

Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030

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Search Parameters

Searches for relevant model inputs were conducted in PubMed and EMBASE. Search terms were limited to studies of NAFLD / NASH in selected countries. In addition, national and international databases and publications were used to develop longitudinal estimates for the prevalence of adult obesity and type 2 diabetes mellitus (DM) in each country, along with estimates for the number of incident liver cancers and liver transplantations at the national level, where such data were available.

Search Terms	PubMed	EMBASE
NAFLD / NASH	(NAFLD OR NASH OR steatosis OR steatohepatitis OR (fatty liver))	('NAFLD'/exp OR NAFLD) OR ('NASH'/exp OR NASH) OR ('steatosis'/exp OR steatosis) OR ('steatohepatitis'/exp OR steatohepatitis) OR ('fatty liver'/exp OR fatty liver)
Country	China OR Hong Kong OR Taiwan OR France OR Germany OR Italy OR Spain OR United Kingdom OR UK OR England OR Scotland OR United States OR US	'China' OR 'Hong Kong' OR 'Taiwan' OR 'France' OR 'Germany' OR 'Italy' OR 'Spain' OR 'United Kingdom' OR 'UK' OR 'England' OR 'Scotland' OR 'United States' OR 'US'

Data collected – NAFLD and NASH prevalence, as well as data for the distribution of cases by sex, age and disease state were collected, when available. In addition, data for the study population, sample size, dates of data collection, and analysis type (meta-analysis, modeling, review article, surveillance study or other/unknown) were extracted from each publication.

Delphi Process

Expert consensus was developed using a modified Delphi process as described in Table 1.

Table S1. Delphi Process

Activities		
Phase 1 – Data Gathering	1a	<p>Identify country experts who are willing to collaborate</p> <ul style="list-style-type: none"> Experts were identified through NAFLD-related scientific contributions, or through referrals and recommendations from leading researchers.
	1b	<p>Literature Search</p> <ul style="list-style-type: none"> Review the internal database for previously identified sources Review online sources (e.g., CDC, etc.) to capture non-indexed sources Run a literature search to identify recent publications Summarize input data available through the literature Gather empirical data for new HCC cases, liver transplants, percent of HCC and transplants due to NAFLD, percent of cases with obesity or DM Build draft model based on published data Schedule meeting with experts
Phase 2 – Country Meetings and Modeling	2a	<p>Expert Meeting 1 (2-3 hours)</p> <ul style="list-style-type: none"> Provide a background on the project, model and methodology Review data identified in Phase 1b and highlight gaps in data Request data in local non-indexed journals, unpublished data and any other available data (e.g., hospital-level data) that can be used to fill the gaps Gain agreement on data sources that can be used as for extrapolation when no local data are available <p>Follow up with Experts Post Meeting 1</p> <ul style="list-style-type: none"> Send minutes of the meeting and list of remaining action items to experts Follow up with experts to collect missing data and get copies of publications, government reports and unpublished data (e.g., raw hospital or registry-level data) Analyze raw data and send to experts for approval
	2b	
	2c	<p>Disease Burden Modeling</p> <ul style="list-style-type: none"> Populate disease burden model with inputs and calibrate model to empirical data Schedule second meeting Develop a slide deck summarizing all inputs and associated data sources Perform a final check of the model and slide deck and approve internally <p>Expert Meeting 2 (2-3 hours)</p> <ul style="list-style-type: none"> Review all inputs as well as data provided by experts since meeting 1 and results of analyses of any raw data provided Gain agreement on all inputs to be used in the model Update the model using any updated inputs
	2d	
Phase 3 – Follow-up Analyses	3a	<p>Follow-up Analyses</p> <ul style="list-style-type: none"> Update model as necessary and send results to experts Provide support to address follow-up questions Finalize approved inputs and outputs Update analysis as new information becomes available (e.g., new national studies, updated treatment data)

Input Data Sources

The data sources that were approved to be used for each country analysis are shown in Table 2.

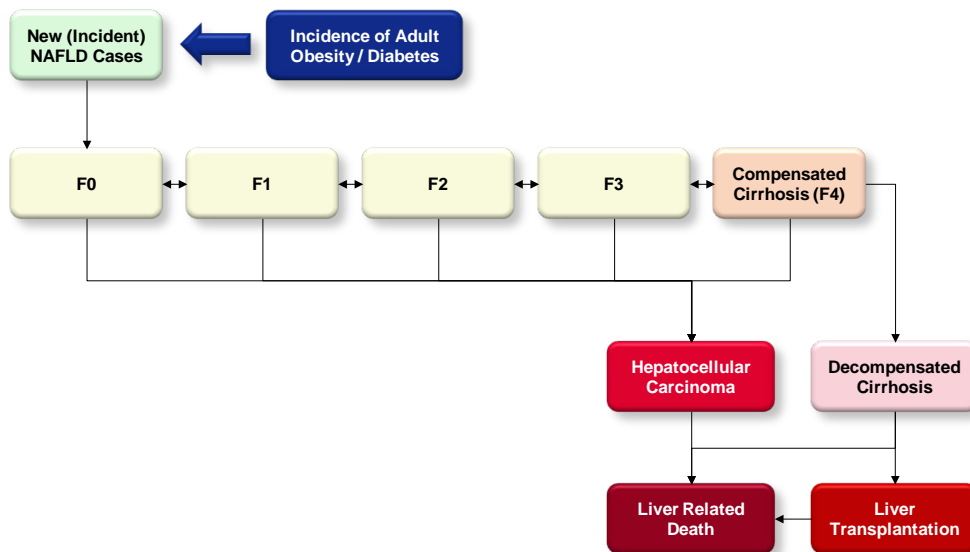
Table S2. Data Sources

	China	France	Germany	Italy	Japan	Spain	UK	US
Adult Obesity Prevalence	[1, 2]	[3-5]	[6]	[7, 8]	[9]	[10]	[11, 12]	[13, 14]
Adult Diabetes Prevalence	[15, 16]	[17, 18]	[19, 20]	[21]	[22]	[23, 24]	[25]	[26, 27]
HCC Incidence		[28, 29]		[29-31]	[32]	[23]	[33]	[34, 35]
% HCC NAFLD / NASH Related							[36]	[37]
Total Transplants	[38]	[39]	[40]	[41, 42]	[43]	[44]	[45]	[34, 46]
% NAFLD related		[39]				[44]	[47]	[48]
NAFLD Prevalence by Age and Gender	[49]					[50]		[51]

Markov Model

The Markov model (Figure 1) was built using Microsoft Excel® (Microsoft Corp., Redmond, WA) to track the annual NAFLD population by fibrosis stage and NASH status (steatosis only [NAFL] or NASH) from 1950-2030.

Fig. S1. NAFLD Disease Progression Model



Beginning with the estimated annual new NAFLD cases (defined as the onset of steatosis rather than newly diagnosed), fibrosis progression of all cases was modeled through 2030. Cases by stage of disease were calculated annually by age and gender,

with one-year age cohorts through age 84 and cases aged ≥ 85 years tracked as a single cohort. Annually, the population in each age group (excluding the ≥ 85 year cohort) was advanced to the next age to simulate the impact of aging. Historical and medium-fertility projection population data for all countries were obtained from the United Nations' population database by gender and one year age cohort [52].

Disease progression through fibrosis and advanced liver disease (decompensated cirrhosis and HCC) (Figure 1) was estimated with adjustment for all-cause mortality (including general background, excess cardiovascular and liver-related mortality). New cases by disease stage ($New\ Cases_{stage\ x}$) were calculated by multiplying progression rates and the total cases at prior stages of the disease in the previous year ($Total\ Cases_{stage\ x-1, Year\ Y-1}$) as shown in Equation 1.

Equation 1

$$Total\ Cases_{Stage_x \& Year_y \& Age\ Cohort_z} = \left(Total\ Cases_{Stage_x \& Year_{y-1} \& Age\ Cohort_{z-1}} \right) + New\ Cases_{Stage_x \& Year_y \& Age\ Cohort_z} - All\ Cause\ Mortality_{Stage_x \& Year_y \& Age\ Cohort_z} - Progressed_{Stage_x \& Year_y \& Age\ Cohort_z}$$

where:

$$New\ Cases_{Stage_x \& Year_y \& Age\ Cohort_z} = (Total\ Cases_{Stage_{x-1} \& Year_{y-1} \& Age\ Cohort_z})(Progression\ Rate_{Stage_{x-1} \rightarrow Stage_x \& Age\ Cohort_z})$$

$$Background\ Mortality_{Stage_x \& Year_y \& Age\ Cohort_z} = (Total\ Cases_{Stage_x \& Year_{y-1} \& Age\ Cohort_z})([Background\ Mortality\ Rate][CVD\ Multiplier]_{Age\ Cohort_z})$$

$$Progressed_{Stage_x \& Year_y \& Age\ Cohort_z} = (Total\ Cases_{Stage_{x-1} \& Year_{y-1} \& Age\ Cohort_z})(Progression\ Rate_{Stage_{x-1} \rightarrow Stage_{x+1} \& Age\ Cohort_z})$$

$$Liver\ Related\ Mortality_{Stage_x \& Year_y \& Age\ Cohort_z} = \left(Total\ Cases_{Stage_x \& Year_{y-1} \& Age\ Cohort_{z-1}} - Adjusted\ Background\ Mortality_{Stage_x \& Year_y \& Age\ Cohort_z} - Progressed_{Stage_x \& Year_y \& Age\ Cohort_z} \right) (Liver\ Related\ Mortality\ Rate_{Year_{y-1} \& Age\ Cohort_{z-1}})$$

Transition Rates

The annual transition probabilities were based on published estimates and expert consensus as shown in Table 3.

Table S3. Disease Stage Annual Transitions Rates

Disease Stage Transition	Annual Rate	Source
F0 to F1	0.3-2.2%	Back-calculated
F0 to HCC	0.0004%	[37, 53]
F1 to F2	2.8-13.3%	Back-calculated
F1 to HCC	0.011%	[37, 53]
F2 to F3	2.8-13.3%	Back-calculated
F2 to HCC	0.022%	[37, 53]
F3 to F4 (Cirrhosis)	3.8-9.9%	Back-calculated
F3 to HCC	0.044%	[37, 53]
Cirrhosis to Decomp Cirrhosis	3.80%	[54]
Cirrhosis to HCC	0.34%	[37, 53]
Decomp Cirrhosis to Liver Rel. Death	20.0%	[54]
HCC to Liver Rel. Death (Yr 1)	61.0%	[37]
HCC to L.R. Death (Sub Yrs)	16.2%	[55]

However, single annual transition rates resulted in poor validation of the models – comparison of modeled and reported HCC cases, as described below.

Thus, age and gender specific fibrosis progression rates were developed based on assumptions for the distribution of cases by NASH status and fibrosis stage, as described below. Fibrosis progression rates are available from studies analyzing consecutive liver biopsies, but report highly varied rates, including negative progression (e.g. regression) [56]. For the purpose of the model, progression rates were assumed to be the sum of forward progression minus the rate of regression. Where data or expert input were available for the incidence of NAFLD-related HCC, decompensated cirrhosis and related mortality, progression rates were modified to align with reported data and expert consensus (Table 3). A long term follow up study of individuals with NASH-

related cirrhosis reported that 45% experienced liver failure or decompensated cirrhosis, defined as an increase in Child-Turcotte-Pugh score by 2 points over twelve years of follow up in patients with Child Class A Cirrhosis [54]. An annual progression rate of 3.8% decompensation among cirrhotics was calculated and applied in the model.

Fibrosis progression rates was further adjusted with overweight individuals (BMI 25 to $<30\text{kg/m}^2$) having 2.35 greater odds and obese individuals (BMI $\geq 30\text{kg/m}^2$) having 5.70 greater odds of advanced fibrosis [57] (Table 4). It was assumed that relative differences at the national level in the proportion of overweight and obese individuals would be reflective of each country's NAFLD populations.

For every country, it was assumed that 64% of incident HCC cases would occur among cirrhotics [53]. Using US data as an analogue, the annual transition rate from F4 to HCC was estimated at 0.33%. The remaining 36% of incident HCC cases occurred among F0-F3 cases. The incidence rate among F3 cases was back-calculated and progression decreased exponentially with each decreasing level of fibrosis from 0.038% (F3 to HCC) to 0.00035% (F0 to HCC) (Table 3). NAFLD-related HCC cases may experience greater mortality as compared to HCV-related HCC; first year mortality (61%) was applied to new HCC cases, with subsequent years mortality rates based on long-term survival data [37, 55]. A long term follow up study of individuals with NASH-related cirrhosis reported an annual progression rate of 3.8% for clinical decompensation [54] (increase of 2 in Child Turcotte Pugh score among Child Class A Cirrhosis [58, 59]) and this rate was applied in the model. The annual calculated transition rates, by country, are shown in Table 4.

Table S4. Fibrosis Transition Probabilities by Country, Disease Stage, Sex and Age Group

China Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%
High	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Females	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
High	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%
Low	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%
High	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%
Females	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%
Low	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%
High	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%	8.8%
Low	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%
High	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%
Females	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%
Low	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%
High	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%	11.3%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.4%	3.4%	3.4%	3.4%	3.4%	3.4%	3.4%	3.4%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%
Low	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%
High	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	10.5%	10.5%	10.5%	10.5%	10.5%	10.5%	10.5%	10.5%	10.5%	10.5%
Females	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%
Low	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	1.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%
High	5.4%	5.4%	5.4%	5.4%	5.4%	5.4%	5.4%	5.4%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%

France Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
High	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
Females	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
High	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%
Low	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%
High	6.0%	6.0%	6.0%	6.0%	6.0%	6.0%	6.0%	6.0%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%
Females	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%
Low	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%
High	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%	10.3%
Low	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%
High	6.0%	6.0%	6.0%	6.0%	6.0%	6.0%	6.0%	6.0%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%
Females	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%	8.6%
Low	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%
High	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%
Low	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%	4.4%
High	9.0%	9.0%	9.0%	9.0%	9.0%	9.0%	9.0%	9.0%	14.7%	14.7%	14.7%	14.7%	14.7%	14.7%	14.7%	14.7%	14.7%	14.7%
Females	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	3.9%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%
Low	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	3.7%	3.7%	3.7%	3.7%	3.7%	3.7%	3.7%	3.7%	3.7%	3.7%
High	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	12.2%	12.2%	12.2%	12.2%	12.2%	12.2%	12.2%	12.2%	12.2%	12.2%

Germany Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%
High	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%
Females	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
High	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%
High	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%
Females	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%
Low	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%
High	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%	11.4%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%	6.7%
High	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%	17.5%
Females	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	3.6%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%	9.5%
Low	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%	5.6%
High	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%	14.5%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	8.5%	8.5%	8.5%	8.5%	8.5%	8.5%	8.5%	8.5%	8.5%	8.5%
Low	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%
High	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%
Females	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	7.1%	7.1%	7.1%	7.1%	7.1%	7.1%	7.1%	7.1%	7.1%	7.1%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%
High	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%	13.5%

Italy Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
High	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%	2.1%
Females	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
High	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%	1.7%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%
Low	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%
High	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%
Females	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%
Low	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%
High	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%
Low	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%
High	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%	19.4%
Females	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%
Low	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%	6.2%
High	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%	16.2%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	7.9%	7.9%	7.9%	7.9%	7.9%	7.9%	7.9%	7.9%	7.9%	7.9%
Low	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%
High	9.2%	9.2%	9.2%	9.2%	9.2%	9.2%	9.2%	9.2%	15.1%	15.1%	15.1%	15.1%	15.1%	15.1%	15.1%	15.1%	15.1%	15.1%
Females	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%	6.6%
Low	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	2.3%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%
High	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%	12.5%

Japan Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
High	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%
Females	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
Low	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.2%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%
High	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%
Low	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%
High	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%
Females	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%
Low	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%
High	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%
Low	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%	4.9%
High	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%	12.7%
Females	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%
Low	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%	4.1%
High	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%	10.6%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	3.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%	5.2%
Low	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
High	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%
Females	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%
Low	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
High	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	8.2%	8.2%	8.2%	8.2%	8.2%	8.2%	8.2%	8.2%	8.2%	8.2%

Spain Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%	1.4%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
High	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%
Females	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
High	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%
Low	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%
High	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%
Females	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%
High	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%
Low	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%
High	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%	20.4%
Females	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%	11.1%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%
High	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%
Low	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%	4.8%
High	9.7%	9.7%	9.7%	9.7%	9.7%	9.7%	9.7%	9.7%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%	15.8%
Females	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	4.3%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%
Low	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%	4.0%
High	8.1%	8.1%	8.1%	8.1%	8.1%	8.1%	8.1%	8.1%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%	13.2%

UK Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%
High	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	0.9%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%	2.4%
Females	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%
Low	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
High	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%
Low	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%
High	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%
Females	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Low	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%
High	5.8%	5.8%	5.8%	5.8%	5.8%	5.8%	5.8%	5.8%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	4.5%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%	11.9%
Low	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	2.7%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%	7.0%
High	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	6.9%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%	18.3%
Females	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	3.8%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Low	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%	5.9%
High	5.8%	5.8%	5.8%	5.8%	5.8%	5.8%	5.8%	5.8%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%	15.3%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	5.5%	8.9%	8.9%	8.9%	8.9%	8.9%	8.9%	8.9%	8.9%	8.9%	8.9%
Low	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	3.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%
High	10.4%	10.4%	10.4%	10.4%	10.4%	10.4%	10.4%	10.4%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%	17.0%
Females	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	4.6%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%	7.4%
Low	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	2.6%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%
High	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	8.7%	14.1%	14.1%	14.1%	14.1%	14.1%	14.1%	14.1%	14.1%	14.1%	14.1%

US Fibrosis Transition Probabilities by Disease Stage, Sex and Age Group

F0 to F1	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%
Low	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%
High	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	1.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%	3.3%
Females	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%	1.8%
Low	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	0.4%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%
High	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%	2.8%
F1 to F2	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%
Low	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%
High	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%
Females	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%
High	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%
F2 to F3	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%	13.3%
Low	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%	7.8%
High	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	7.7%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%	20.3%
Females	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	4.2%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%	11.0%
Low	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%	6.5%
High	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	6.4%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%	16.9%
F3 to F4 (Cirrhosis)	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Males	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%	9.9%
Low	3.5%	3.5%	3.5%	3.5%	3.5%	3.5%	3.5%	3.5%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%	5.7%
High	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	11.5%	18.8%	18.8%	18.8%	18.8%	18.8%	18.8%	18.8%	18.8%	18.8%	18.8%
Females	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	5.1%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%	8.3%
Low	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	2.9%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%	4.7%
High	9.6%	9.6%	9.6%	9.6%	9.6%	9.6%	9.6%	9.6%	15.7%	15.7%	15.7%	15.7%	15.7%	15.7%	15.7%	15.7%	15.7%	15.7%

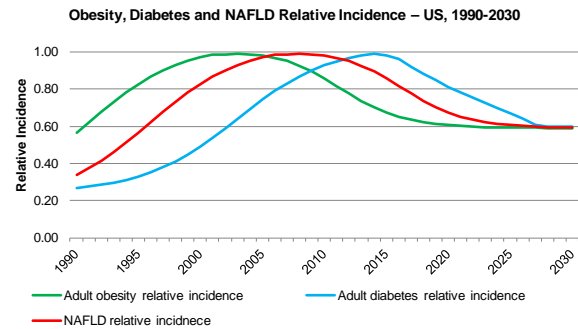
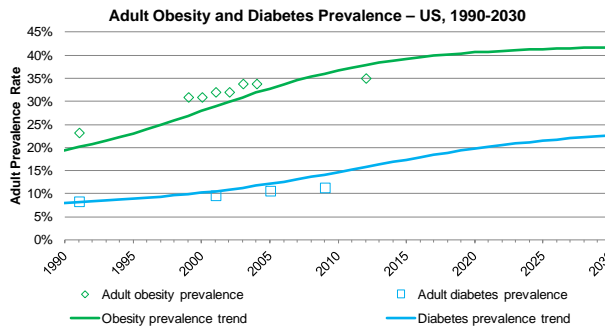
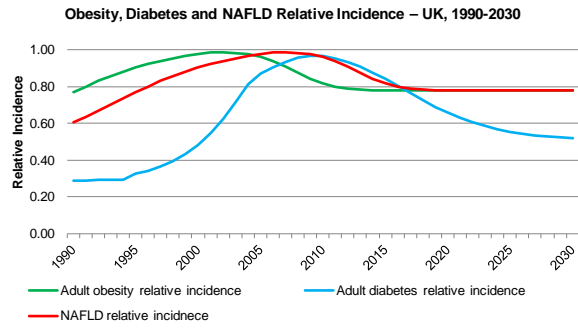
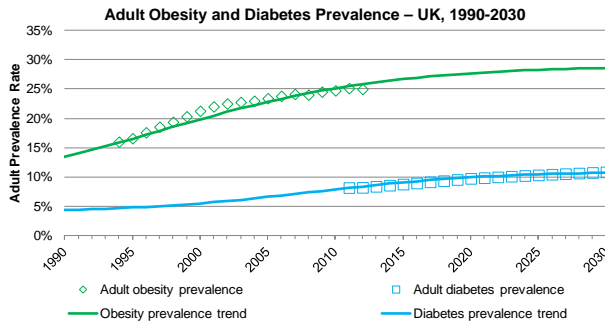
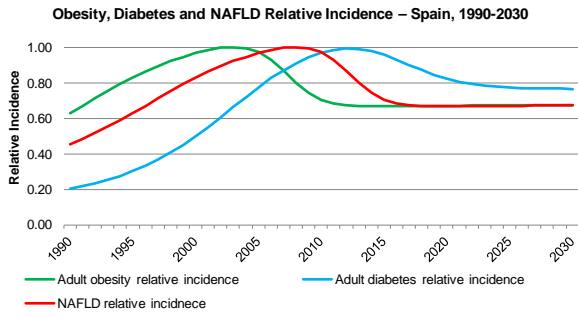
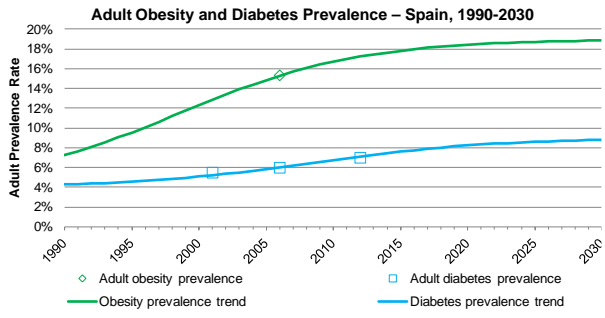
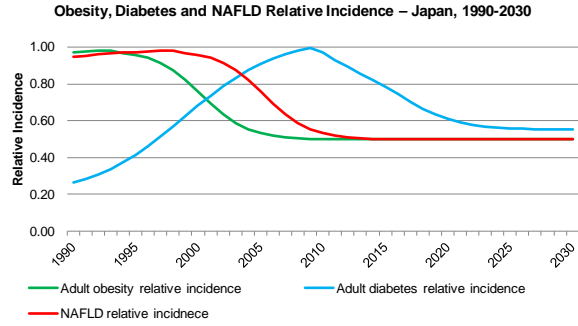
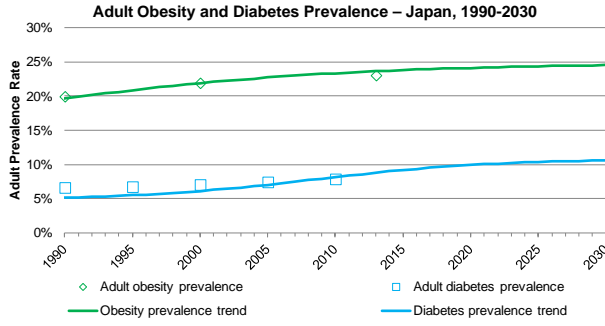
Incidence (New Cases) Calculations

Recent and accurate estimates of NAFLD incidence and prevalence were either unavailable, had limitations that precluded application to the general population, or were subject to varied diagnostic techniques. Therefore, annual changes in the number of new cases were back calculated using the change in obesity and DM as a surrogate for the change in new NAFLD cases. Total prevalent cases were assumed to be the sum of existing and new NAFLD cases after accounting for mortality, and were calibrated to the estimated prevalence of NAFLD in 2015. Incidence was used to describe new NAFLD cases (onset of steatosis) and not the time of first diagnosis.

In every country studied, the reported rates of adult obesity and diagnosed diabetes have increased over time (Figure 2). Unlike obesity, DM data are less readily available due to changes in awareness, screening, and diagnosis levels. In most countries, reliable estimates of true DM prevalence (diagnosed and undiagnosed) were unavailable until recent decades. Long term changes in adult obesity and DM prevalence were plotted and trend lines were examined to identify the time period in which the rate of increase was greatest (Figure 2). The growth in NAFLD new cases was assumed to follow the growth in obesity and lag behind the growth in DM as shown in Figure 2. Future trends in adult obesity and DM were forecasted using best-fit sigmoidal functions. The change in annual prevalence was used to estimate the change in new cases/incidence of adult obesity and DM. Due to the lower prevalence of DM, the incidence was scaled from 0 to 1 to allow side by side comparison. As shown in Figure 2, except for China, the rate of new (incidence) obesity and DM is forecasted to decrease while total cases (prevalence) will continue to increase (Figure 3).

Fig. S2. Relative Incidence and Prevalence Changes in Adult Obesity and Diabetes – 1990-2030





Published data suggest that males have a higher NAFLD prevalence than females and prevalence rates increase with age [49-51]. Relative incidence values describe changes in the annual number of new NAFLD cases. A curve was fitted from 1950 to the estimated peak and a second curve followed the decline in relative incidence (Figure 2). Relative changes in the number of total NAFLD cases and the distribution of NAFL versus NASH within the population were imputed from data related to trends for obesity and DM (Figure 2) for which more robust data existed. For China, urbanization level (proportion of individuals residing in urban areas) was also used to estimate increases in the adoption of obesigenic lifestyles [62].

Annual relative incidence values were used to describe changes in the annual number of new NAFLD cases over time. The Excel® Solver add-in was used to solve for the constant, which when multiplied by the annual relative incidence, resulted in the known prevalence after adjusting for mortality. This constant multiplied by the relative incidence provided the number of new NAFLD cases per year. Data related to the distribution of NAFL vs. NASH in these populations were used to impute the trends for these histological phenotypes [51, 63, 64].

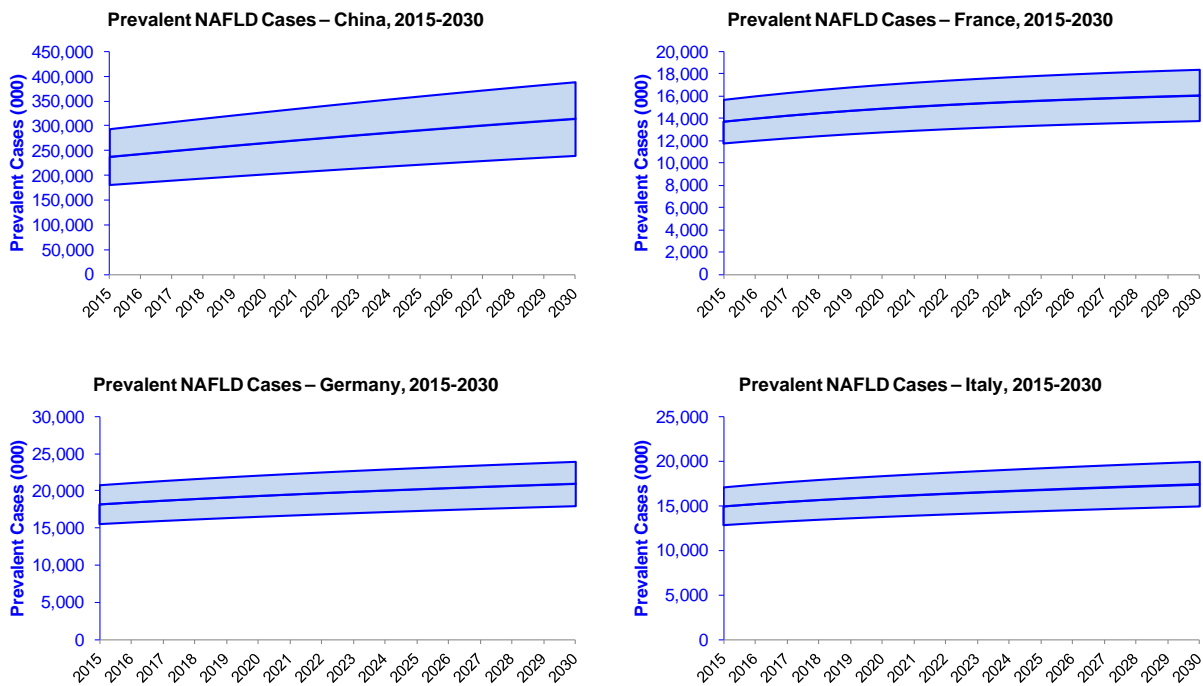
Next, annual incident cases were distributed by age and gender to fit the adjusted NAFLD prevalence. A weighting factor was applied to reported prevalence by age and gender in order to reach estimated NAFLD prevalence in the adult age groups in 2015. The percentage of the incident population allocated to each age and gender cohort in years 1950-1965 was set equal to 1966 and trended linearly in 5 five-year increments until 2011, at which point the percent of incident cases allocated to each age and gender cohort were held constant until 2030.

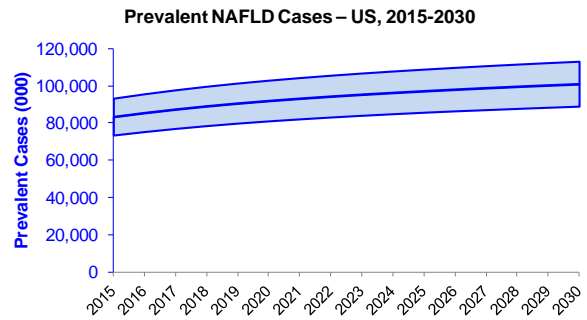
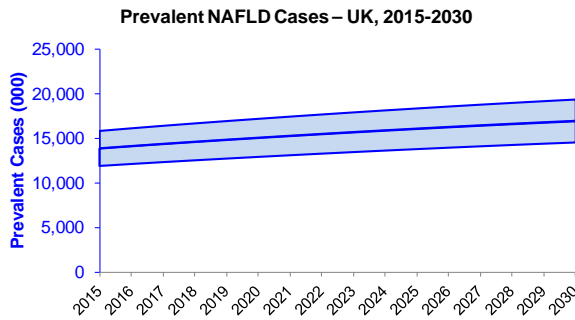
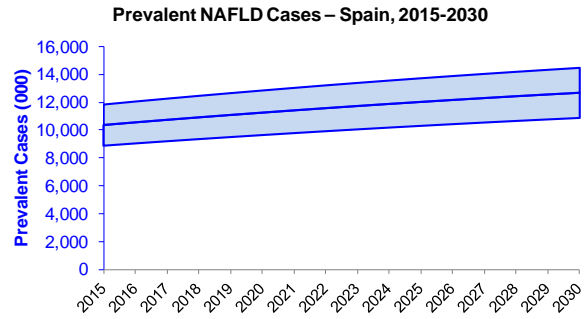
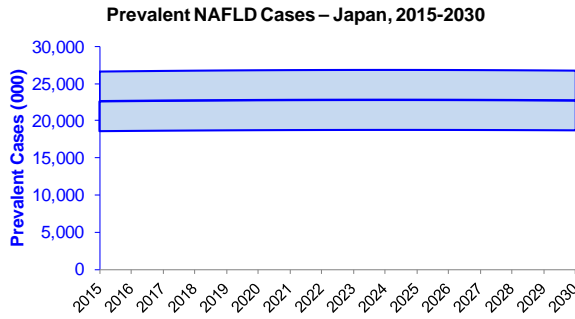
The relative impact of incident NAFLD cases occurring prior to 1950 was negligible and not included.

Uncertainty and Sensitivity Analysis

Uncertainty intervals (UI) were generated using Beta-PERT distributions around key uncertainties by Monte Carlo analysis using Oracle Crystal Ball® (Oracle Corp., Redwood City, CA, Release 11.1.3708.0). The prevalent NAFLD cases between 2016-2030 and the corresponding uncertainty intervals are shown in Figure 3. Asian countries (China and Japan) had higher uncertainty which will be reduced as the additional epidemiology studies are conducted. In addition, the movement of people from rural to urban area was also a key uncertainty in China as obesity is increasing more dramatically in the urban settings.

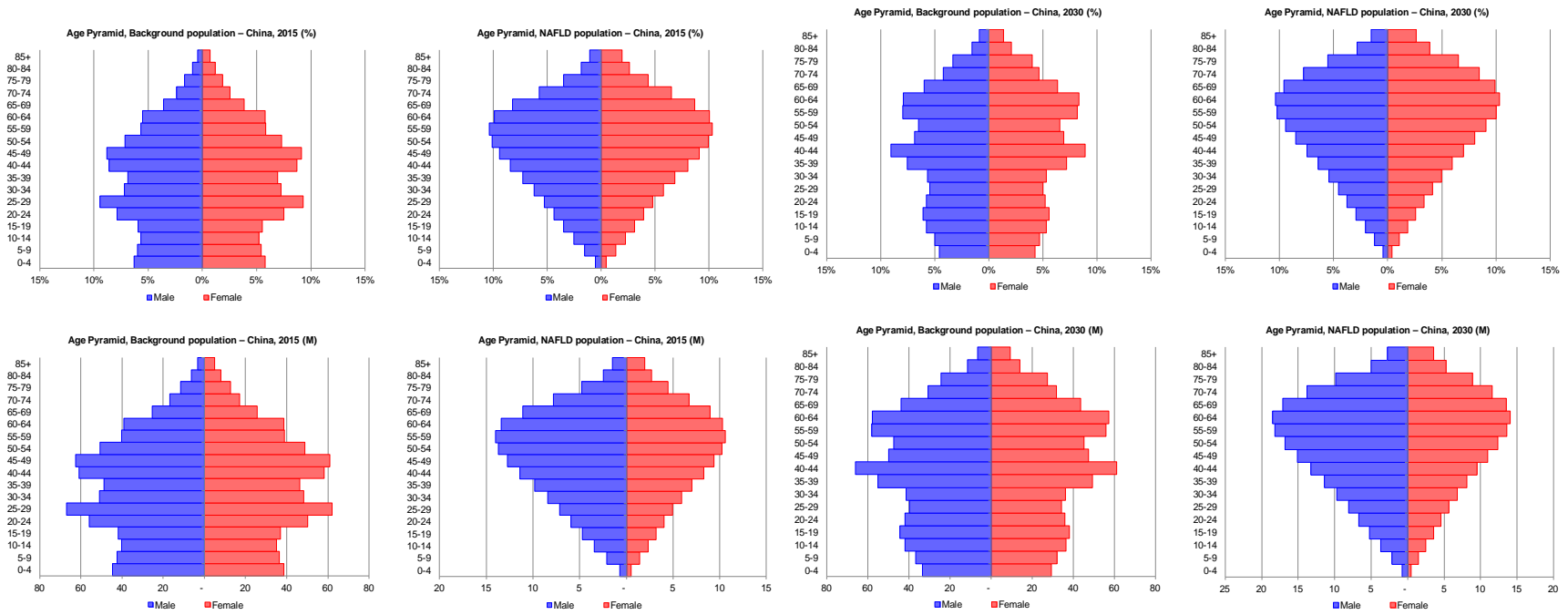
Fig. S3. Prevalent NAFLD Cases with Uncertainty Intervals, 2015-2030

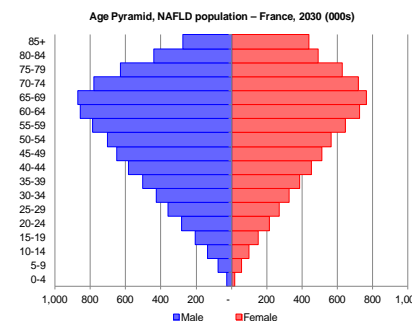
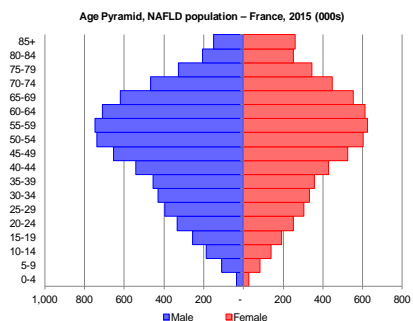
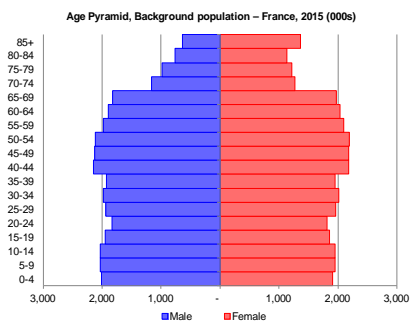
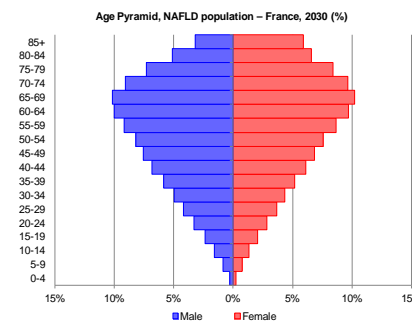
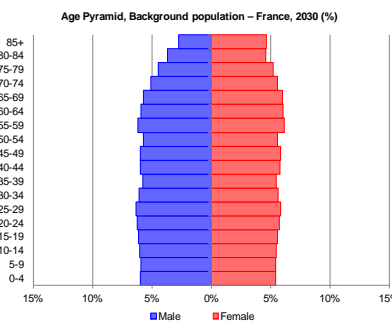
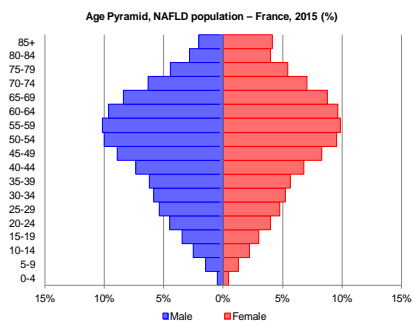
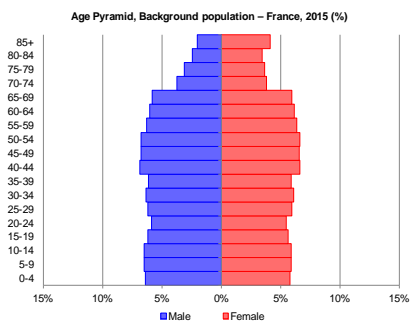


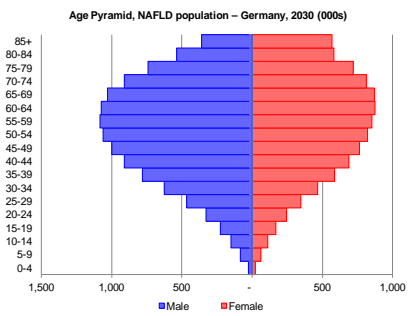
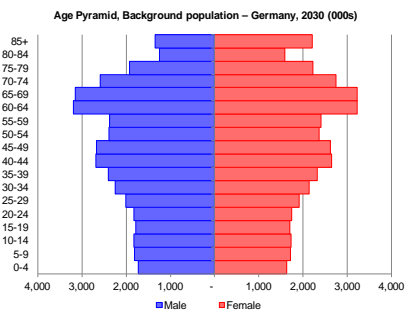
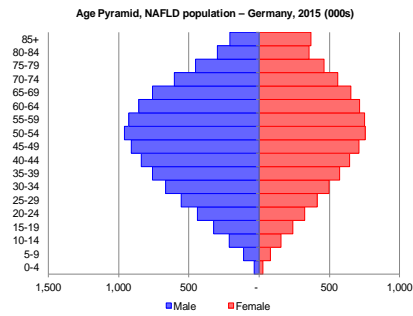
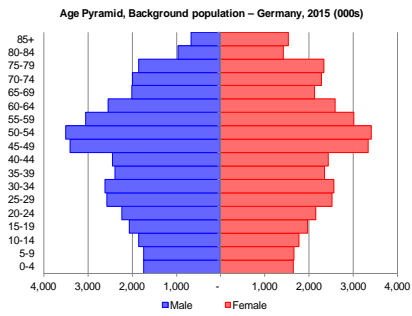
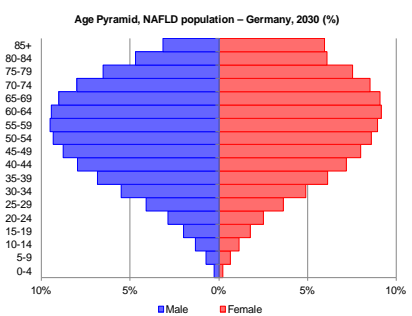
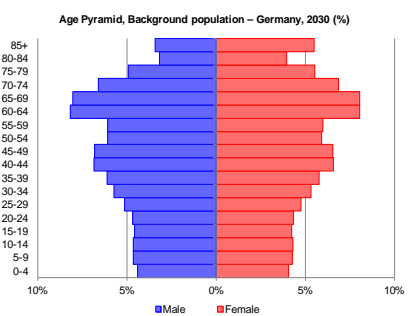
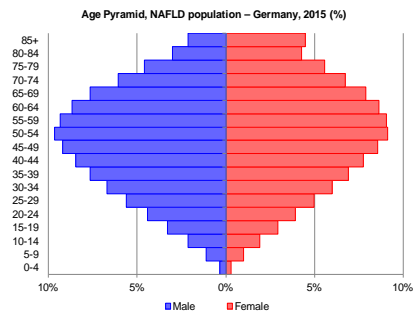
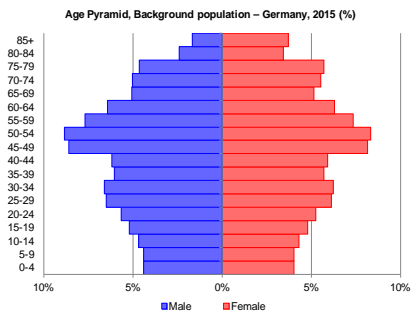


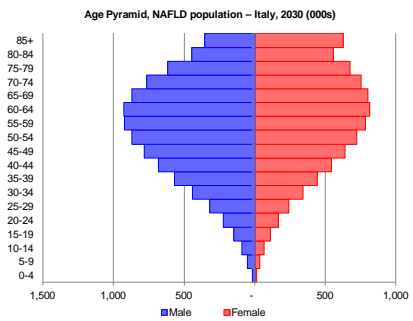
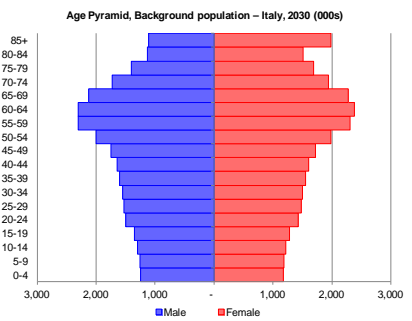
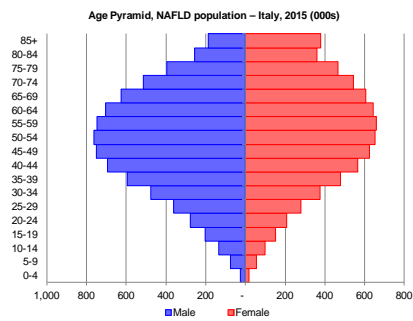
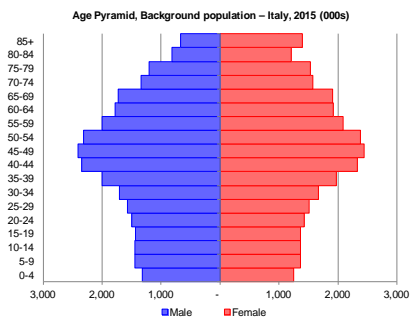
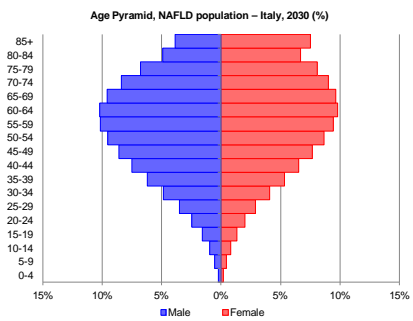
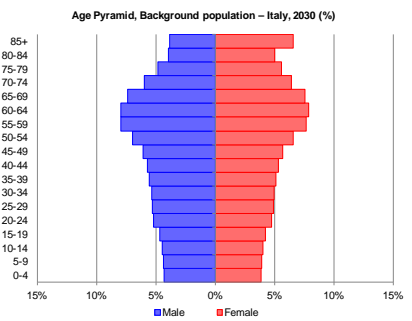
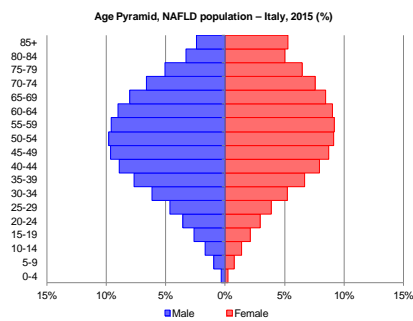
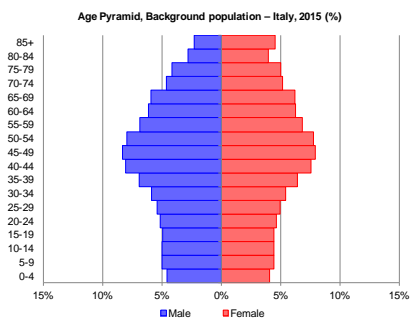
The age pyramid of the countries' and the NAFLD population are shown in Figure 4. Although there are considerable differences in countries' populations, the NAFLD populations have a more similar age distribution due to similar risk factors for NAFLD development across countries.

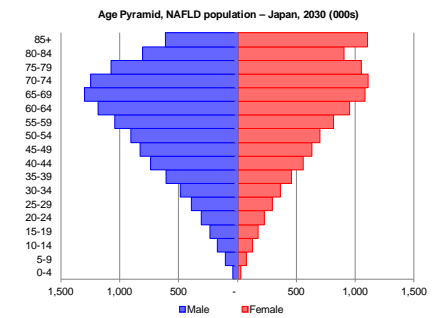
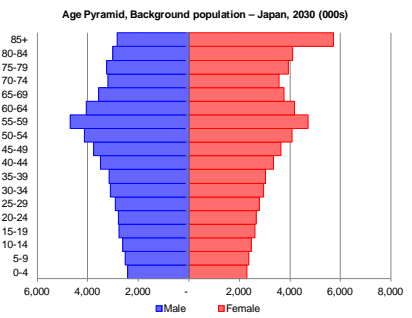
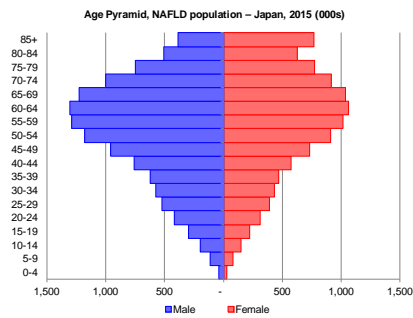
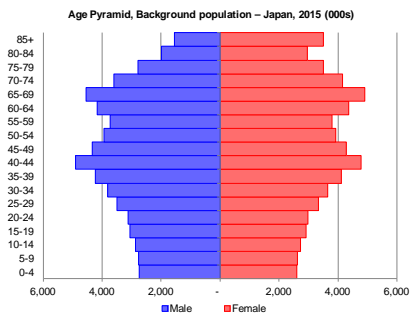
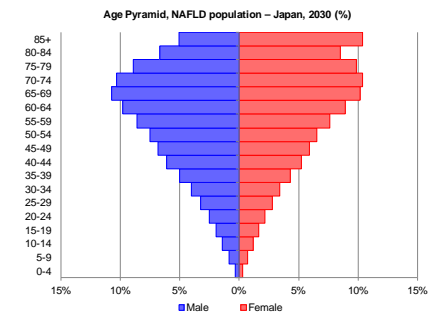
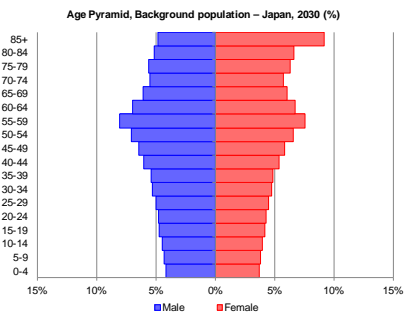
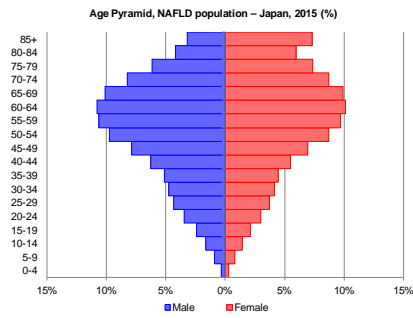
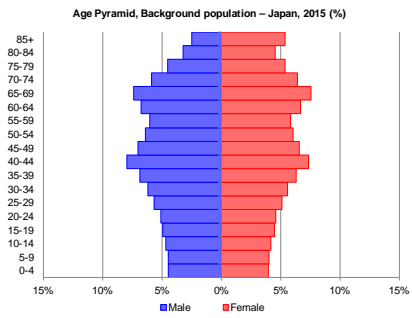
Fig. S4. Distribution of General and Prevalent NAFLD Populations by Sex and Age Group – 2015 & 2030

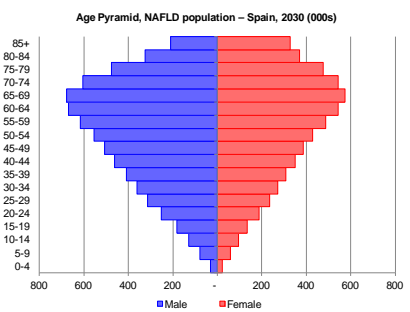
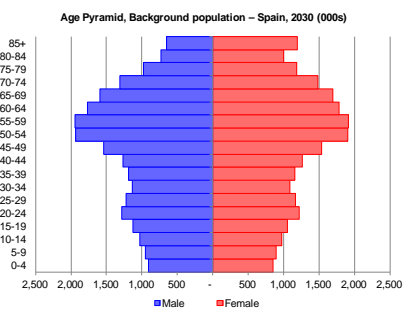
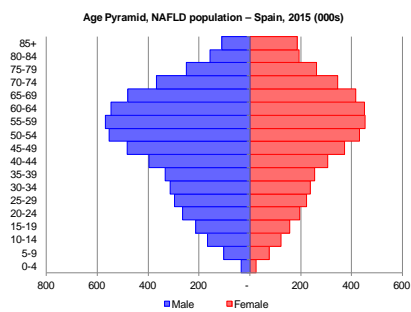
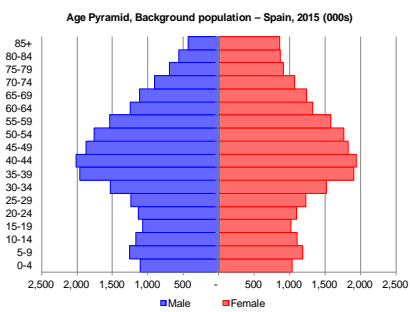
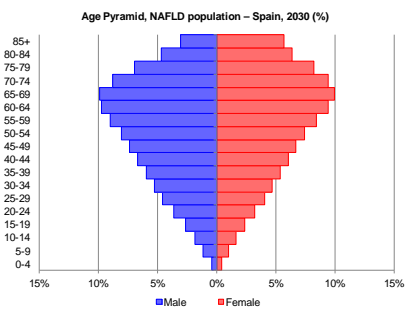
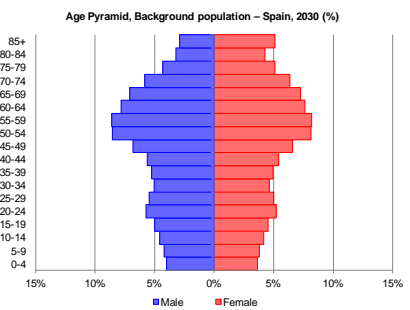
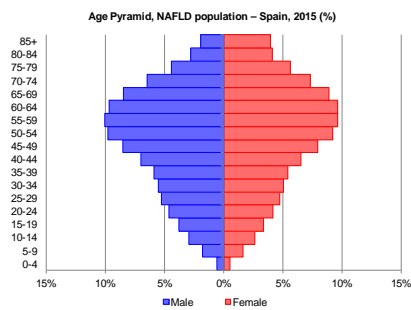
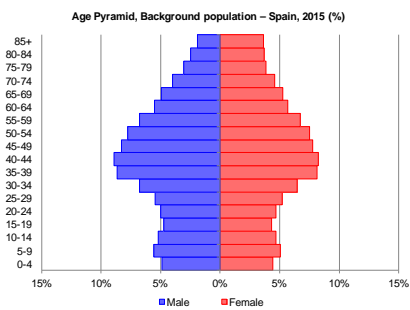


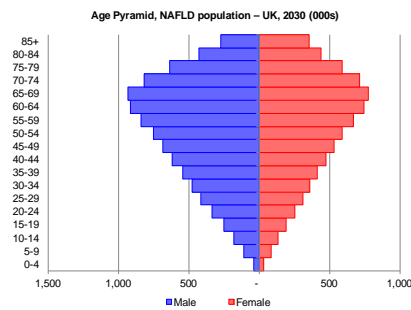
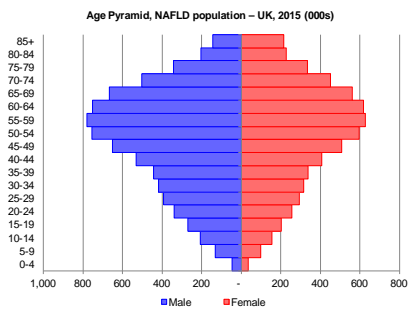
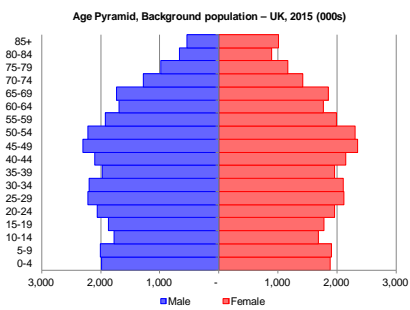
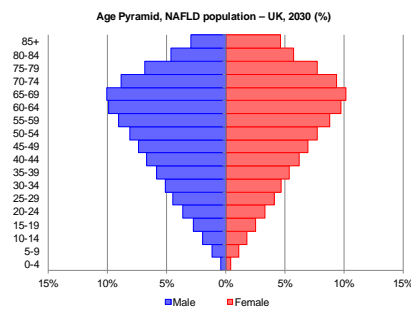
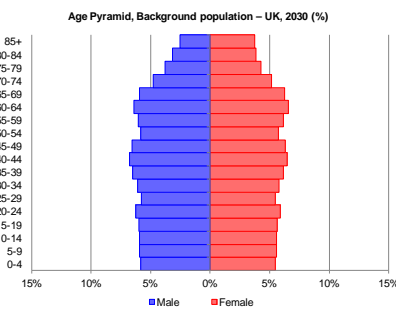
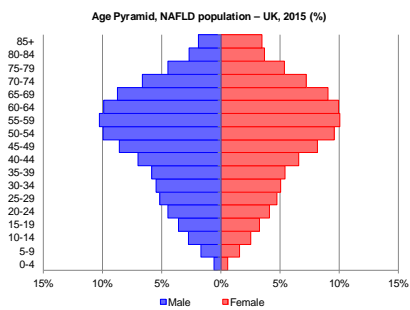
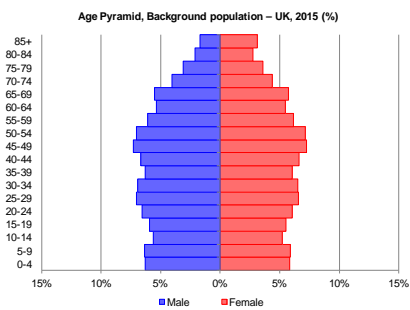


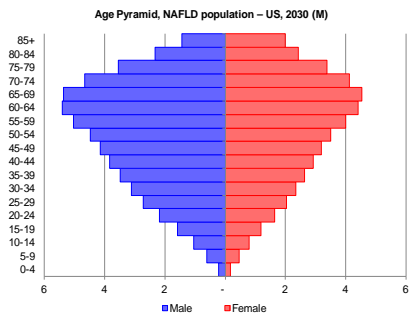
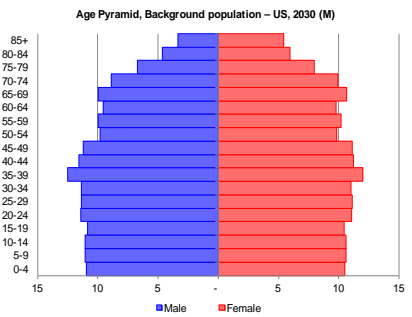
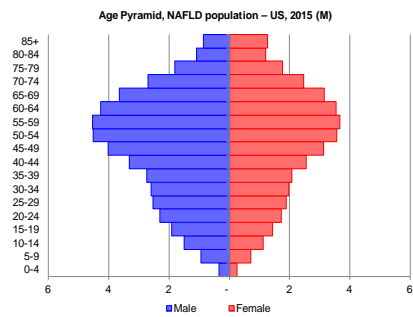
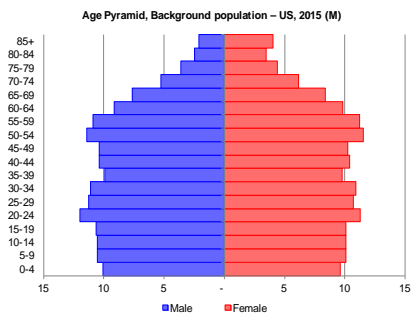
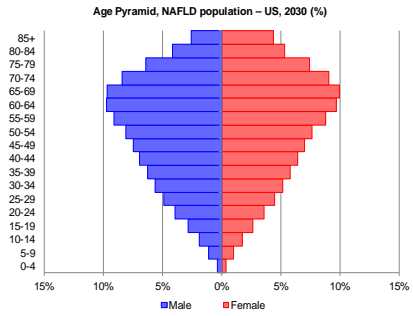
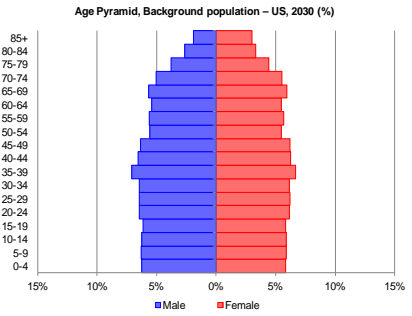
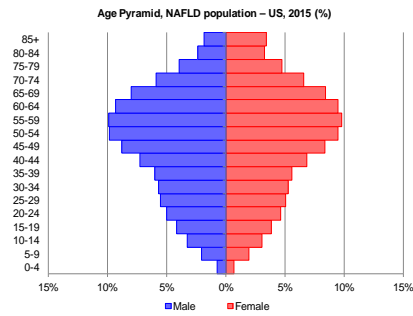
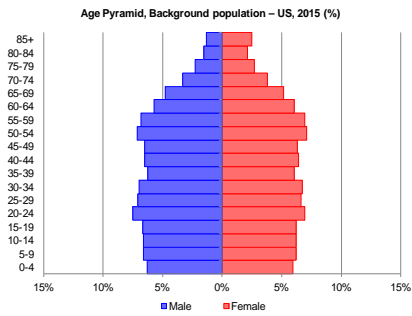












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