Modeling the epidemic of NAFLD and burden on healthcare system

H. Razavi & C. Estes

June 30, 2016

Disclosure

- H. Razavi is the Managing Director of CDA and has received no personal remuneration.

- CDA has received research funding from AbbVie, Boehringer Ingelheim, Gilead and Intercept.

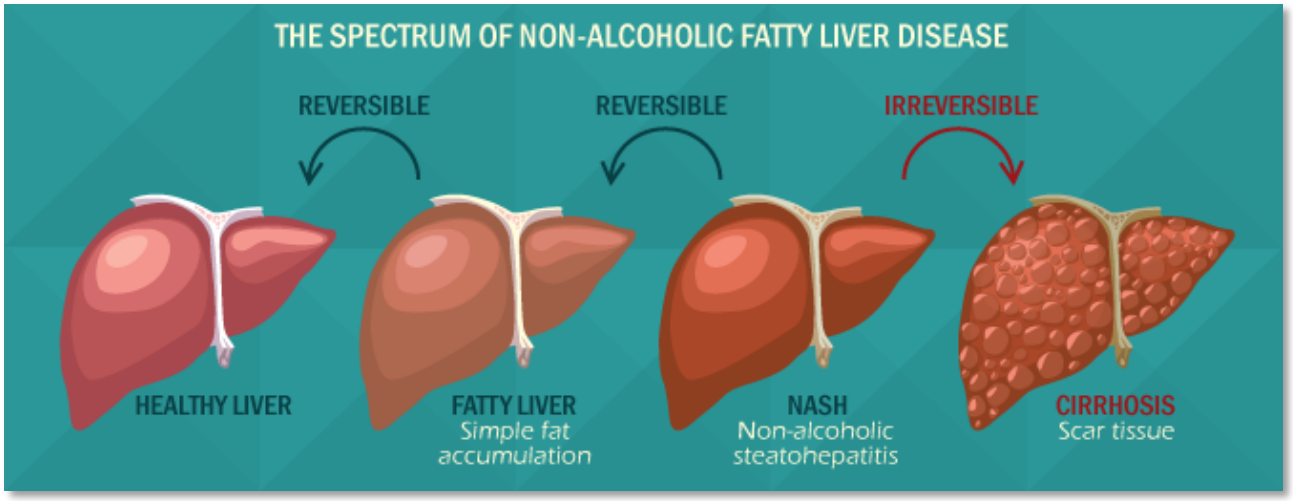
- This study was supported by Boehringer Ingelheim, Gilead and Intercept.

Acknowledgement

- **Principle investigator:** Arun Sanyal
- **United States:** Rohit Loomba, Arun Sanyal, Zobair Younossi
- **France:** Vlad Ratziu, Lawrence Serfaty
- **Germany:** Andreas Geier, Michael Manns, Christian Trautwein, Stefan Zeuzem
- **Italy:** Stefano Bellentani, Antonio Craxi, Giulio Marchesini, Salvatore Petta
- **Spain:** Maria Arias-Loste, Joan Caballeria, Javier Crespo, Manuel Romero Gomez
- **United Kingdom:** Quentin Anstee, Christopher Day, Jude Oben, Philip Newsome
- **China:** Wei Lai, George Lau

Project Objectives

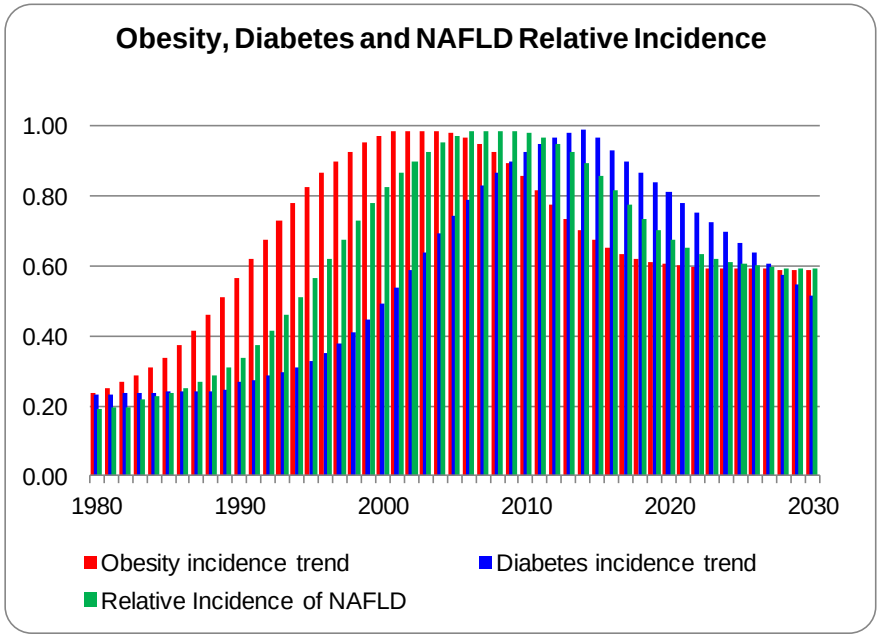
- Develop a tool to estimate NAFLD disease progression
- Collect published epidemiology data for NAFLD
- Calibrate the model for each country
- Update the model based on expert feedback



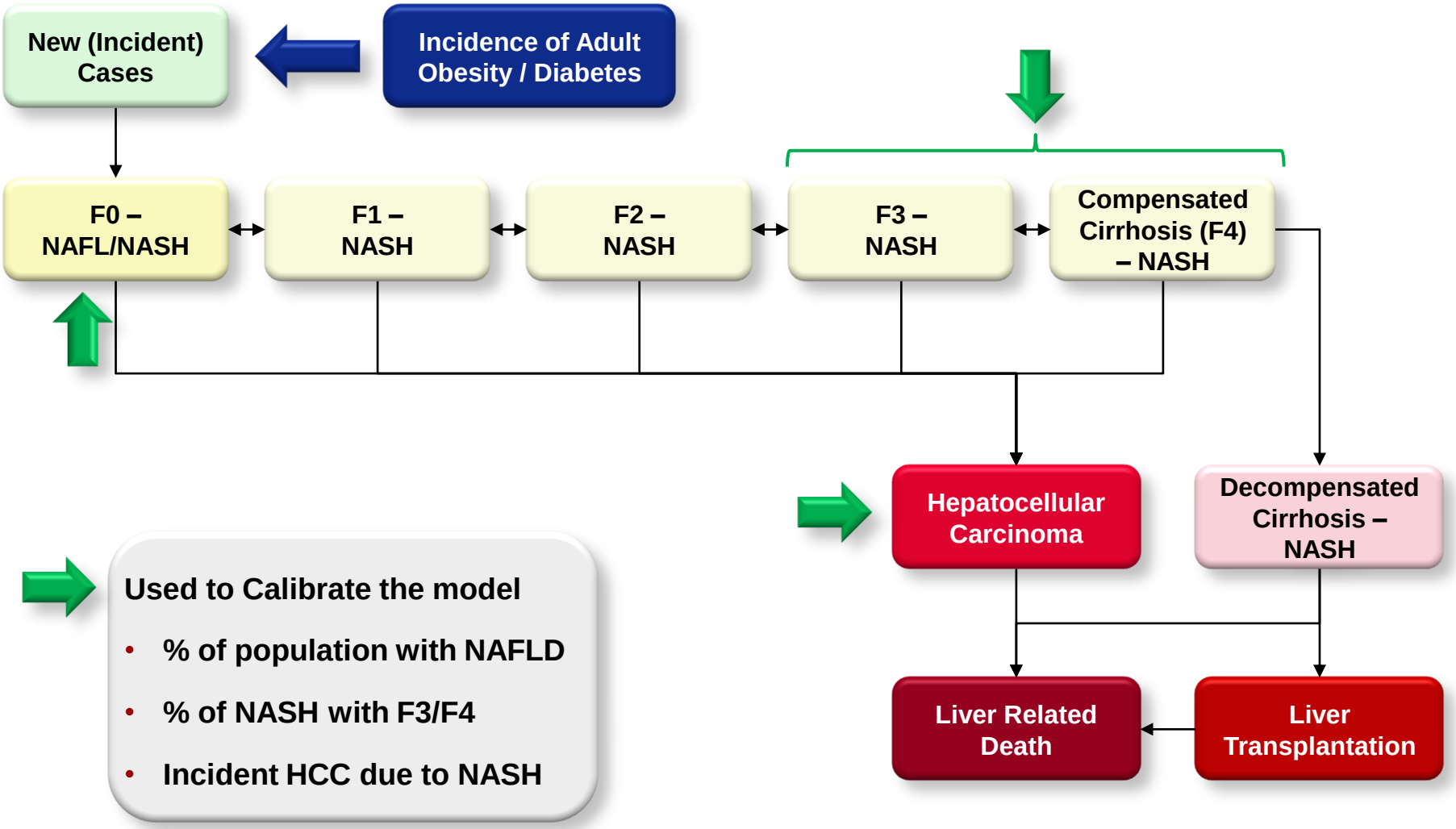
Modeling Approach

- 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

$$Prevalence_{Year\ x} = \sum_{t=1950}^{x} (Incidence_t - Mortality_t)$$



NAFLD Disease Progression



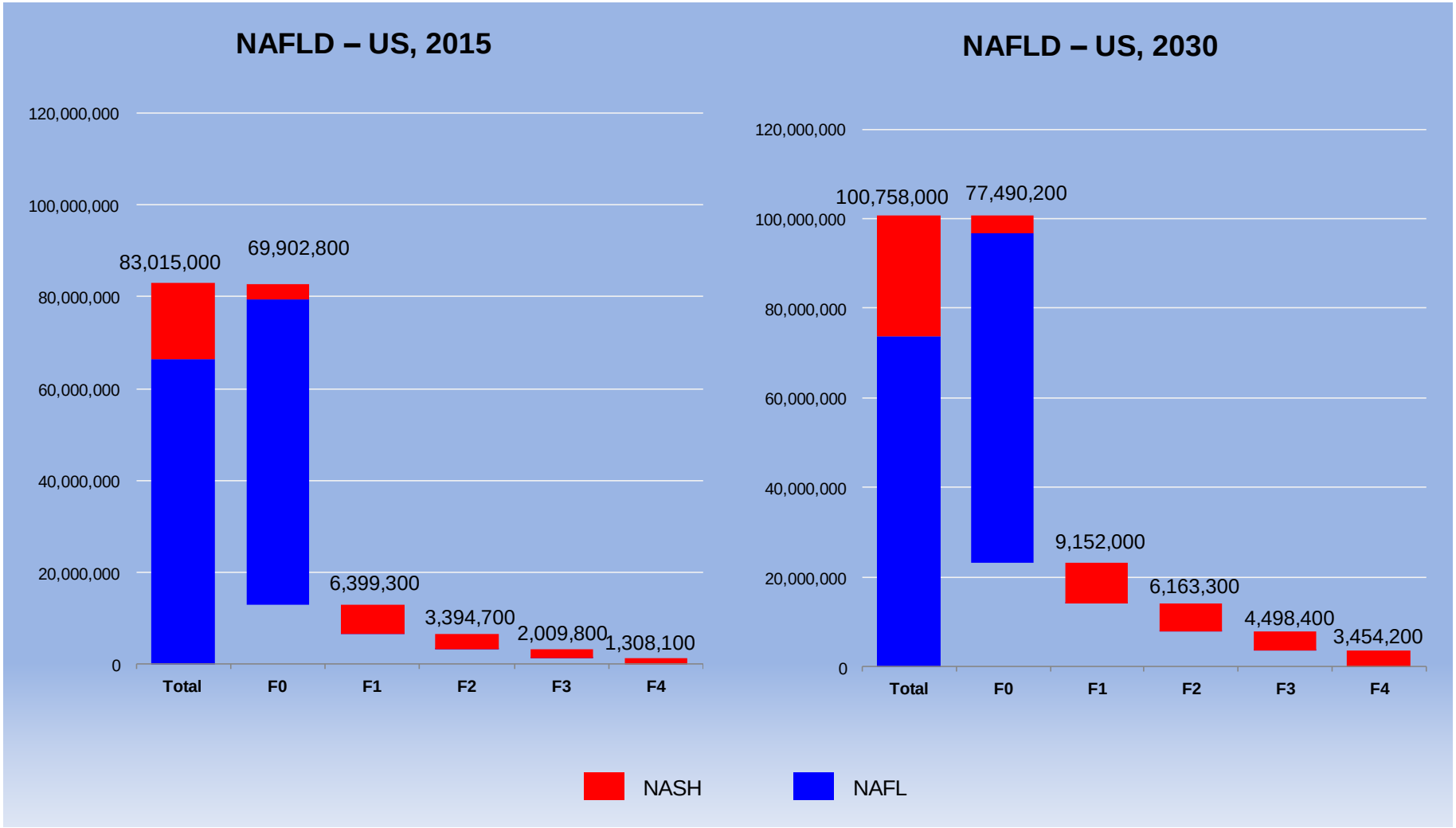
Prevalence assumptions across countries

	% of Total Population ≥15+ with NAFLD	% of Total Population ≥15+ with NASH	
US	30%	6.3%	NHANES III - Lazo 2013, Younossi 2015
France	25%	4.8%	Poynard 2010, Ratziu 2012, Blachier 2013
Germany	25%	5.3%	Haring 2009
Italy	29%	5.6%	Bedogni 2005
Spain	25%	5.0%	Caballeria 2010
UK	25%	5.3%	Armstrong 2012
China	21%	3.4%	Fan 2009, Fan 2013

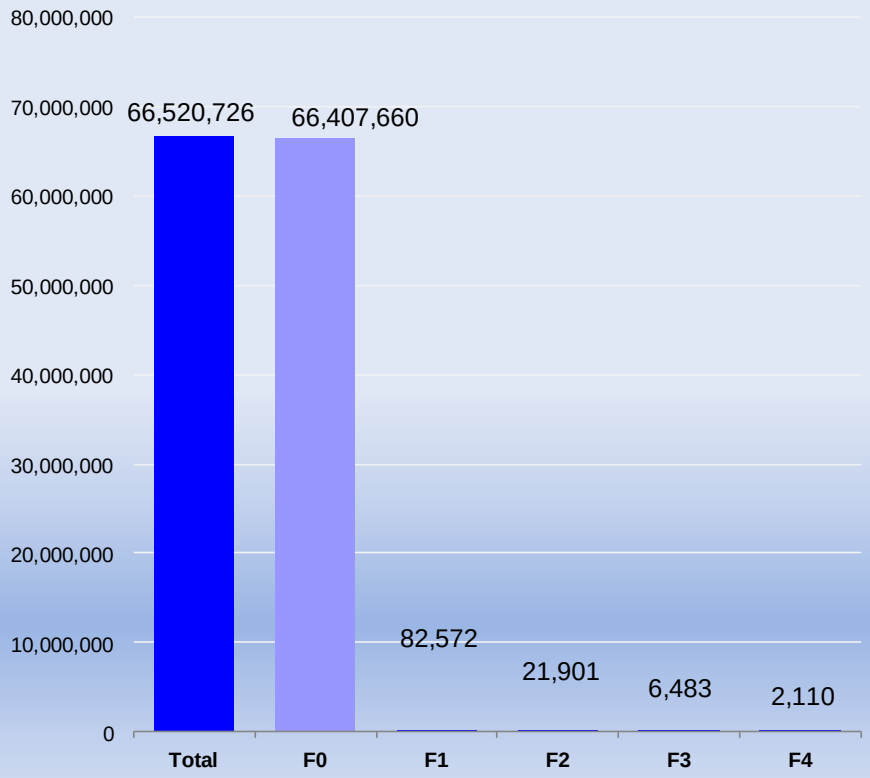
NASH

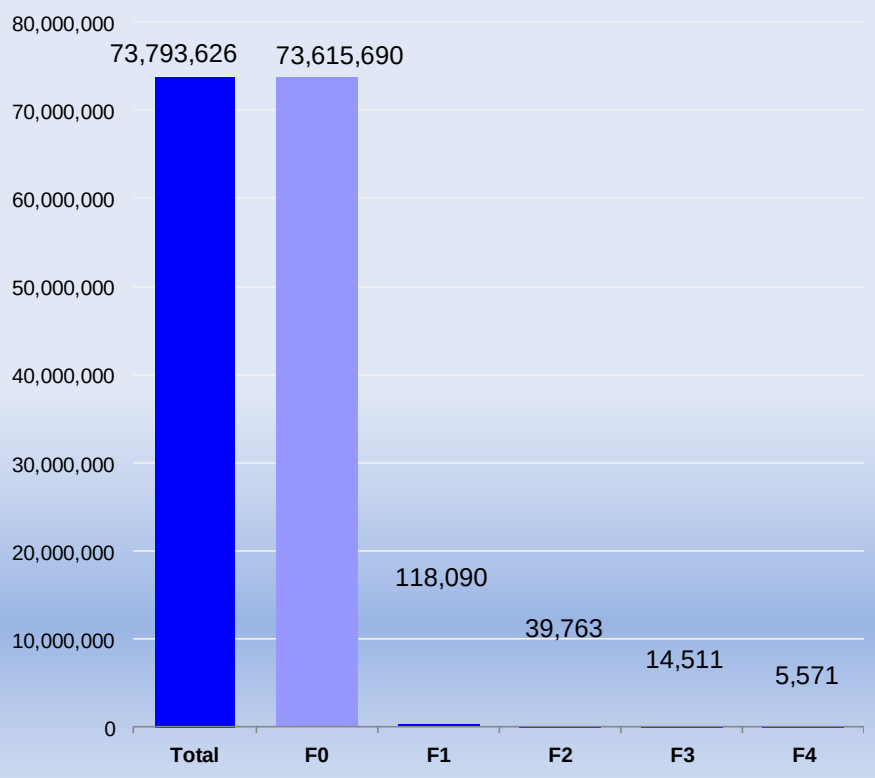
- 15.6% of 776 aircrew who died in 525 fatal aircraft accidents had fatty liver and 19.2% of NAFLD cases had NASH (Ground 1990 as reported in Grant 2004)
- 328 cases completed ultrasound at Brooks Army Medical center; 26.5% of NAFLD cases had NASH (Williams 2011)
- Among 576 liver biopsies with definite NASH, 21% were classified as F3/F4 (Kleiner 2005)

Model outputs – Prevalence by disease state – US

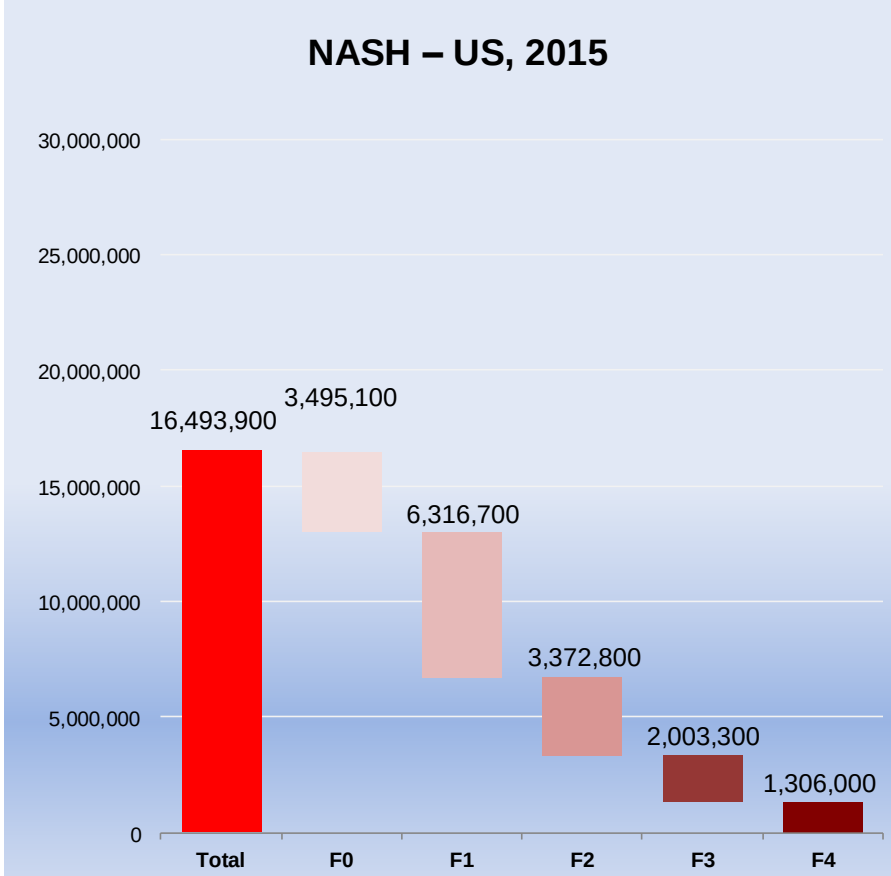


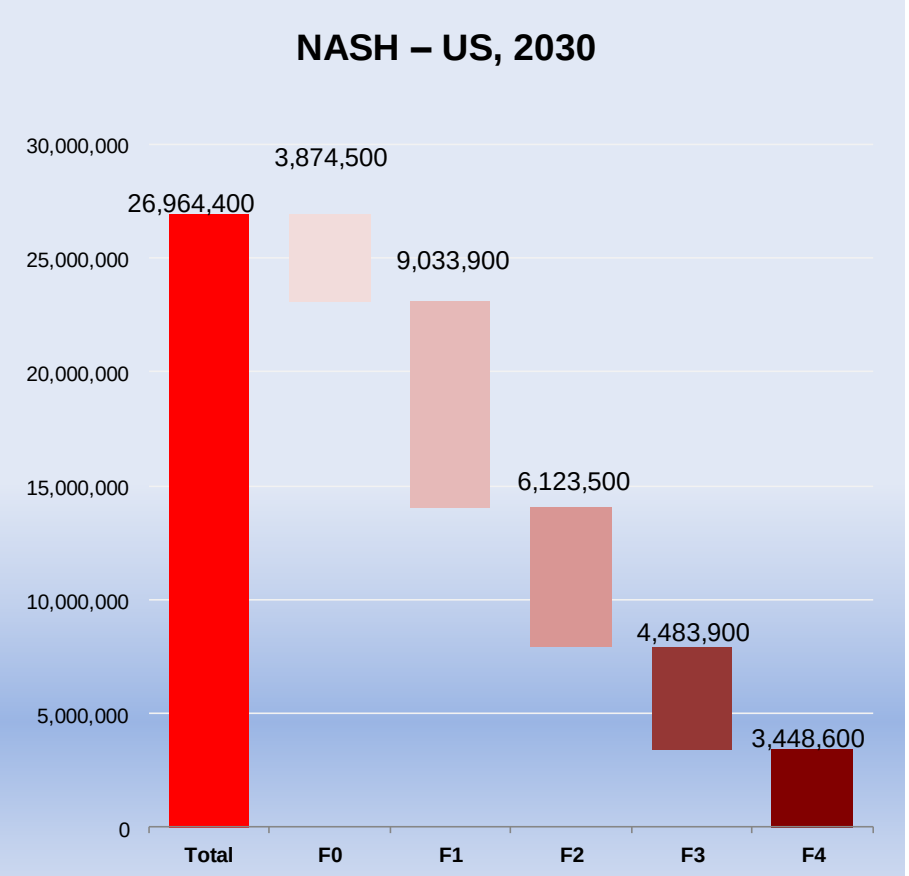
Model outputs – Prevalence by disease state – US



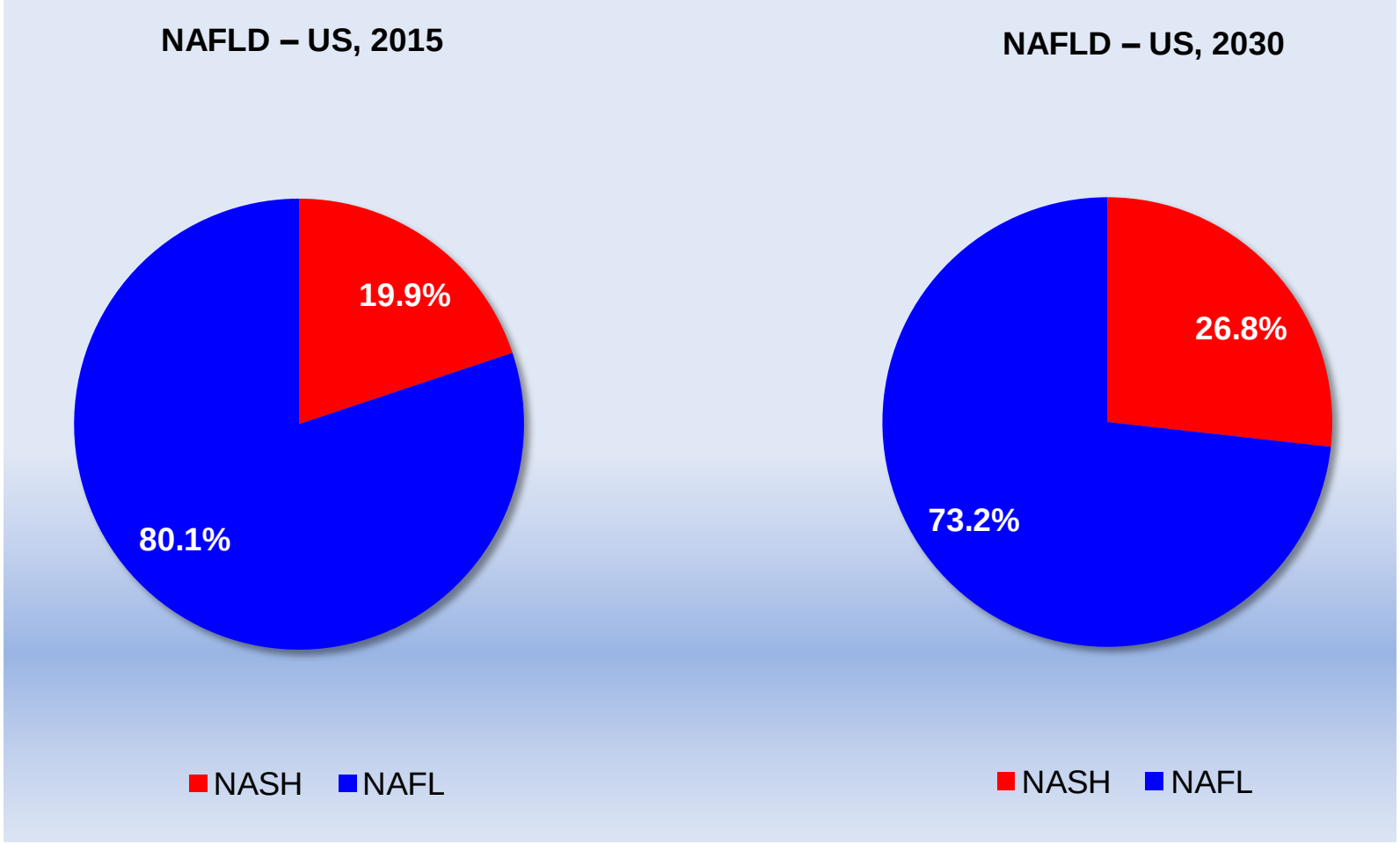


Model outputs – Prevalence by disease state – US

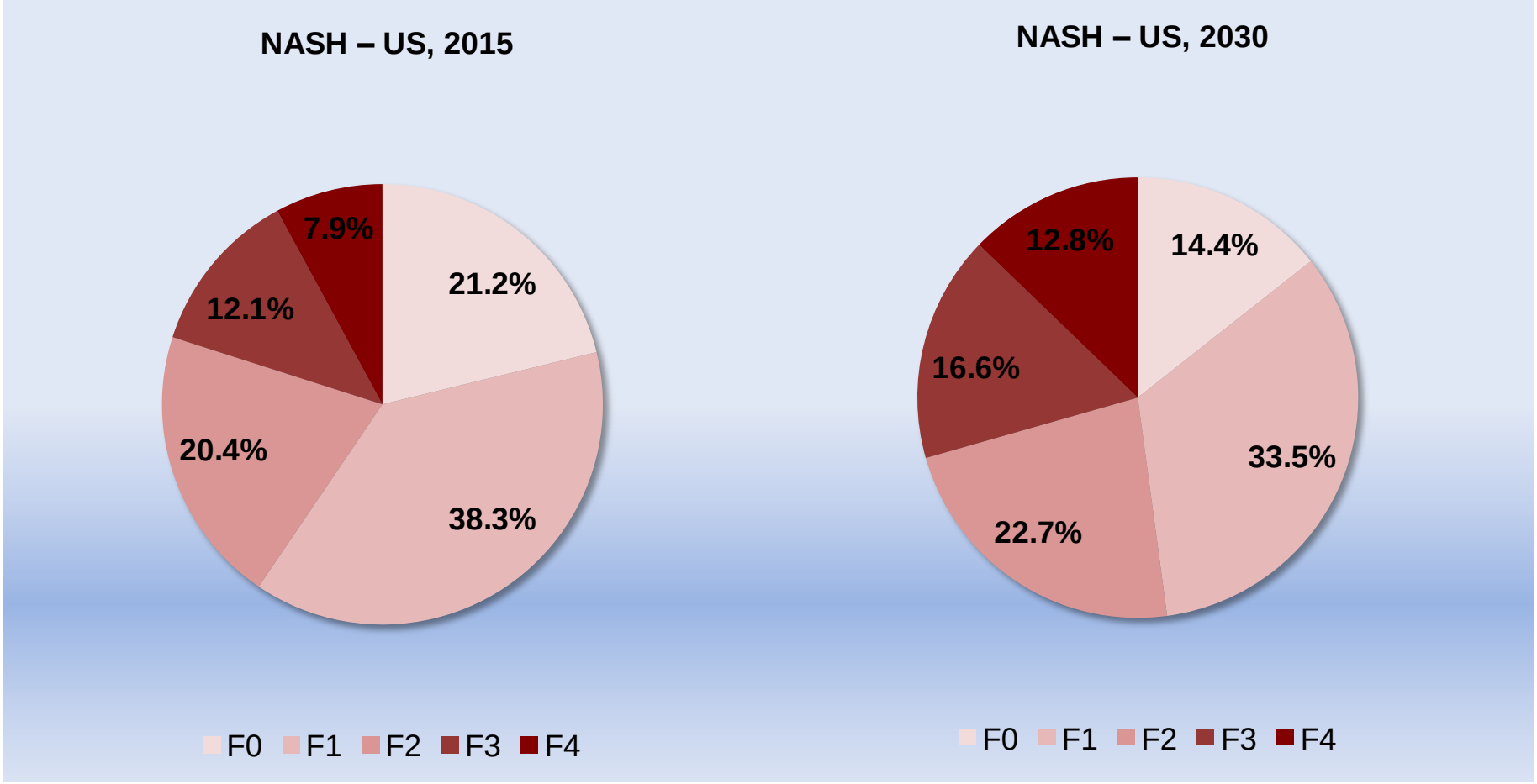




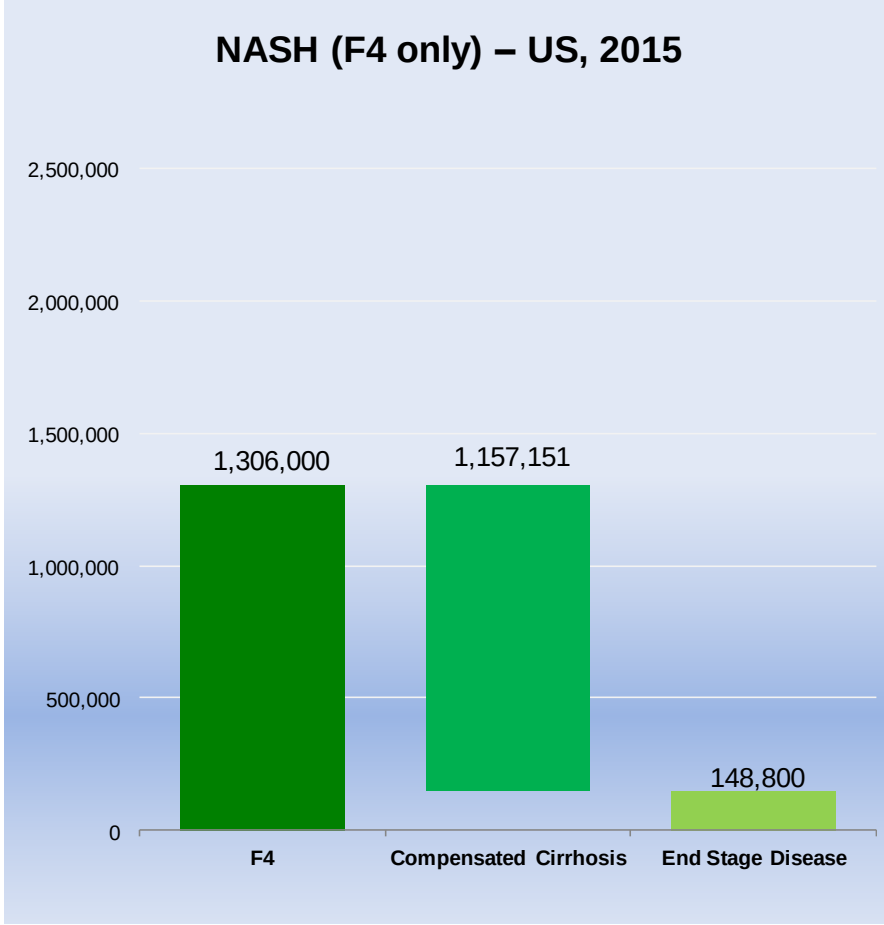
Model outputs – Prevalence by disease state – US

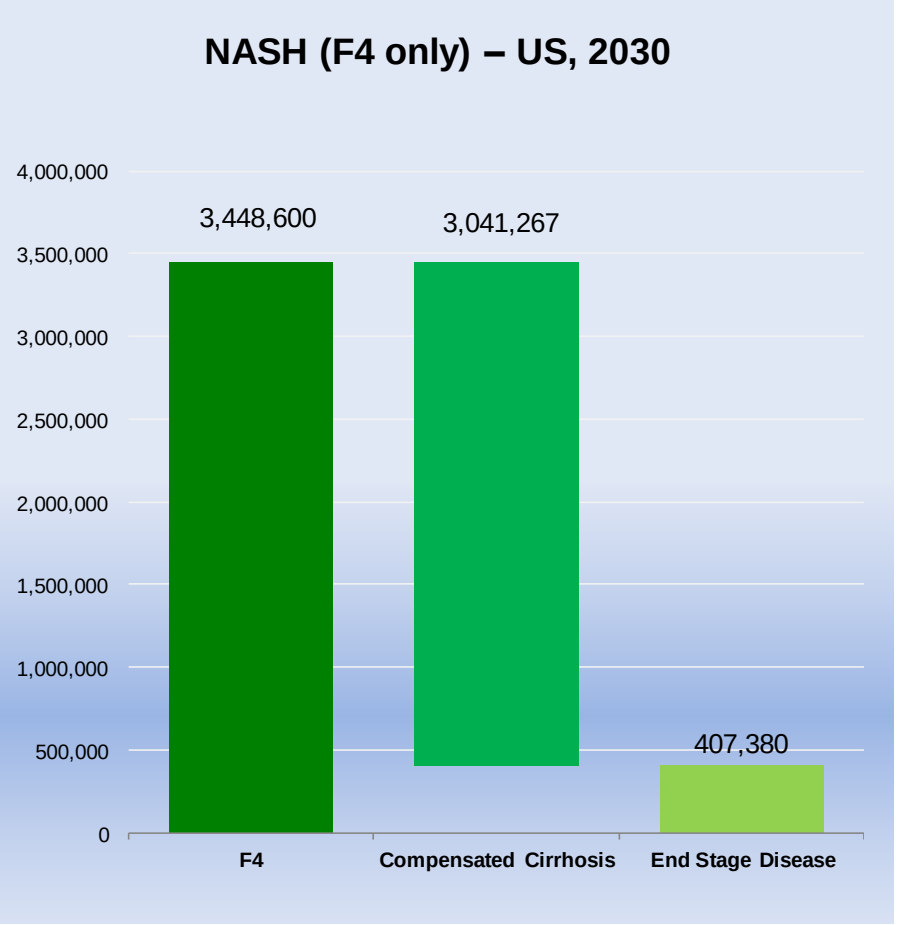


Model outputs – Prevalence by disease state – US

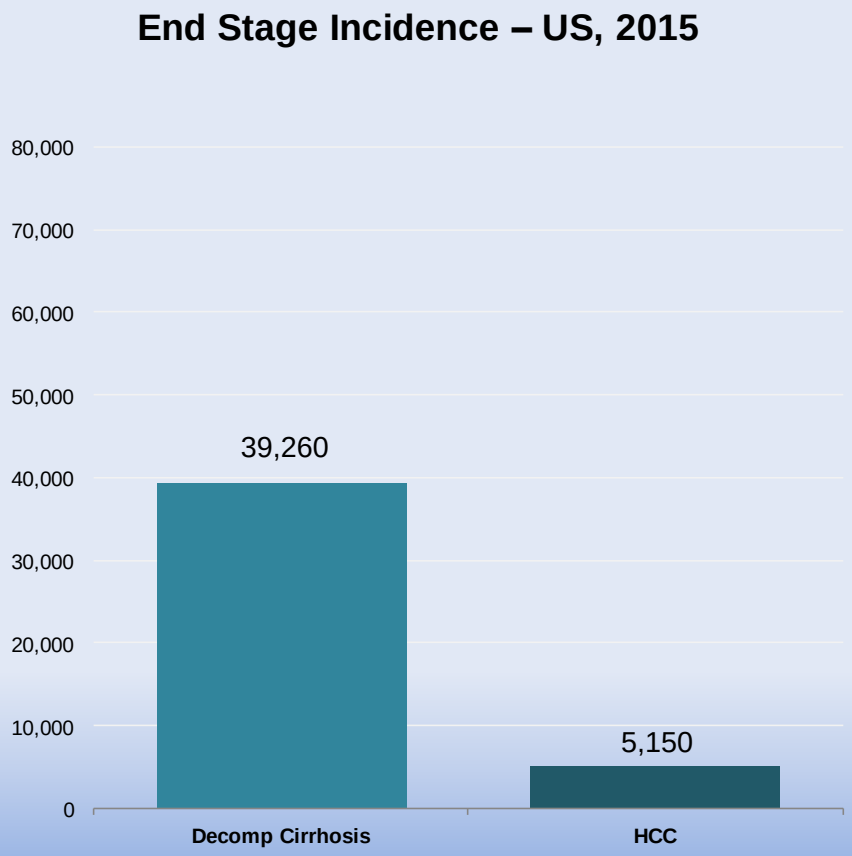


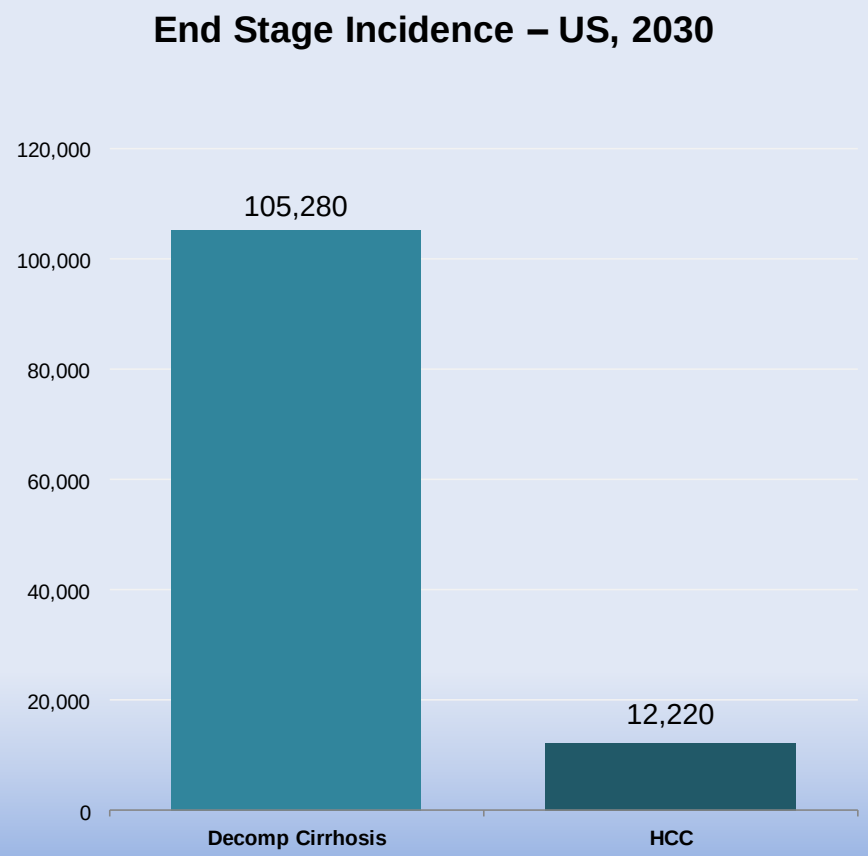
Model outputs – Prevalence by disease state – US



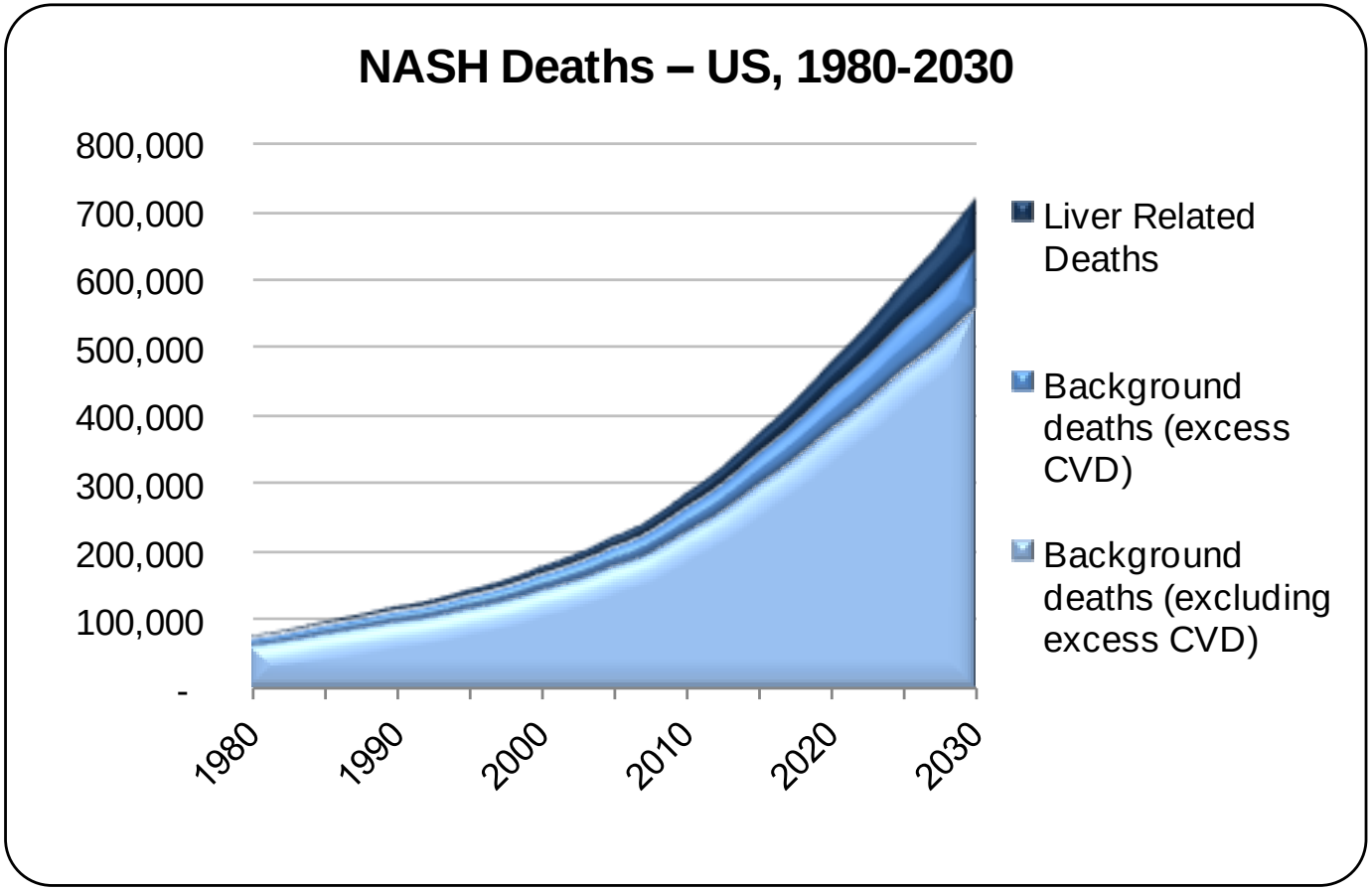


Model outputs – Prevalence by disease state – US



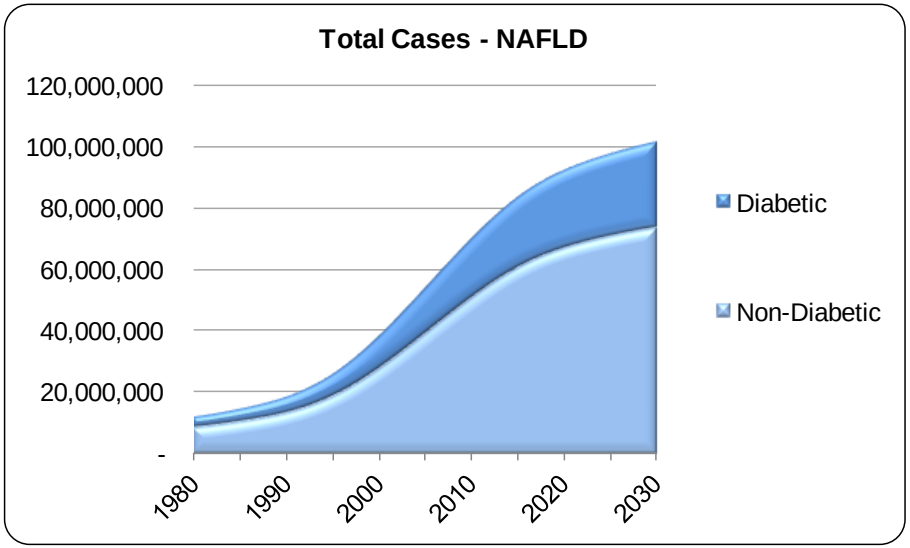


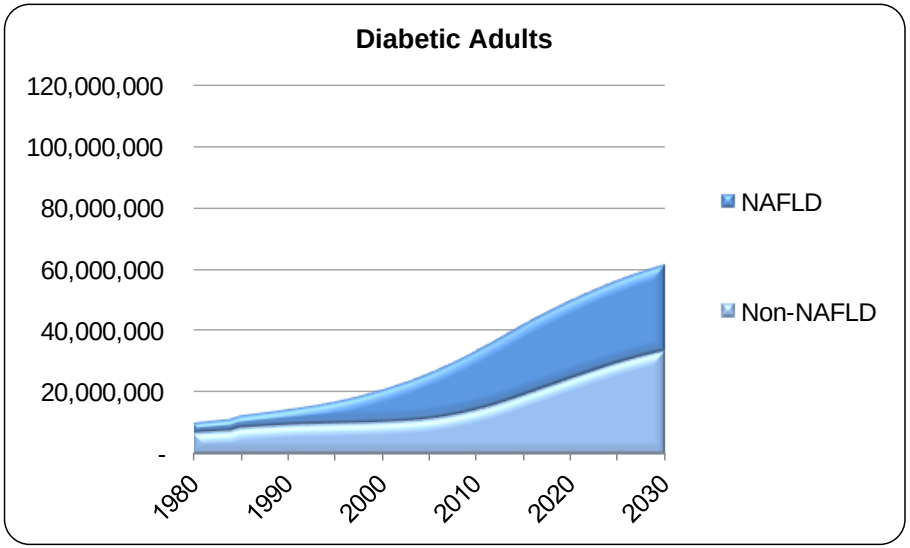
NASH – Total Deaths – US

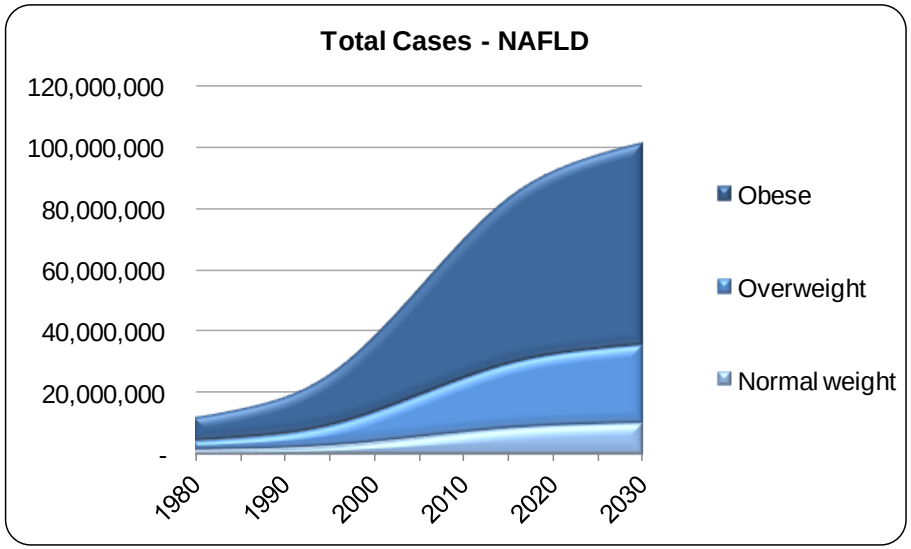


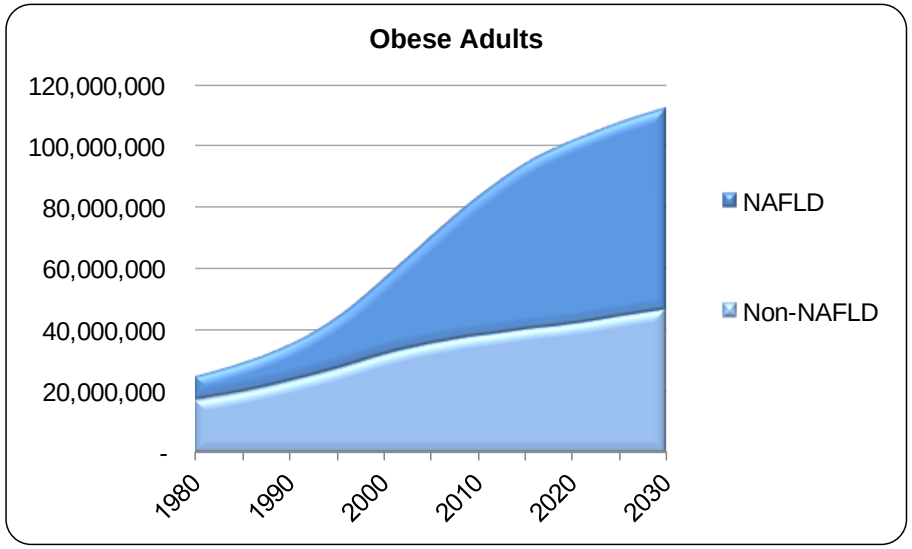
Among the NASH population in 2015, estimate 28,150 liver deaths, 44,100 excess CVD deaths, and 293,900 background deaths.

Prevalence – NAFLD – US

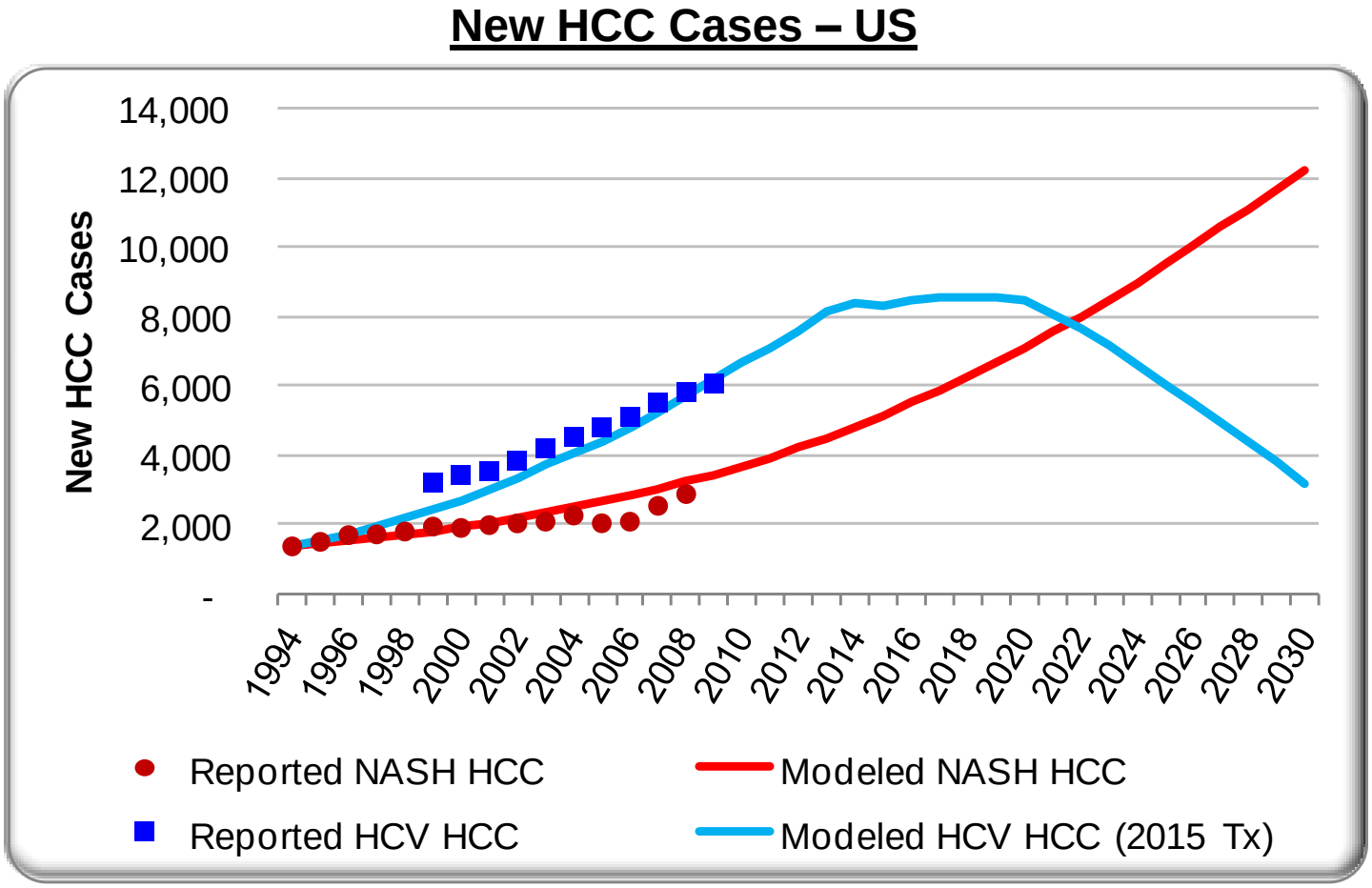








Without intervention, the number of NASH related HCC cases is expected to surpass HCV related HCC in 2022



Reported HCC cases were derived from reported liver cancer cases – SEER database http://seer.cancer.gov/data/

Conclusions:

- As the rate of increase in obesity and diabetes starts to level off, we will see a slow down in the new number of NAFLD cases – 20% increase in total case in the next 15 years
- However, the existing NAFLD population will continue to progress to more advanced liver disease stages
  - » 65% increase in NASH cases from est. 16.5 million in 2015
  - » 140% increase in new HCC cases from est. 5,150 cases in 2015
  - » 165% increase in total cirrhotic cases from est. 1.3 million in 2015
  - » 170% increase in new decompensated cirrhosis cases from est. 39,000 cases in 2015
  - » 175% increase in liver related deaths from an est. 28 thousands in 2015
- Similar growth in disease burden was also seen in other countries analyzed