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Estimating the Humanistic Burden of NASH for the US population

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INTRODUCTION

- Non-alcoholic steatohepatitis (NASH) is the progressive form of non-alcoholic fatty liver disease (NAFLD) defined by a buildup of fat in the liver and signs of inflammation, liver damage and progressive fibrosis.
- NASH is associated with non-specific symptoms making diagnosis difficult and leading to undetected disease progression.
- Patients with NASH may develop cirrhosis, leading to clinical decompensation, liver cancer, and liver failure, affecting morbidity and mortality.

OBJECTIVE

- **The goal of this study was to estimate the burden of NASH in the US, which is not well understood.**
- **We wanted to present that burden separately by age and by sex in the form of a 'population pyramid'**
- **We further sought to disaggregate the burden by morbidity & mortality**

METHODS

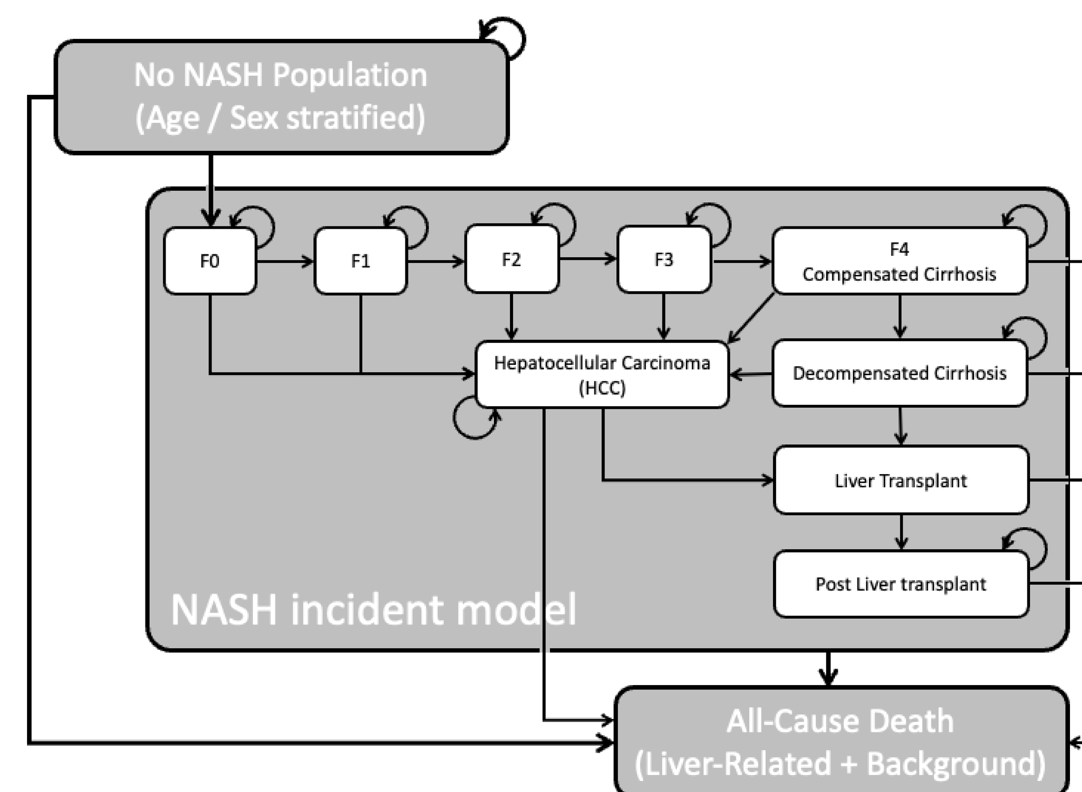
Incident model

- An incident model of NASH was developed using standard definitions of fibrosis (stages F0 through to F4) plus decompensated cirrhosis, liver transplant, post-liver transplant and hepatocellular carcinoma (HCC) health states (See Figure 1)
- All NASH states are considered to increase the chances of HCC
- Stages F0 through to F3 are not associated with increased risk of liver-related death (non-HCC)
- Later stages of disease are associated with increased risk of death from liver-related disease
- Transition probabilities were taken from lifetables (background mortality) and the literature in line with other NASH models (see Table 1)
- Quality of life utility values for states were also sourced from the literature

Population model

- The incident model of NASH was nested within a population model who are assumed to start the model without NASH (Figure 1)
- Incidence estimates are assumed to rise with age in line with obesity and diabetes rates in the population (see poster MSR38)
- Underlying incidence was calibrated to literature estimates of emergent NASH disease (see poster MSR38)
- Background mortality was taken from published US lifetables [3]
- US population norm quality of life utilities were used for the non-NASH population [13]
- Burden is quantified in terms of quality-adjusted life years (QALYs) disaggregated into the morbidity and mortality burden of NASH (see poster MSR38)

Figure 1. Population model with nested incident NASH model



Note: Model assumes a 'net-effect' of fibrosis progression and regression

Table 1. Transition probabilities for the NASH model

Transitions		Probability	Source
Fibrosis progression	F0-F1	9.60%	[1, 2]
	F1-F2	3.90%	[1, 2]
	F2-F3	5.60%	[1, 2]
	F3-F4	11.00%	[1, 2]
	F4-DC	3.80%	[3, 4, 5]
Risk of HCC	F0-HCC	0.01%	[3]
	F1-HCC	0.01%	[3]
	F2-HCC	0.02%	[3]
	F3-HCC	0.20%	[6]
	F4-HCC	1.80%	[6, 7]
	DC-HCC	2.60%	[5, 7, 8]
Liver transplant	DC-LT	43.00%	[7, 9]
	HCC-LT	56.00%	[7, 9]
Liver-related mortality	F4-Death	4.00%	[10]
	DC-Death	4.00%	[10]
	HCC-Death	57.60%	[11]
	LT-Death	9.70%	[12]
	PLT-Death	4.00%	[12]

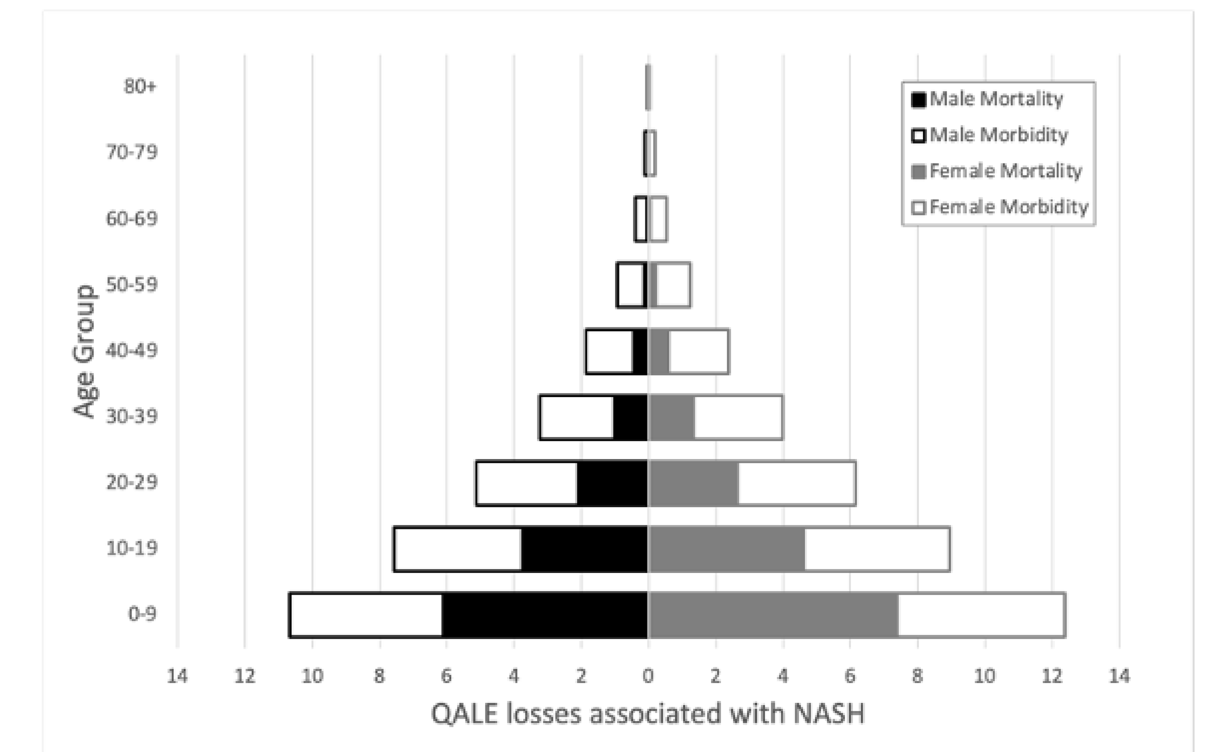
HCC, hepatocellular carcinoma; DC, decompensated cirrhosis; LT, liver transplant; PLT, post liver transplant

RESULTS

Incident model

- The population pyramid for NASH burden over the lifetime conditional on age and sex at incidence of disease is presented in Figure 2
- Bottom heavy shape reflects the insidious nature of NASH
- Acquiring the disease at earlier ages gives longer time for disease to progress to the later more serious sequelae of the disease
- Age-sex specific pyramids, conditional on timing of incidence, can show the burden at different decades of life (see poster MSR38)

Figure 2. Burden of incident NASH by age and sex



Population model

- The population pyramid for the circa. 334M population of the US is shown in Figure 3
- Combining incident frequency at different ages, age-sex specific burden at different decades of life (see poster MSR38), with this population pyramid gives the US population life-course burden of NASH shown in Figure 4
- The 'spinning top' shape of the life-course burden reflects the insidious nature of the disease
- The greatest burden of NASH is predicted to occur in the 60-69 year old decade

Figure 3. US population pyramid

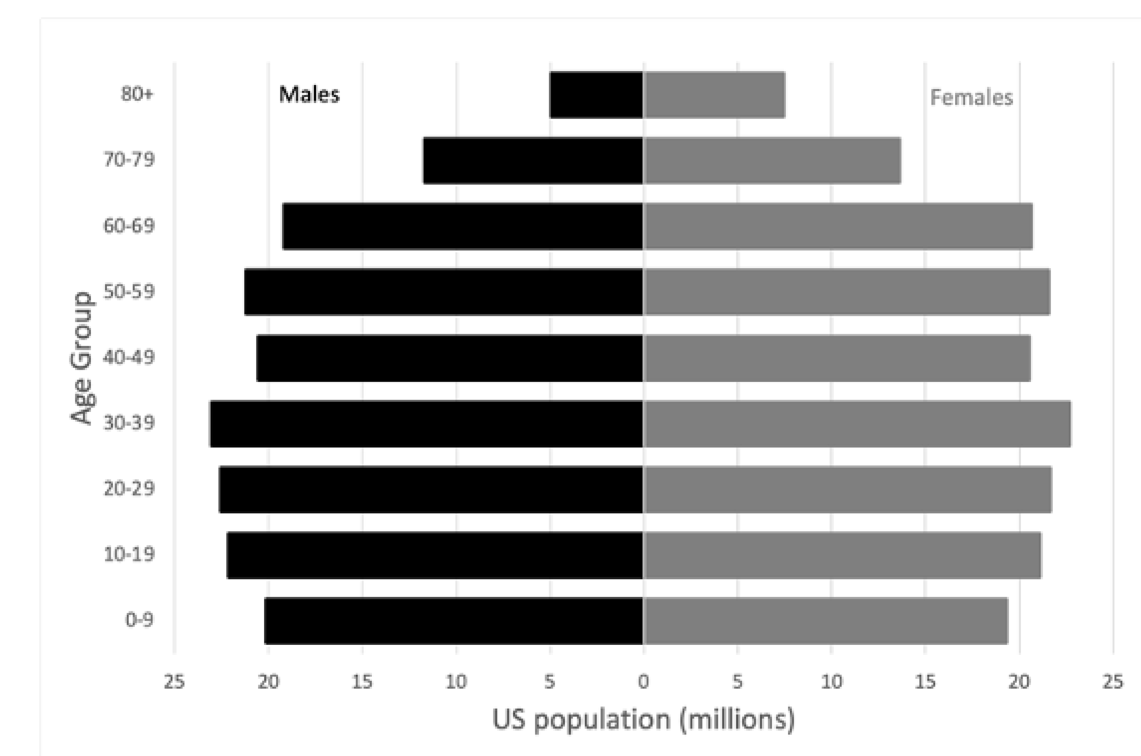
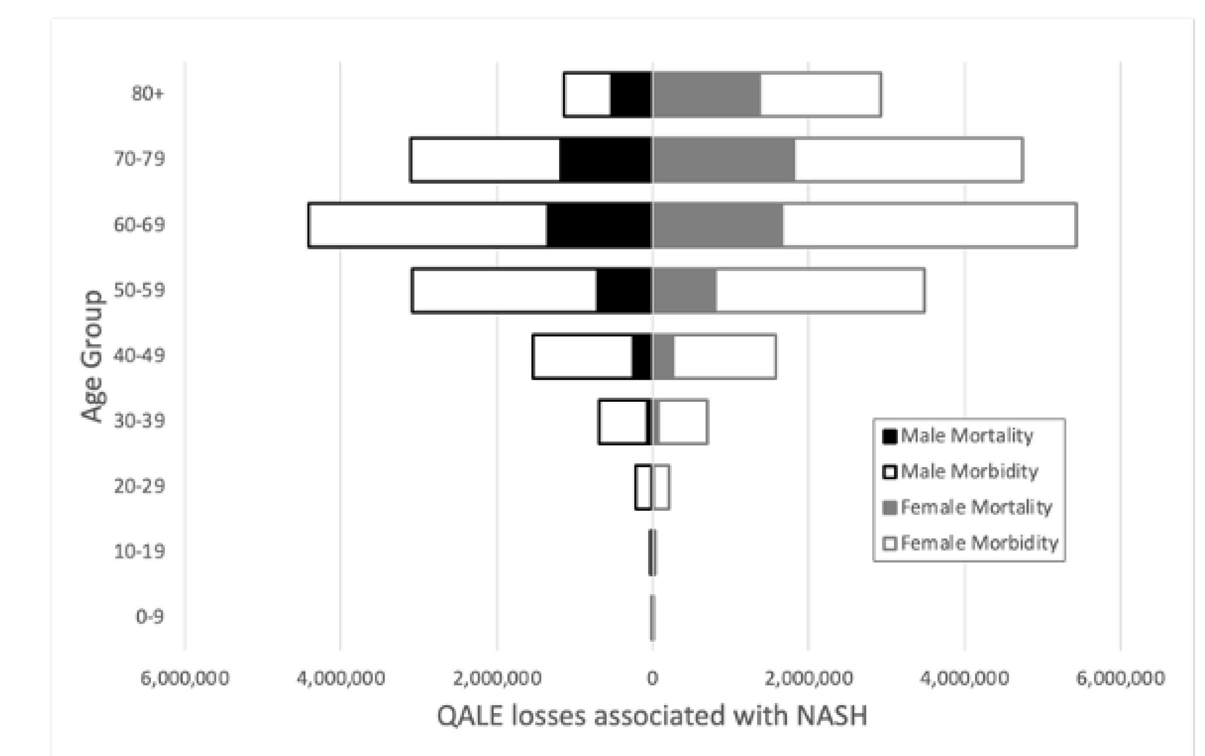


Figure 4. US population life course NASH burden



DISCUSSION AND CONCLUSIONS

- Our population analysis of NASH burden is based on similar incident models of NASH that have appeared in the literature
- Our population pyramid approach to presenting the burden shows a number of insights
- Morbidity is a greater burden than mortality for NASH
- Due to the insidious nature of NASH, the burden is likely to be concentrated in 7th decade of life (60-69 year olds)
- Due to the relative longevity of women, the burden for females is higher than for males without differential incidence

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DISCLOSURES

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