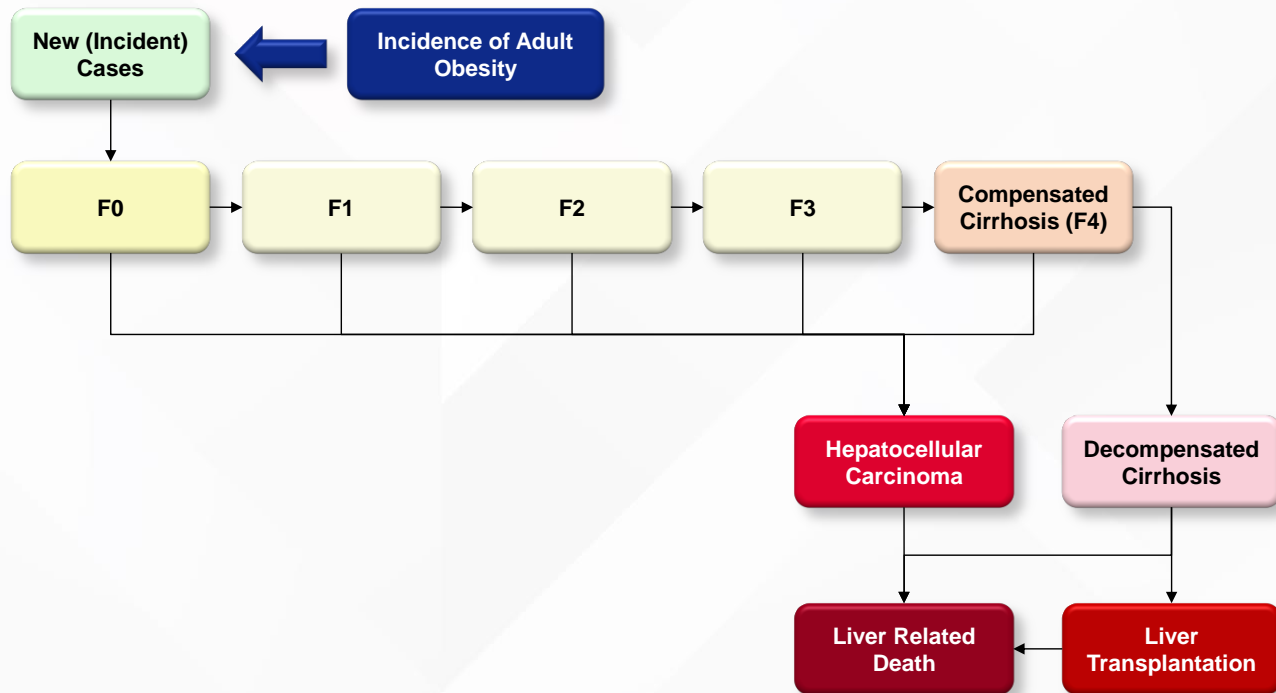
Background:

- There has been a lot of excitement around the use of GLP-1/SGLT2 therapies to treat diabetes and reduce weight.
- Since MASH is highly correlated with obesity, the question that keeps coming up is will expanded treatment with GLP-1/SGLT2 therapies reduce MASH disease burden
 - **If they result in weight reduction and reduction in steatosis.**
 - **If they result in halting or reversal of fibrosis.**

We utilized a Markov model to forecast the impact of various product profiles for GLP-1 therapies

GLP-1 Product Profile

1. Impact on weight loss and steatosis only.
2. Impact on weight loss and steatosis + halting or reversing fibrosis.

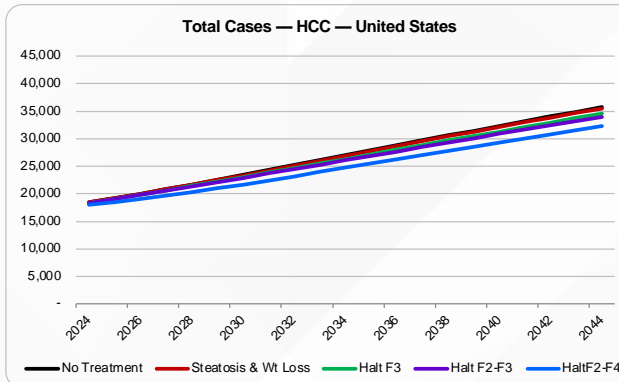
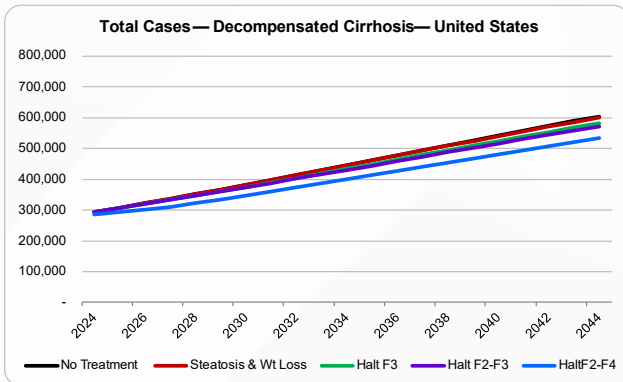
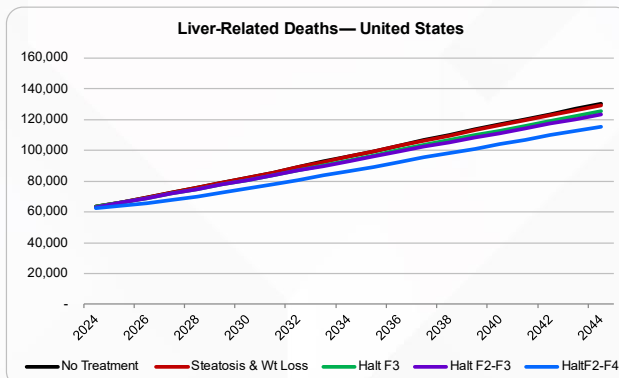
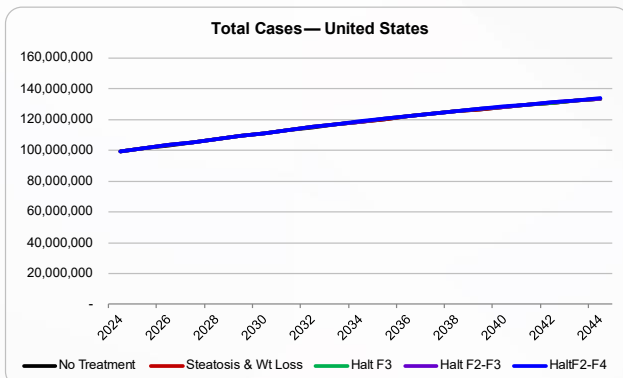


We examined the impact of halting fibrosis at various stages

Scenario	2024	2034	2044
No Treatment	0	0	0
GLP-1 / SGLT2 impact of steatosis and weight loss only	2,633,000 (2,208,500-2,811,500)	3,239,500 (2,754,200-3,413,500)	3,783,300 (3,207,400-4,001,500)
GLP-1/SGLT2 if halting F3 fibrosis	2,633,000 (2,208,500-2,811,500)	3,239,500 (2,754,200-3,413,500)	3,783,300 (3,207,400-4,001,500)
GLP-1/SGLT2 if halting F2-F3 fibrosis	2,633,000 (2,208,500-2,811,500)	3,239,500 (2,754,200-3,413,500)	3,783,300 (3,207,400-4,001,500)
GLP-1/SGLT2 if halting F2-F4 fibrosis	2,633,000 (2,208,500-2,811,500)	3,239,500 (2,754,200-3,413,500)	3,783,300 (3,207,400-4,001,500)

Assumed 70% of treated patients demonstrated halting of fibrosis.

With current diagnosis and treatment rates, the impact of GLP-1 therapies will be minimal over the next 20 years



If GLP-1 therapies were labeled for halting fibrosis tomorrow, the overall impact on MASH disease burden would remain small without a significant increase in the diagnosis and treatment of MASH.

Treatment with GLP-1 therapies also reduces cardiovascular-related mortality, which is not shown here

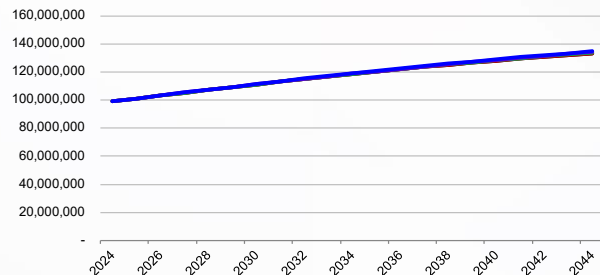
We analyzed the impact of varying levels of treatment scale-up by fibrosis stage

Scenario	2024	2034	2044
No Treatment	0	0	0
GLP-1 / SGLT2 impact of steatosis and weight loss only	2,633,000 (2,208,500-2,811,500)	3,239,500 (2,754,200-3,413,500)	3,783,300 (3,207,400-4,001,500)
GLP-1/SGLT2 if halting F3 fibrosis	2,633,000 (2,208,500-2,811,500)	1,308,200 (804,700-1,727,500)	2,448,000 (1,535,300-3,169,500)
GLP-1/SGLT2 if halting F2-F3 fibrosis	2,633,000 (2,208,500-2,811,500)	2,970,300 (1,827,000-3,922,300)	5,228,900 (3,313,400-6,840,200)
GLP-1/SGLT2 if halting F2-F4 fibrosis	2,633,000 (2,208,500-2,811,500)	3,950,000 (2,429,500-5,216,000)	6,812,300 (4,272,700-8,820,300)

We assumed that 70% of treated patients demonstrated halting of fibrosis.

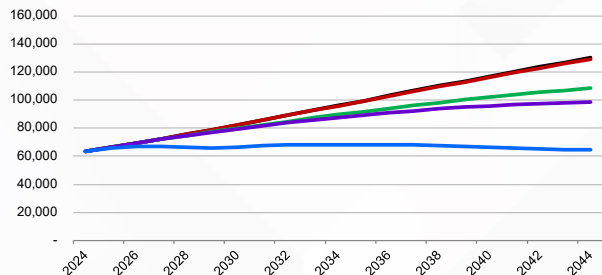
Increased diagnosis and treatment rates are essential to achieve a substantial reduction in disease burden

Total Cases—United States



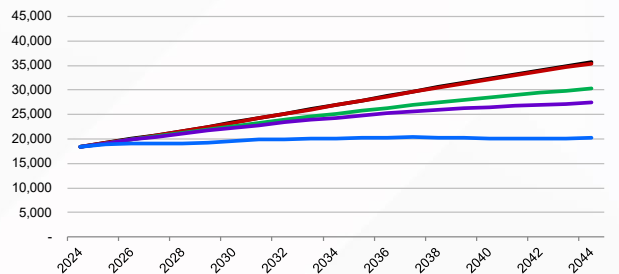
— No Treatment — Steatosis & Wt Loss — Halt F3 — Halt F2-F3 — Halt F2-F4

Liver-Related Deaths—United States



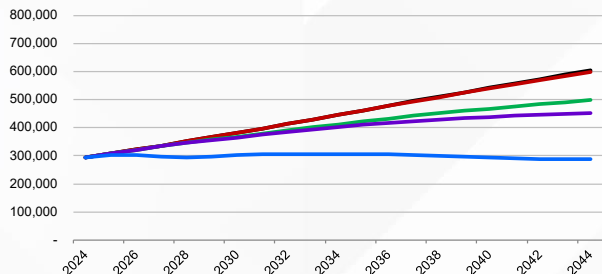
— No Treatment — Steatosis & Wt Loss — Halt F3 — Halt F2-F3 — Halt F2-F4

Total Cases—HCC—United States



— No Treatment — Steatosis & Wt Loss — Halt F3 — Halt F2-F3 — Halt F2-F4

Total Cases—Decompensated Cirrhosis—United States



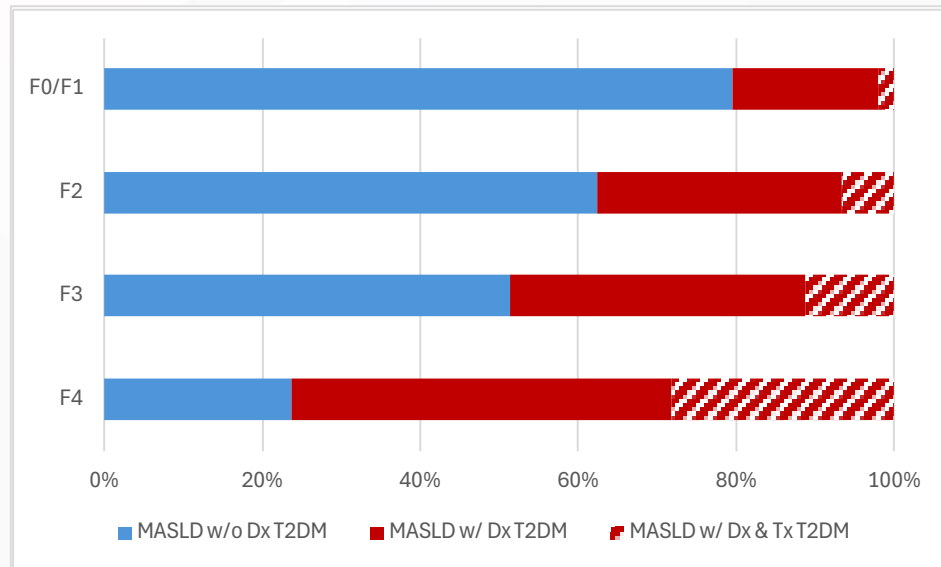
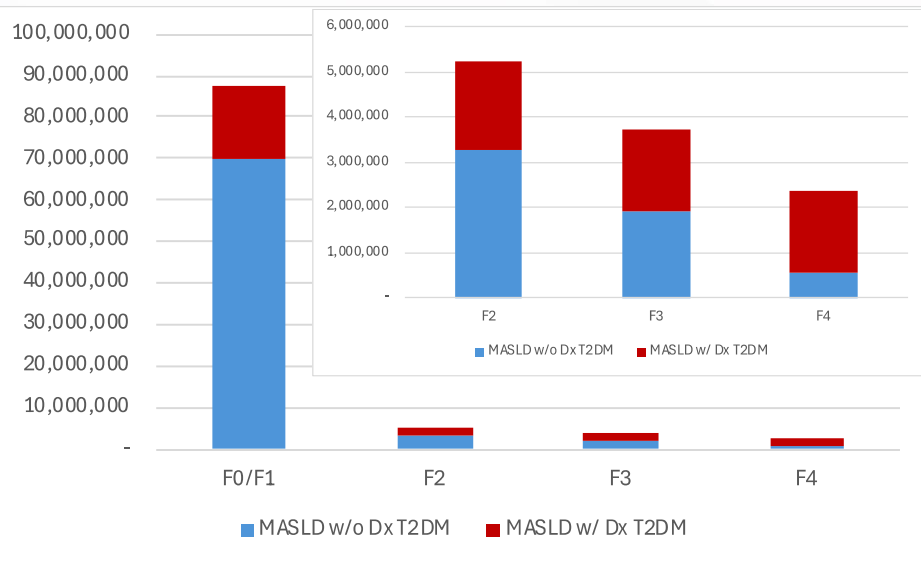
— No Treatment — Steatosis & Wt Loss — Halt F3 — Halt F2-F3 — Halt F2-F4

It is reasonable to assume that treatment will increase if GLP-1 therapies demonstrate halting of fibrosis. With enhanced screening and treatment, a significant reduction in disease burden is forecasted.

Increasing treatment and the ability to halt fibrosis will significantly impact both the disease and economic burden

Scenario	Cumulative Liver Related Deaths (Millions)	Cumulative HCC Cases	Cumulative DCC Cases (Millions)	Cumulative Liver Related Deaths Averted	Cumulative HCC Cases Averted	Cumulative DCC Cases Averted	Cumulative Direct Costs (USD Billions)	Cumulative Costs Averted (USD Billions)	Cumulative DALYs Averted
No Treatment	2.023	325,100	2.506	-	-	-	\$520.3	-	-
Steatosis & Weight Loss	2.017 (0.912-3.731)	323,400 (179,500-576,800)	2.496 (1.060-4.630)	6,000 (2,700-11,400)	1,800 (1,000-3,200)	10,000 (4,200-18,700)	\$512.8 (\$266.9-\$881.2)	\$7.6 (\$4.0-\$13.0)	12,900 (5,500-30,400)
Halt F3	1.855 (0.835-3.517)	291,100 (159,200-531,500)	2.225 (0.945-4.176)	167,800 (75,600-318,200)	34,000 (18,600-62,200)	281,000 (119,400-527,500)	\$479.9 (\$253.8-\$826.1)	\$40.5 (\$21.4-\$69.6)	339,100 (162,800-583,200)
Halt F2-F3	1.790 (0.806-3.394)	273,900 (149,800-500,000)	2.115 (0.898-3.970)	232,600 (104,800-440,900)	51,300 (28,100-93,700)	390,900 (166,100-733,800)	\$464.6 (\$245.7-\$799.7)	\$55.8 (\$29.5-\$96.0)	470,300 (225,800-809,000)
Halt F2-F4	1.401 (0.631-2.656)	215,000 (117,600-392,500)	1.523 (0.647-2.859)	621,700 (280,000-1,178,800)	110,200 (60,300-201,200)	982,700 (417,400-1,844,500)	\$421.2 (\$222.8-\$725.1)	\$99.1 (\$52.4-\$170.6)	1,247,300 (598,900-2,145,400)

Individuals with diabetes constitute a significant portion of the MASH population with bridging fibrosis



Diabetic patients would be ideal candidates for an initial MASH screening strategy since they are already under care.

Conclusions

- If GLP-1 therapies are limited to existing treatment rates, even with a fibrosis halting/ reversal indication, their impact on the MASH (liver disease) burden will be minimal.
- Increasing diagnosis and treatment rates, particularly in the F2-F4 populations, can significantly impact the MASH liver disease and economic burden.
- Focusing on screening diabetic patients for MASH may prove to be an efficient initial strategy since this population is already under care.



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