The value proposition of NASH therapy on the burden of disease related to obesity

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Methodology

• Convened a panel of NAFLD experts in each country
• Collect published epidemiology data for NAFLD
• Gathered country specific rates for obesity and diabetes to estimate incidence
• Used published work to estimate progression rates for non-alcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH)
• Modeled the disease progression
• Validates the forecasts against reported NASH related HCC cases
Modeling Approach

- Built a disease progression (Markov) model
- Populations were handled as stocks whereas transition probabilities were handled as flows
- Started in 1950 to track steatosis onset for most individuals
- The population was allowed to age through 1 year age cohorts by gender
- Incidence rates of obesity and diabetes were used to estimate new NAFLD cases
The Markov model took into consideration the reversible nature of the disease.
NASH prevalence and obesity in the EU5 are lower than the US

<table>
<thead>
<tr>
<th></th>
<th>BMI≥30</th>
<th>% of total population ≥15+ with NAFLD</th>
<th>% of NAFLD with NASH</th>
<th>% of total population ≥15+ with NASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>28%</td>
<td>30%</td>
<td>20%</td>
<td>6.3%</td>
</tr>
<tr>
<td>France</td>
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<td>25%</td>
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<td>18%</td>
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<td>Italy</td>
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<tr>
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</tr>
<tr>
<td>UK</td>
<td>21%</td>
<td>25%</td>
<td>18%</td>
<td>4.8%</td>
</tr>
</tbody>
</table>
Parallel Epidemics of Diabetes and Obesity in the US


Obesity has been increasing in European countries as well.

Adult obesity has been increasing but the rate of increase has slowed.
NASH population is expected to grow by 60% while cirrhotic cases will increase by 160% in US.
NASH population is expected to grow by 45% while cirrhotic cases will increase by 120% in EU.
The increase in NAFLD cases is slowing down but NASH, HCC, and liver related deaths will increase.
Cost Inputs

• Annual direct costs per F4 / HCC patient were derived from the literature and inflated to 2016 USD based on Eurostat health inflation

• Costs for compensated cirrhosis were applied to 10% of prevalent cases (2015) increasing to 50% (2030) reflecting increased awareness and diagnosis

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Eurostat. 2017. Database - HICP (2015 = 100) - annual data (average index and rate of change) for Health Category (CP06).
Estimated Direct US Healthcare Cost - NASH

- Annual direct costs increase 260% from $4.9 B (2015) to $17.6 B (2030)
  - Decompensated cirrhosis comprises only ~1% of all prevalent NASH cases and ~10% of F4/HCC cases, but accounts for the majority of direct costs in this analysis
  - Assumed the number of liver transplants can not increase due to limited availability of donors
Estimated Direct US Healthcare Cost - NASH

- Decompensated cirrhosis comprises ~10% of F4/HCC cases but accounts for the majority of direct costs in all years.
Estimated Direct EU5 Healthcare Cost - NASH

- Annual direct costs increase 160% from $1.1 B (2015) to $3.9 B (2030)
  - Decompensated cirrhosis costs increases faster (160%) as compared to HCC (115%), while compensated cirrhosis costs increase ten-fold largely due to increased diagnosis
  - Assumed the number of liver transplants can not increase due to limited availability of donors
Estimated Direct EU5 Healthcare Cost - NASH

- Similar to the US, most direct costs are incurred among decompensated cirrhosis cases in all years.

2015 EU5 Costs
- 77.7% Compensated Cirrhosis
- 10.2% Decompensated Cirrhosis
- 4.7% Hepatocellular Carcinoma
- 7.4% Liver Transplant

2015 EU5 Prevalent Cases
- 88.4% Compensated Cirrhosis
- 10.5% Decompensated Cirrhosis
- 0.9% Hepatocellular Carcinoma
- 0.3% Liver Transplant

2030 US Costs
- 58.7% Compensated Cirrhosis
- 35.1% Decompensated Cirrhosis
- 4.7% Hepatocellular Carcinoma
- 1.5% Liver Transplant

2030 EU5 Prevalent Cases
- 87.9% Compensated Cirrhosis
- 11.2% Decompensated Cirrhosis
- 0.8% Hepatocellular Carcinoma
- 0.1% Liver Transplant
Conclusions

• In the absence of interventions, advanced liver diseases associated with NAFLD will more than double over the next 15 years

• Direct healthcare costs in the US currently estimated at $4.9 billion increasing by 260% to $17.6 billion by 2030 without interventions

• In the European Union, the current healthcare cost is estimate at $1.1 billion, which will increase by 160% to $3.9 billion by 2030 without interventions

• Interventions are required to manage the increase in future disease burden and associated costs
  • Preventing progression to decompensated cirrhosis and HCC are critical for reducing direct healthcare costs

• These same interventions will also have an impact on other non-communicable diseases including cardiovascular diseases and diabetes

• Better reporting systems are required to track NAFLD related disease burden to measure progress