International Think Tank

Paris NASH Meeting

July 5 & 6, 2018
Institut Pasteur

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

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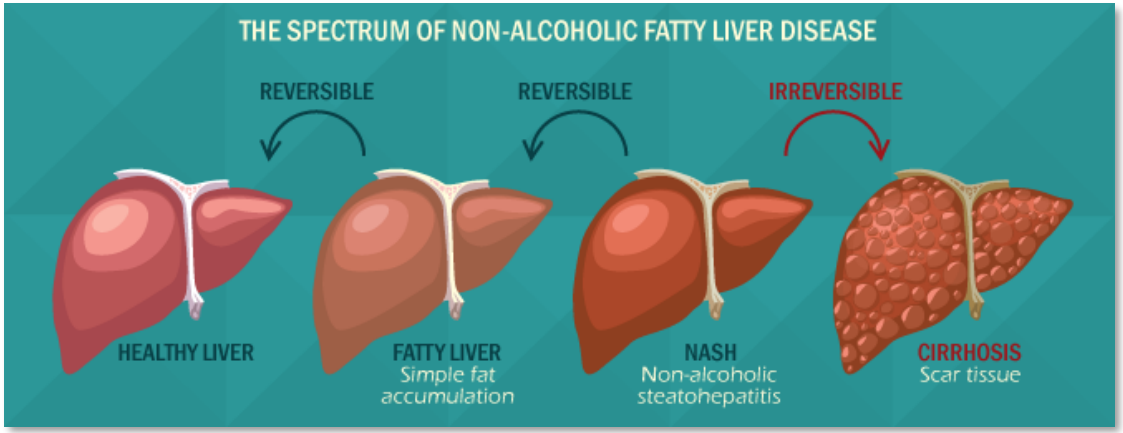
Methodology

- 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



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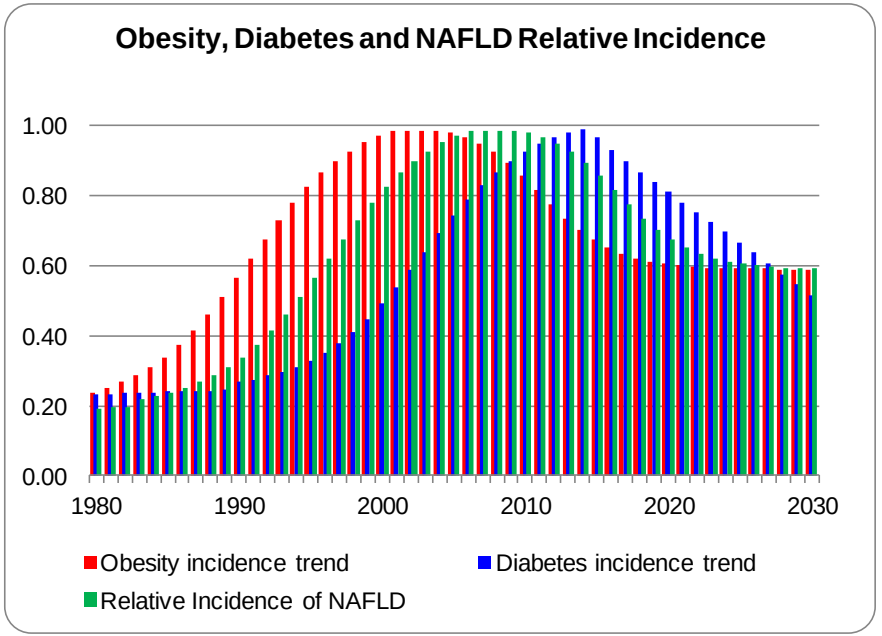
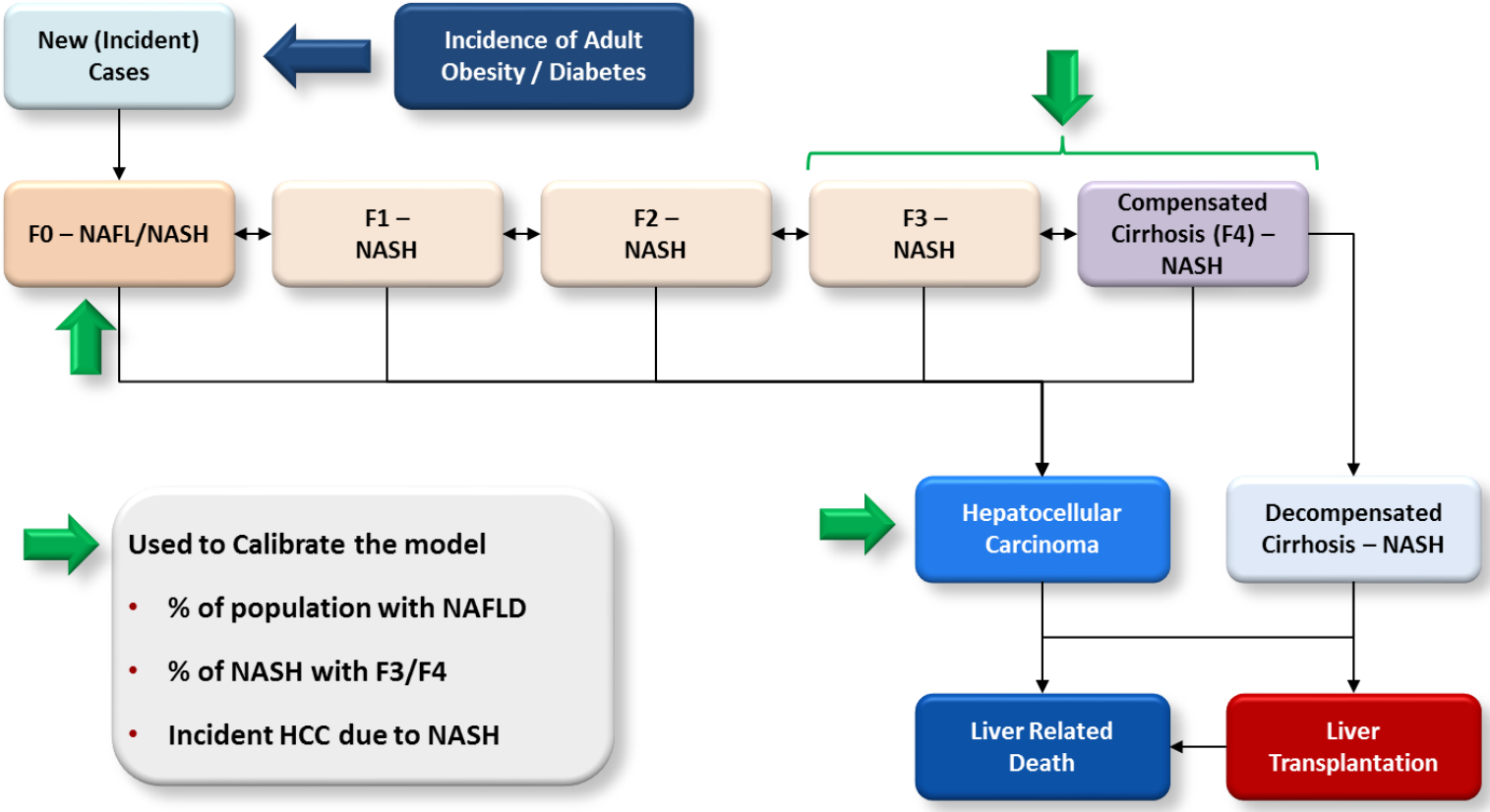
Modeling Approach

- 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



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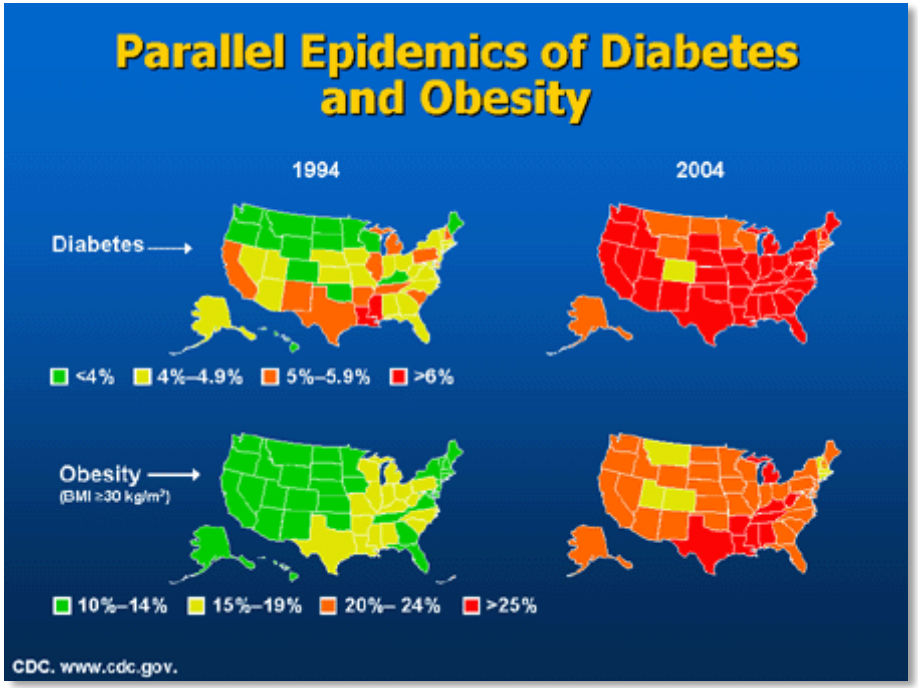
NASH prevalence and obesity in the EU5 are lower than the US

	BMI≥30	% of total population ≥15+ with NAFLD	% of NAFLD with NASH	% of total population ≥15+ with NASH
US	28%	30%	20%	6.3%
France	16%	25%	16%	4.2%
Germany	19%	25%	18%	4.6%
Italy	16%	28%	17%	4.9%
Spain	18%	25%	17%	4.4%
UK	21%	25%	18%	4.8%

Parallel Epidemics of Diabetes and Obesity in the US

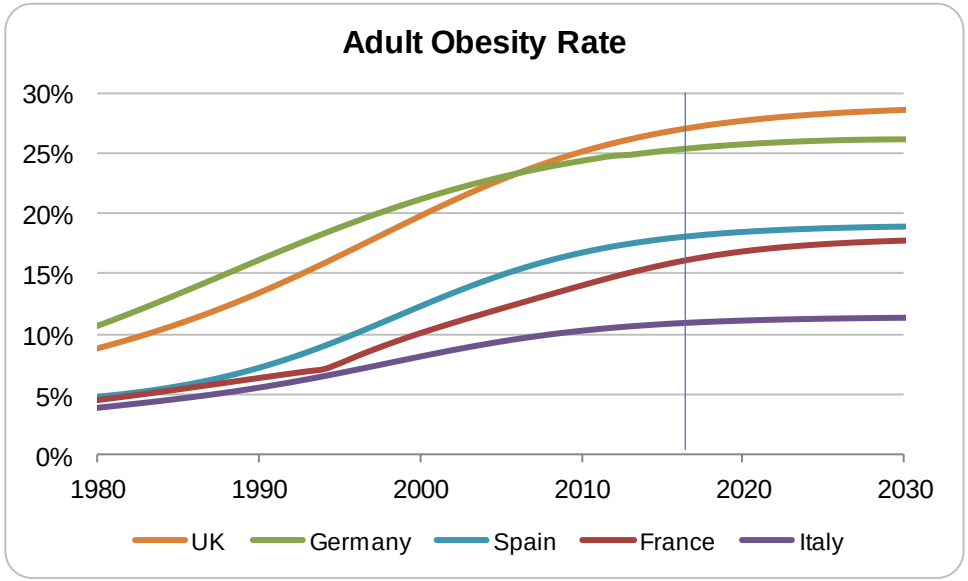


Centers for Disease Control and Prevention, National Center for Health Statistics. National Health Examination Survey and National Health and Nutrition Examination Survey. Health, United States 2006.

Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA, 311(8):806-814, 2014.

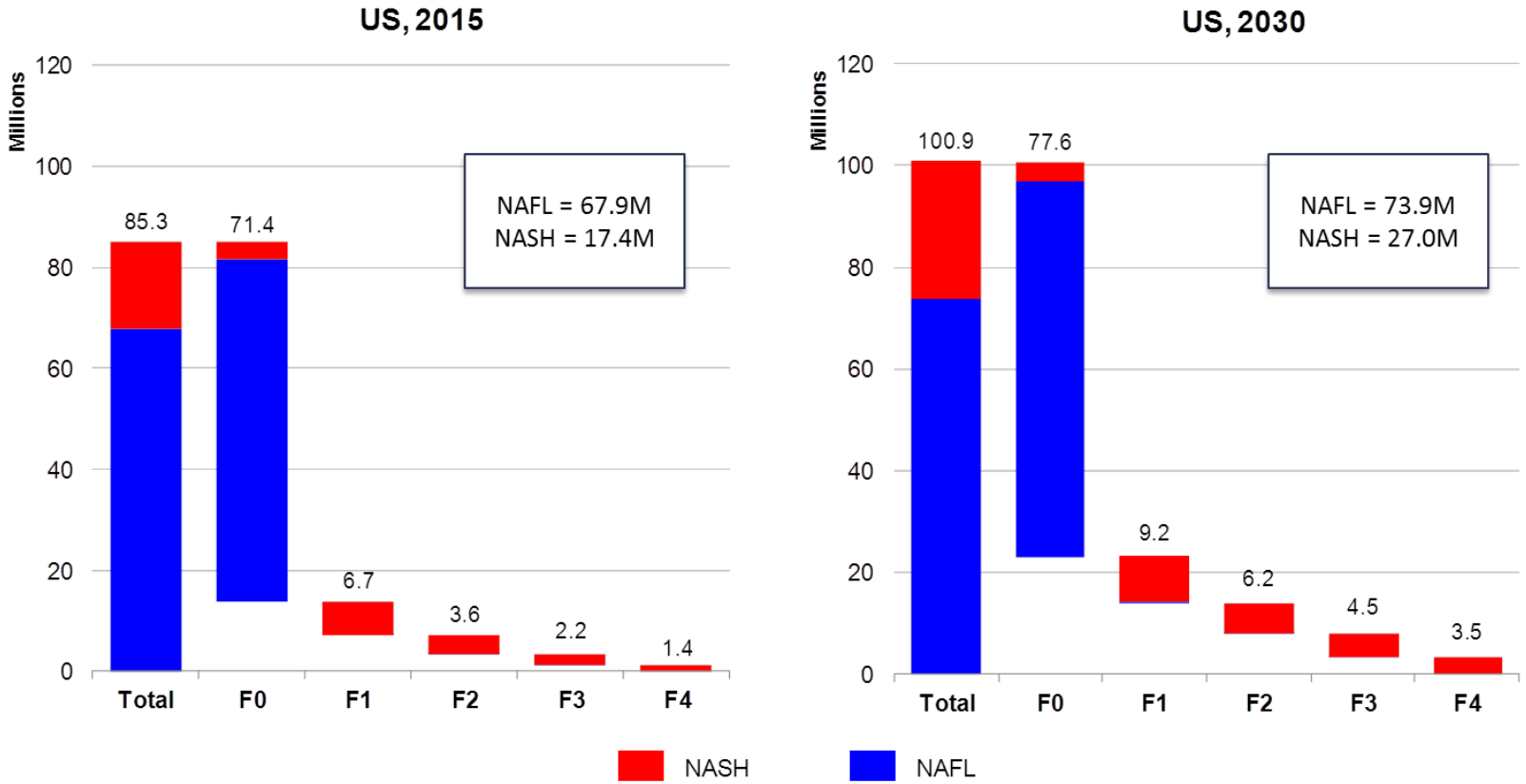
National Center for Health Statistics. Health, United States, 2014. Hyattsville, MD. 2015. Available at: http://www.cdc.gov/nchs/data/hus/hus14.pdf

Obesity has been increasing in European countries as well

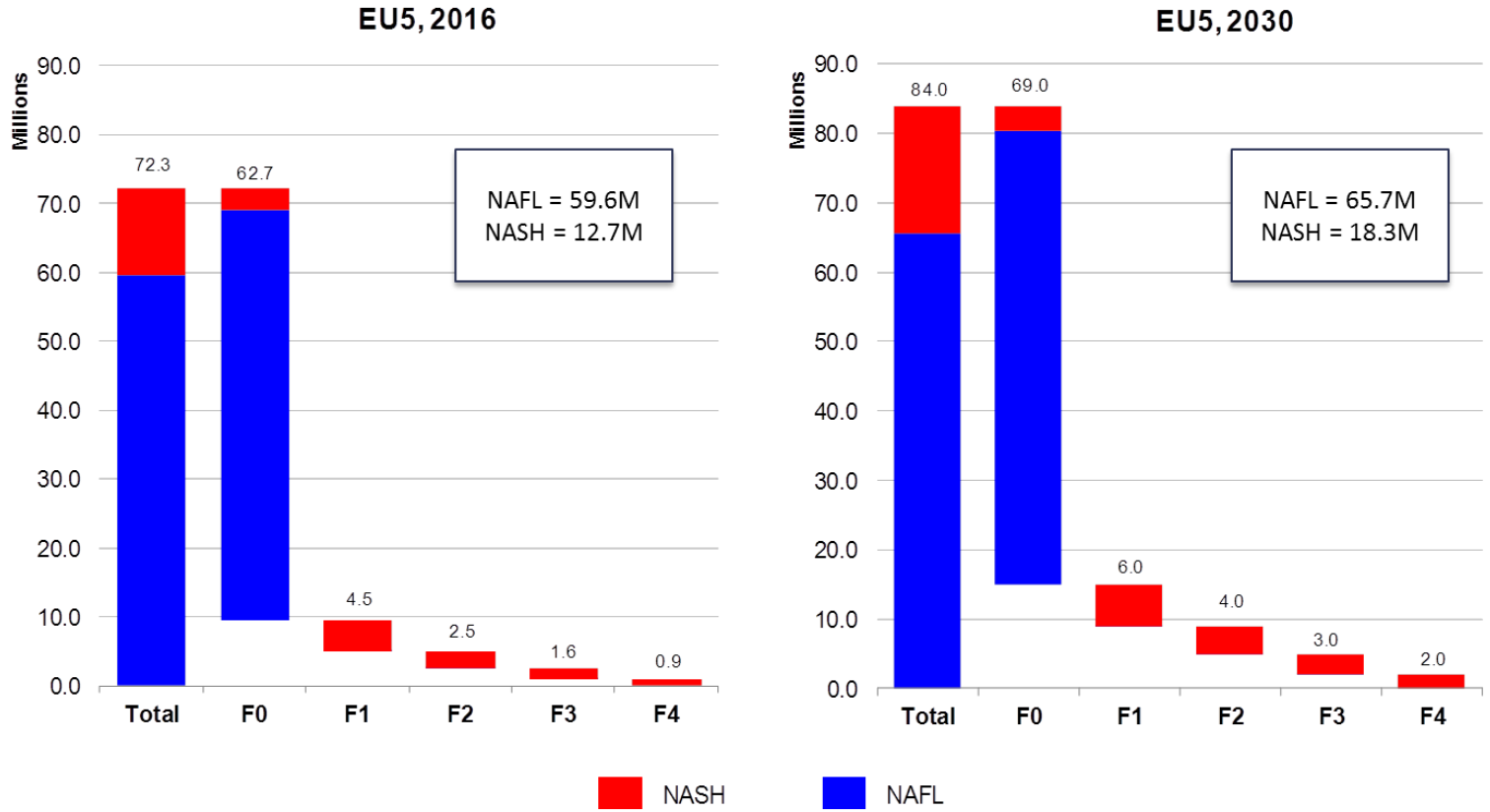


Adult obesity has been increasing but the rate of increase has slowed.

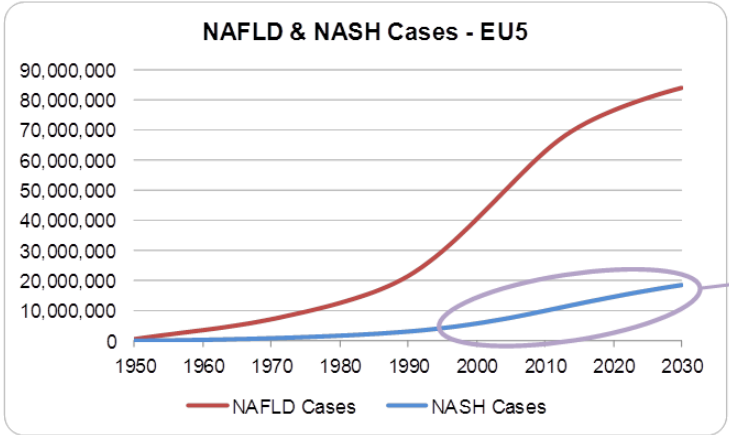
NASH population is expected to grow by 60% while cirrhotic cases will increase by 160% in US

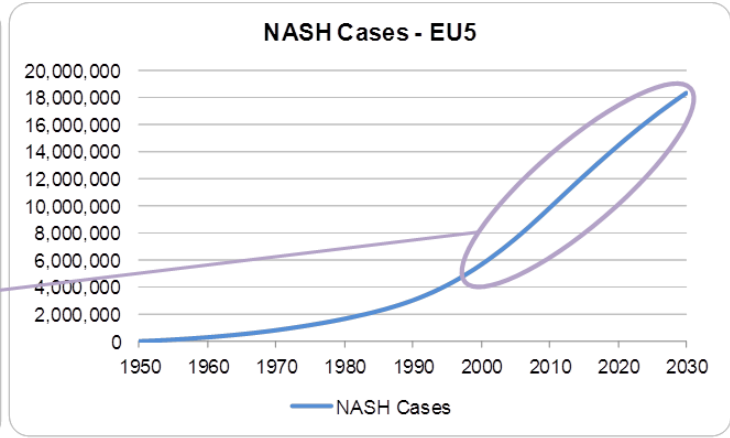


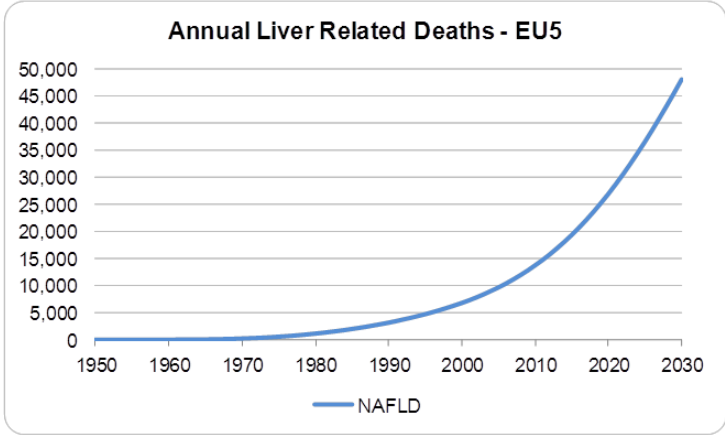
NASH population is expected to grow by 45% while cirrhotic cases will increase by 120% in EU

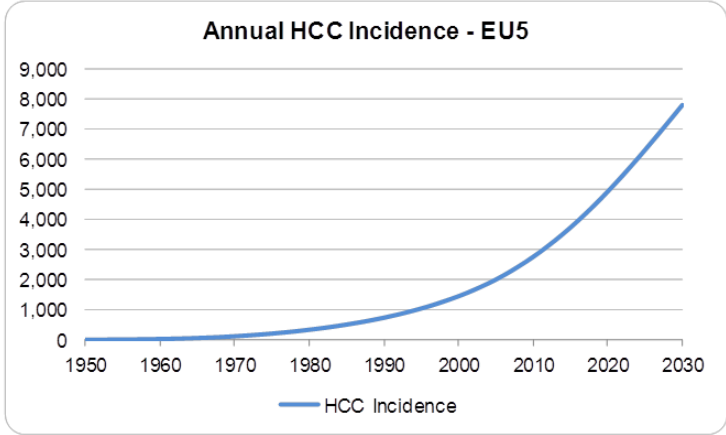


The increase in NAFLD cases is slowing down but NASH, HCC, and liver related deaths will increase



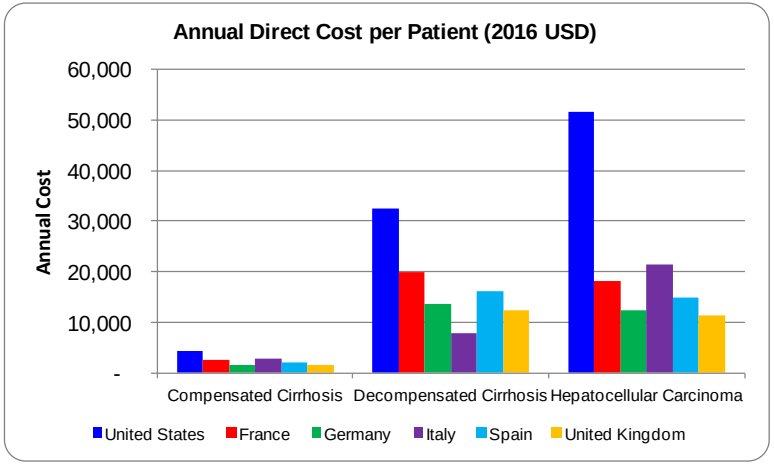


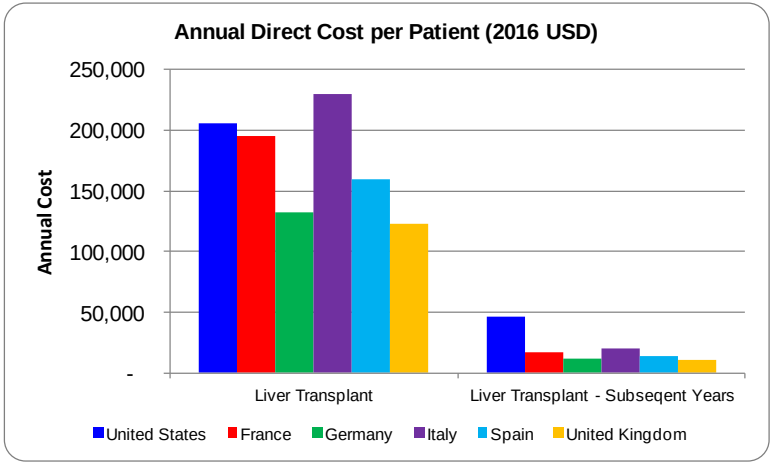




Cost Inputs

- 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





Eckman MH, Talal AH, Gordon SC, Schiff E, Sherman KE. Cost-effectiveness of screening for chronic hepatitis C infection in the United States. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2013;56(10):1382-93.

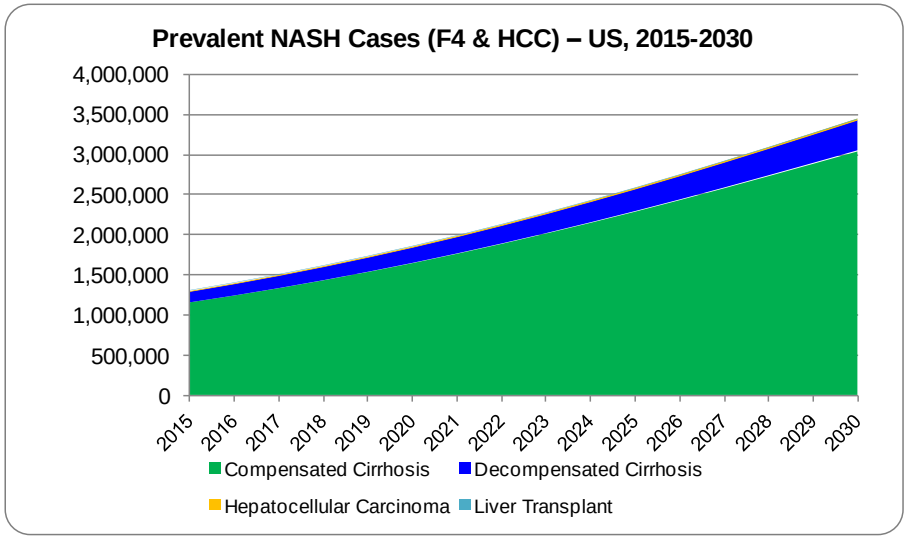
Postma MJ, Wiessing L, Jager J. Updated healthcare estimates for drug-related hepatitis C infections in the European Union. In: Jager J, Limburg W, Kretzschmar M, Postma MJ, Wiessing L, editors. Hepatitis C and injecting drug use: impact, costs and policy options. EMCDDA Scientific Monograph Series, ISSN 1606-1691; No 7. 389 p. : ill. ; 24 cm. Luxembourg: Office for Official Publications of the European Communities; 2004. p. 203-16.

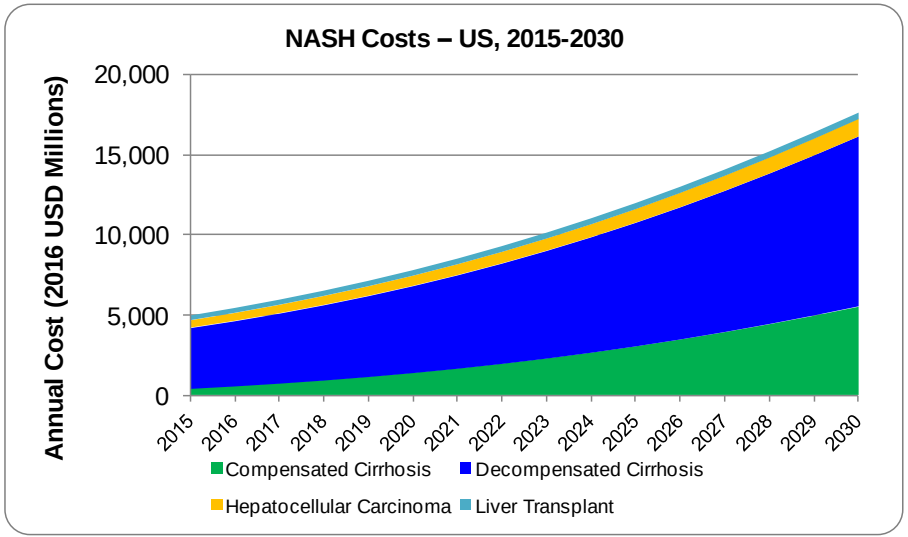
Sullivan SD, Craxi A, Alberti A, et al. Cost effectiveness of peginterferon alpha-2a plus ribavirin versus interferon alpha-2b plus ribavirin as initial therapy for treatment-naive chronic hepatitis C. Pharmacoeconomics 2004; 22: 257-65.

Eurostat. 2017. Database - HICP (2015 = 100) - annual data (average index and rate of change) for Health Category (CP06).

Estimated Direct US Healthcare Cost - NASH

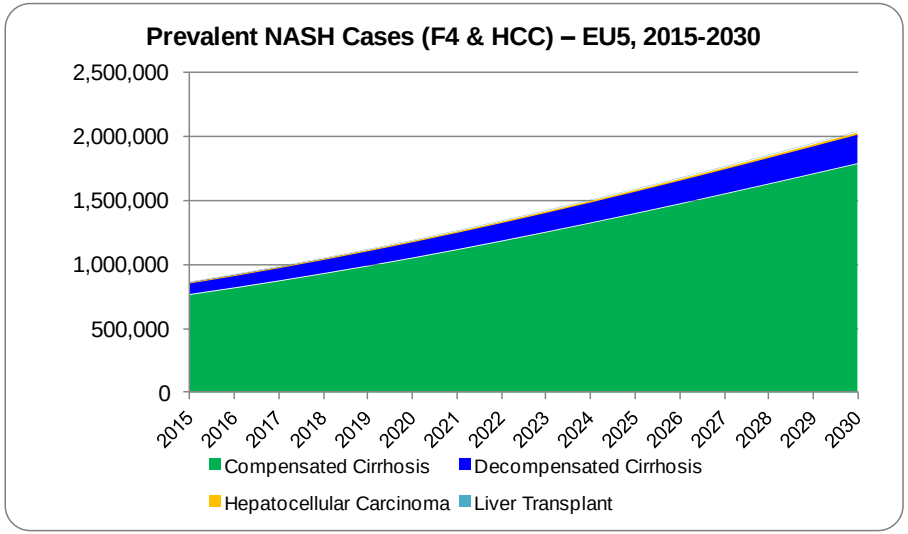
- Annual direct costs increase 260% from $4.9 B (2015) to $17.6 B (2030)
  - Decompensated cirrhosis comprises only ~1% of all prevalent NASH cases and ~10% of F4/HCC cases, but accounts for the majority of direct costs in this analysis
  - Assumed the number of liver transplants can not increase due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

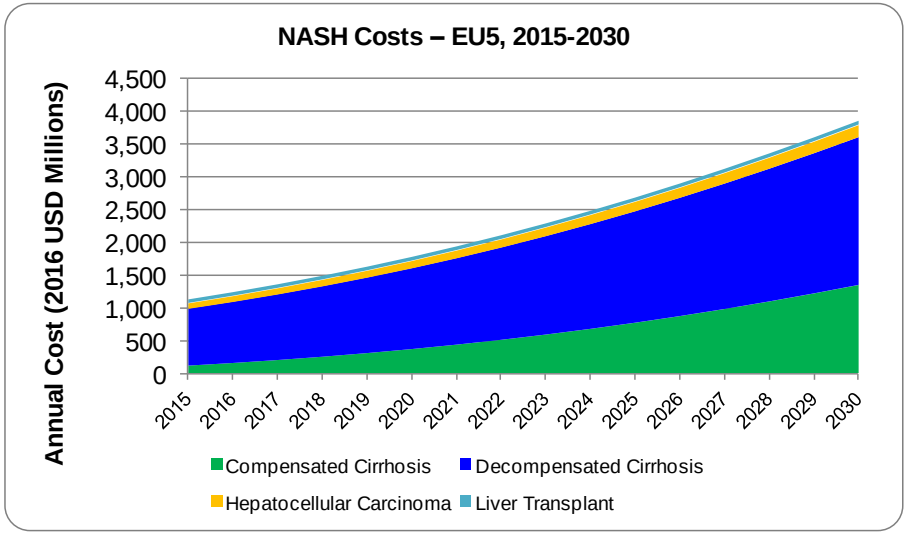




Estimated Direct EU5 Healthcare Cost - NASH

- 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





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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 EU5, 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