

Paris Hepatology Conference

PROGNOSIS OF NASH

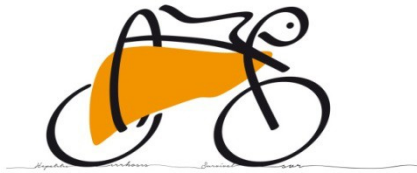
Palais des Congrès
Monday 15th January 2018
14:45-15:00

(NASH)



Prof. Jean-François Dufour

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Visceral Surgery
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Driven to care

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Disclosures

Advisory committees



Bayer HealthCare



Bristol-Myers Squibb



GENFIT
TOWARDS BETTER MEDICINE



GILEAD

Intercept



MERCK



NOVARTIS

Speaking and teaching



Bayer HealthCare

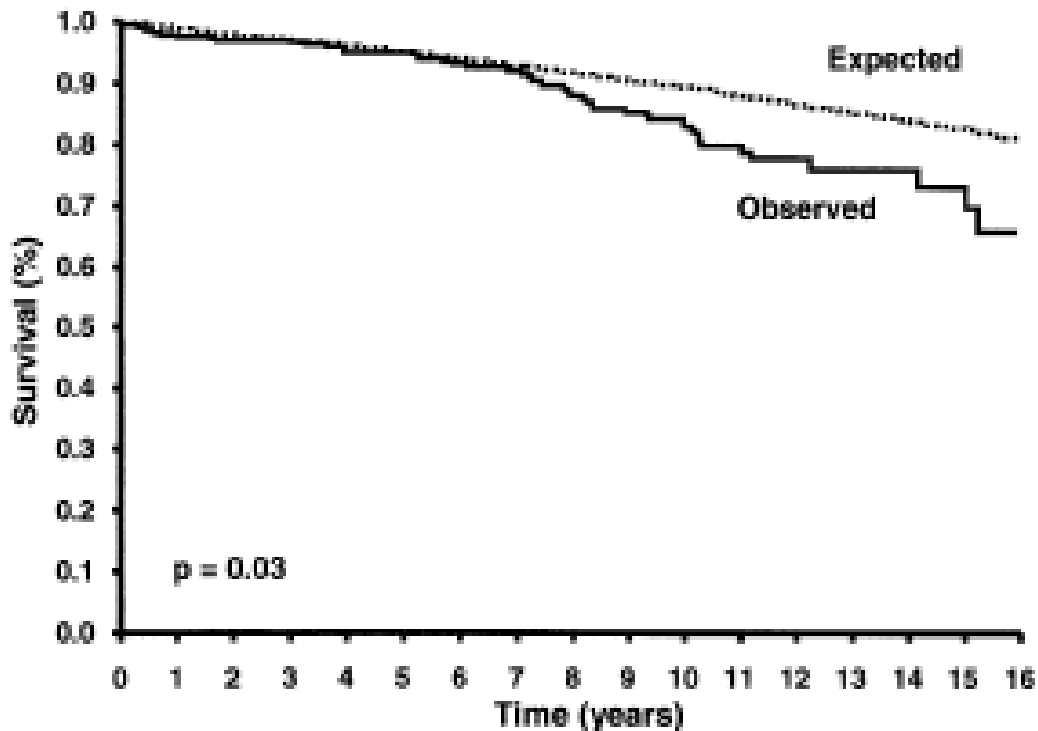
Intercept

Research grant



Bayer HealthCare

NAFLD is associated with higher mortality

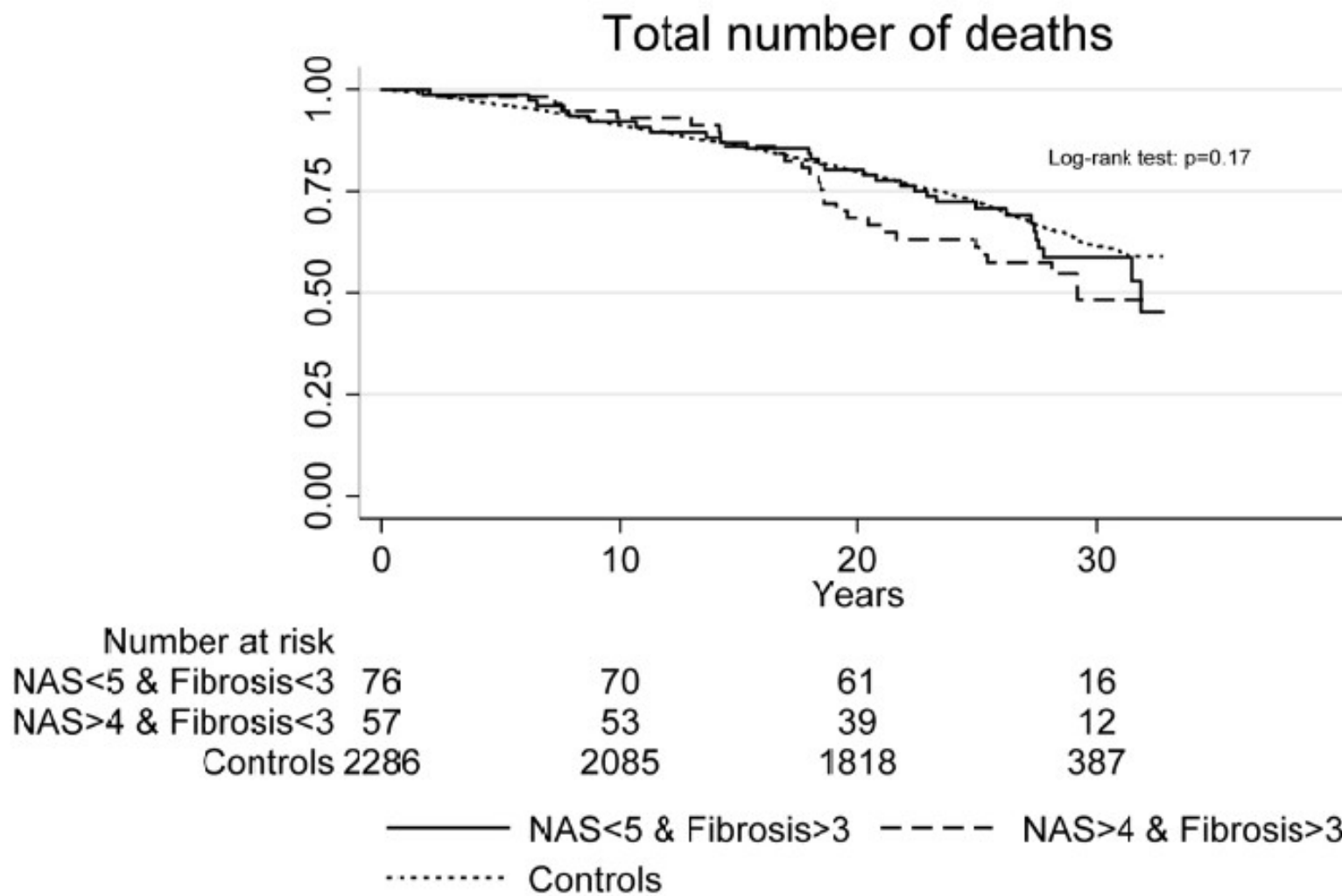


Retrospective

420 patients with steatosis
(Bx, sonography)

Median follow-up 7.6 years

Histological activity as predictor of mortality



Fibrosis stage as predictor of mortality

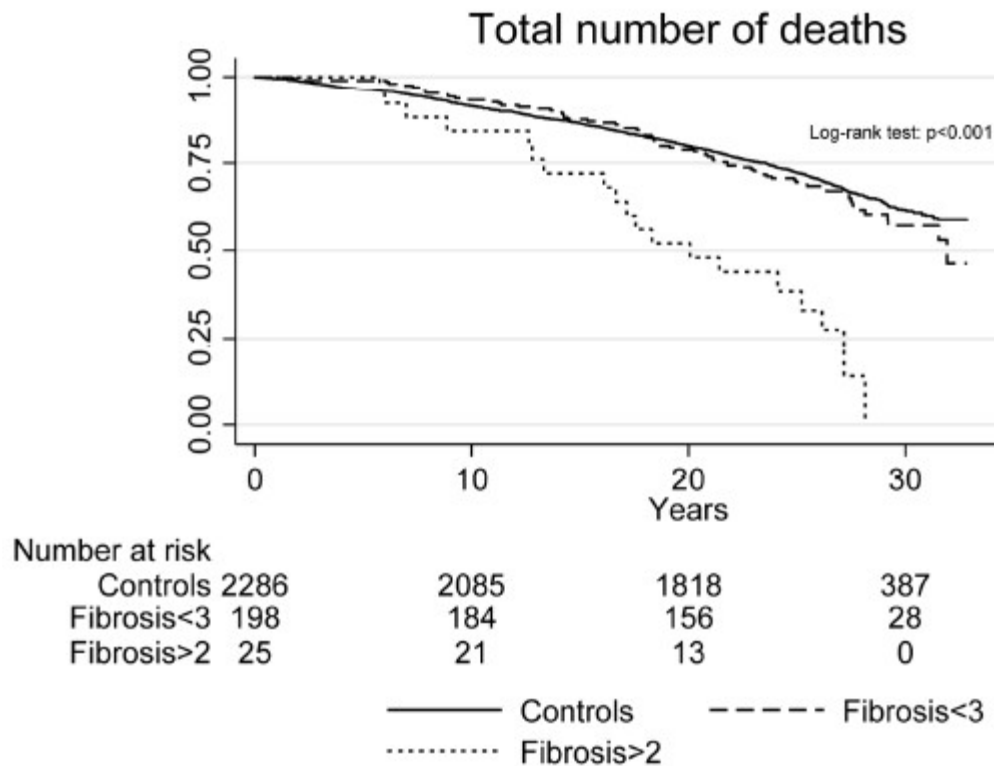


Table 3. Causes of death in NAFLD patients [n (%)].

Cause of death	Number of patients (n = 96)
Cardiovascular disease	41 (43%)
Non-gastrointestinal malignancy	18 (19%)
Hepatocellular carcinoma	5 (5%)
Infection	5 (5%)

NAFLD: Fibrosis determines outcomes

Retrospective longitudinal study

619 patients with biopsy proven NAFLD

From 1975 through 2005, median follow-up 12.6 years

North America, Europe, Asia

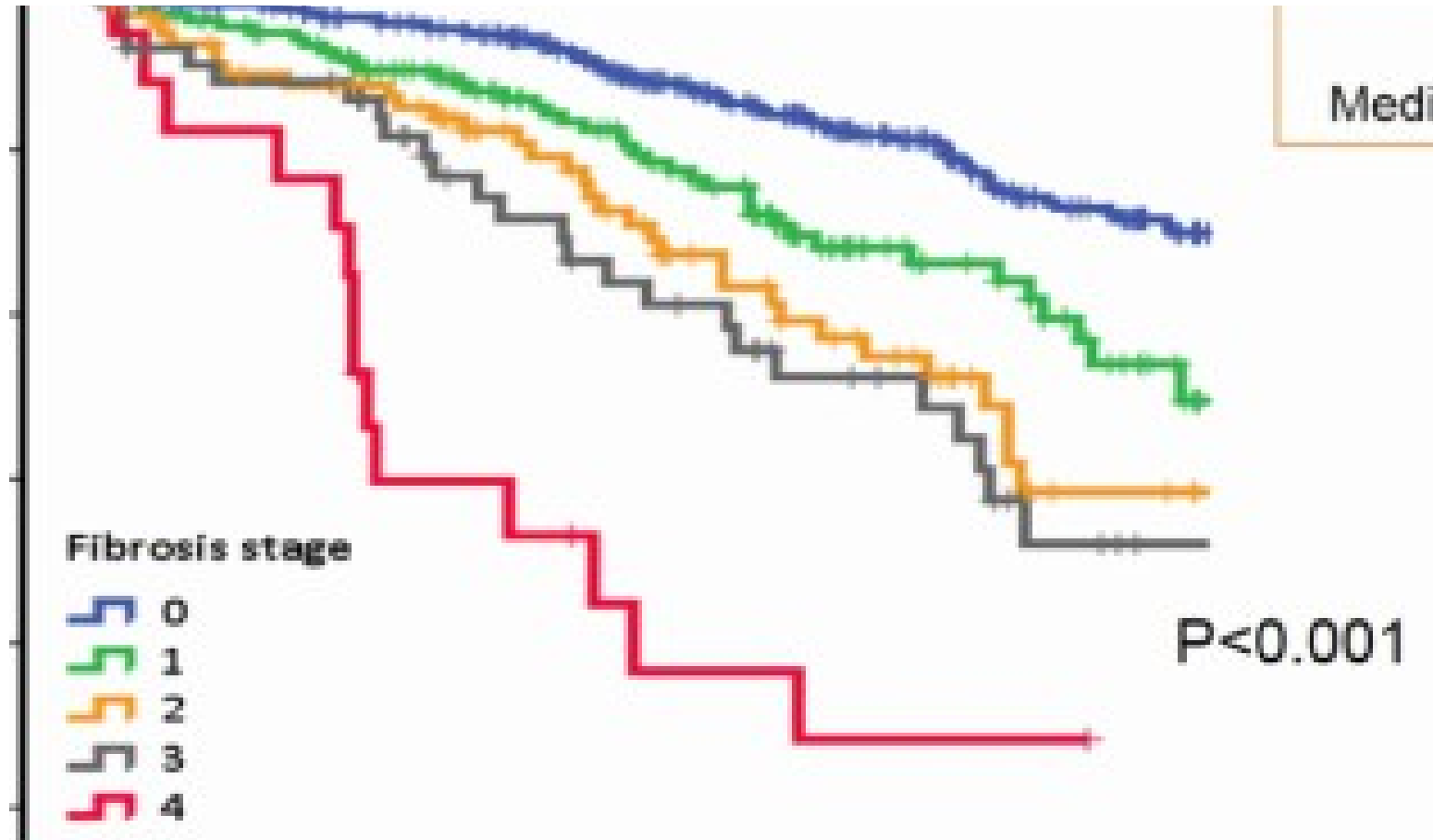
Slides centrally reviewed by 1 pathologist

NAFLD: Predict Mortality/OLT

Multivariate-Adjusted Hazard Ratios and 95% CIs of Outcome Mortality/Liver Transplantation

	Hazard ratio	95% CI of HR	P value
Fibrosis, stage 0	1 (reference)		
Fibrosis, stage 1	1.82	1.18–2.81	.007
Fibrosis, stage 2	1.91	1.20–3.03	.007
Fibrosis, stage 3	1.90	1.16–3.12	.01
Fibrosis, stage 4	6.35	3.35–12.04	<.001
Age, y	1.07	1.05–1.08	<.001
Diabetes, yes	1.60	1.11–2.30	.01
Smoking			
Never	1 (reference)		
Former	1.11	0.71–1.73	.640
Current	2.62	1.67–4.10	<.001
Statin use, yes	0.32	0.15–0.71	.005

Fibrosis determines outcomes

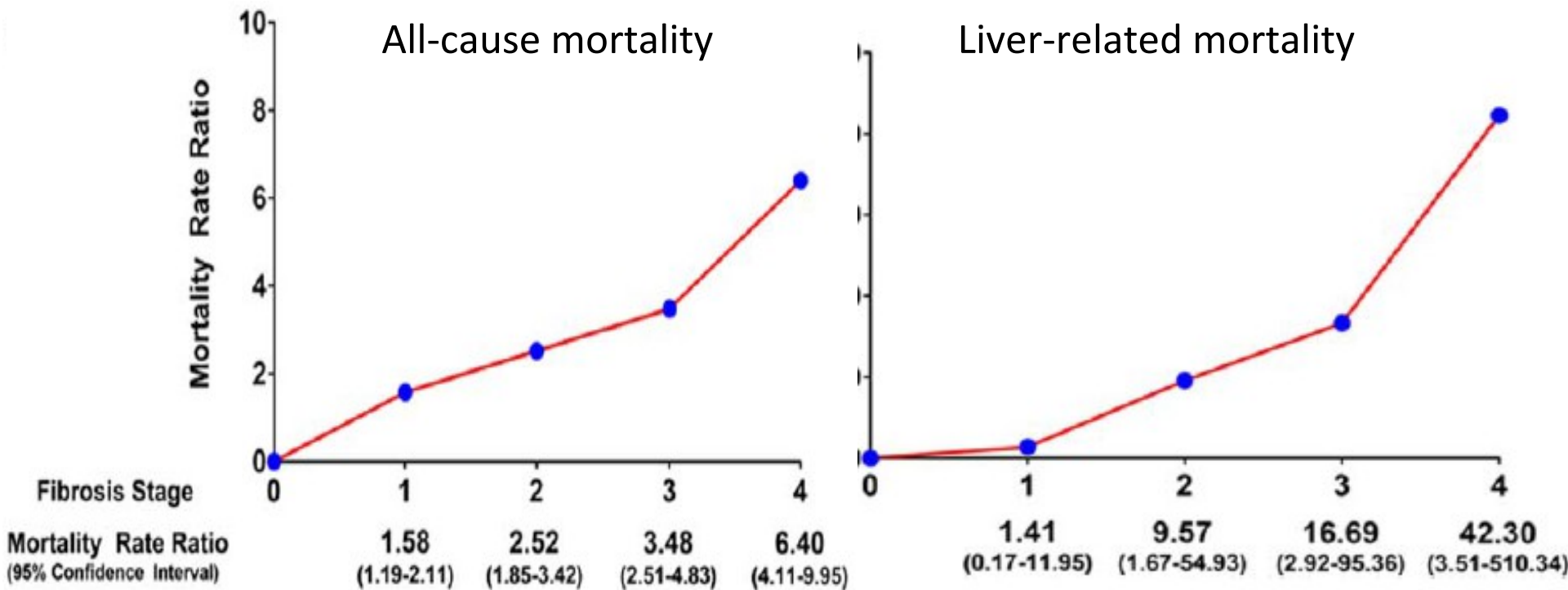


NAFD: Causes of death

Outcome	Number
Death or OLT	(n = 193)
Cardiovascular disease	74 (38.3%)
Nonliver cancer	36 (18.7%)
Cirrhosis complications	15 (7.8%)
HCC	2 (1%)
Liver transplantation	1 (0.5%)
Infections	15 (7.8)
Other	35 (18.1%)

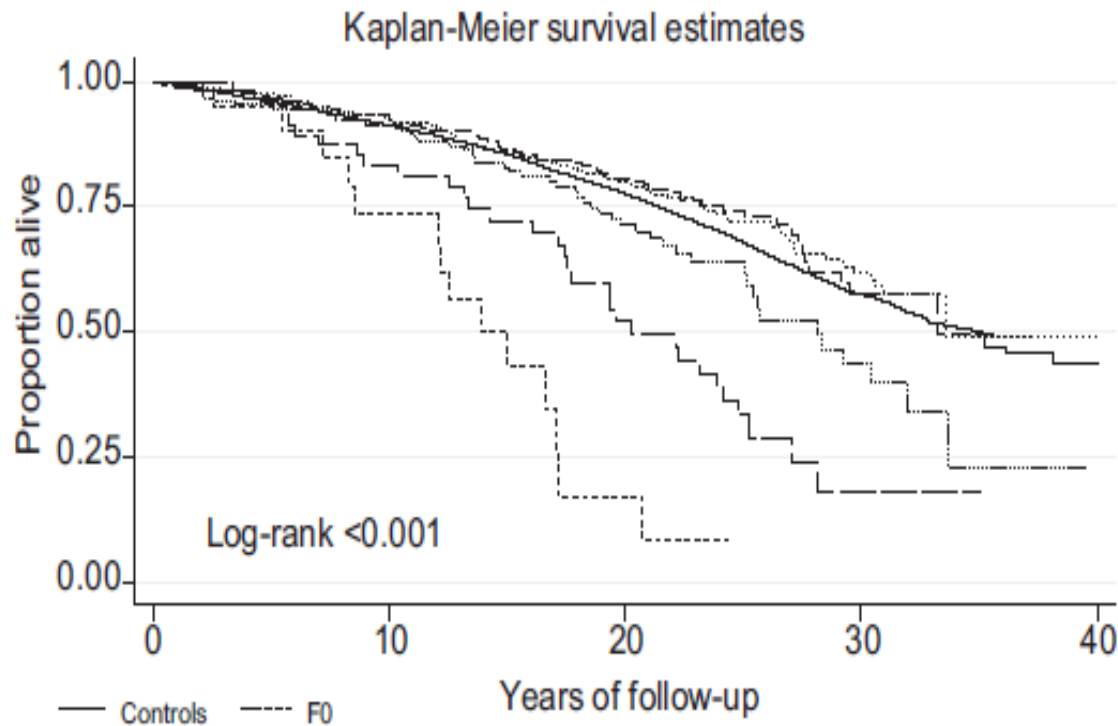
Fibrosis determines outcomes

1,495 NAFLD patients from 5 adult NAFLD cohort studies reporting fibrosis stage-specific mortality



Fibrosis determines outcomes

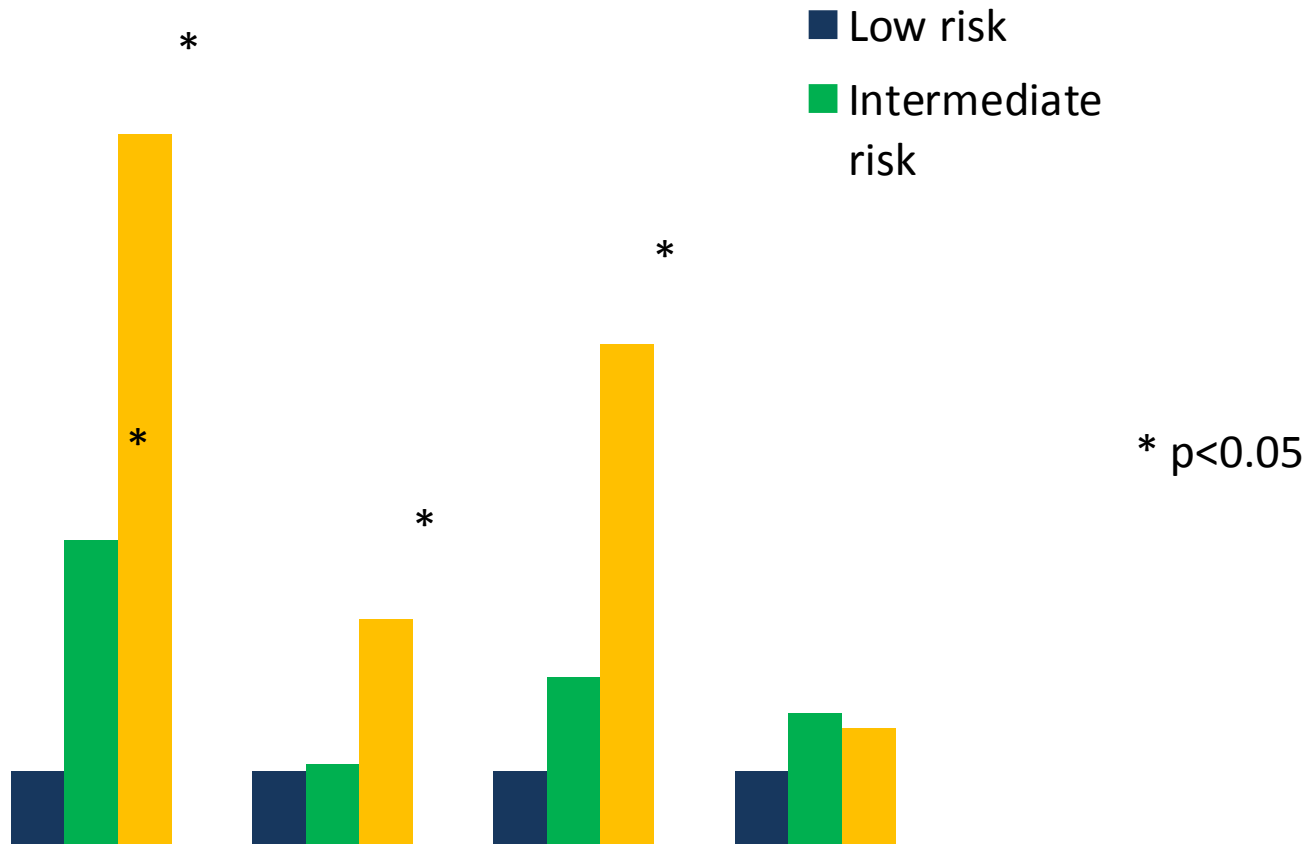
Retrospective cohort study of 646 biopsy-proven NAFLD patients. Each case matched for age, sex and municipality to 10 controls.



Adding presence of NASH to the model with fibrosis stage as the independent variable did not add to the predictive capacity of the model for any stage of fibrosis

Fibrosis Scores predict outcomes

Multivariate adjusted hazard ratios of mortality



Fibrosis Scores predict outcomes

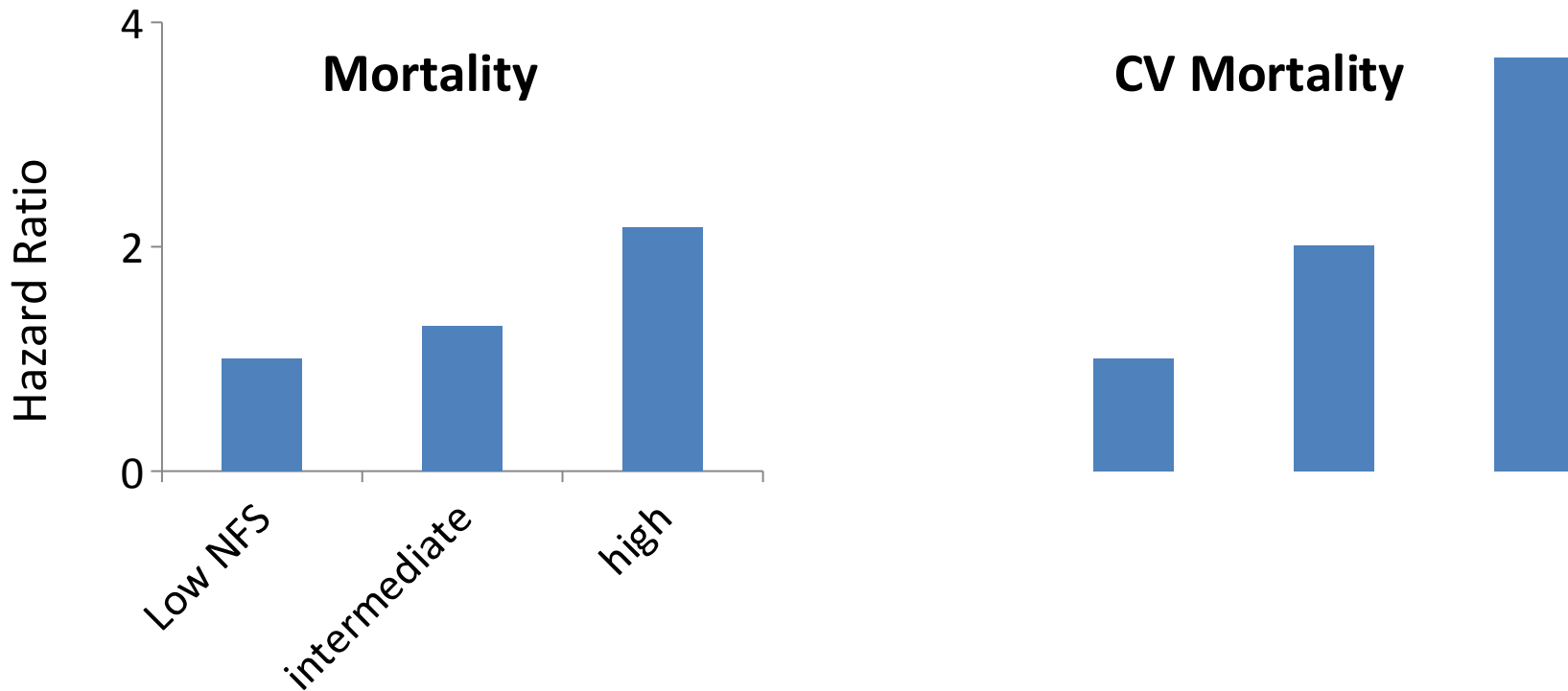
11,154 participants

from National Health and Nutrition Examination Survey 1988–1994

Follow-up data for mortality through December 31, 2006

NAFLD = US detection of steatosis in the absence of other known liver diseases.

Fibrosis determined by the NAFLD fibrosis score (NFS)



NAFLD: Liver stiffness determines outcomes

Longitudinal retrospective study

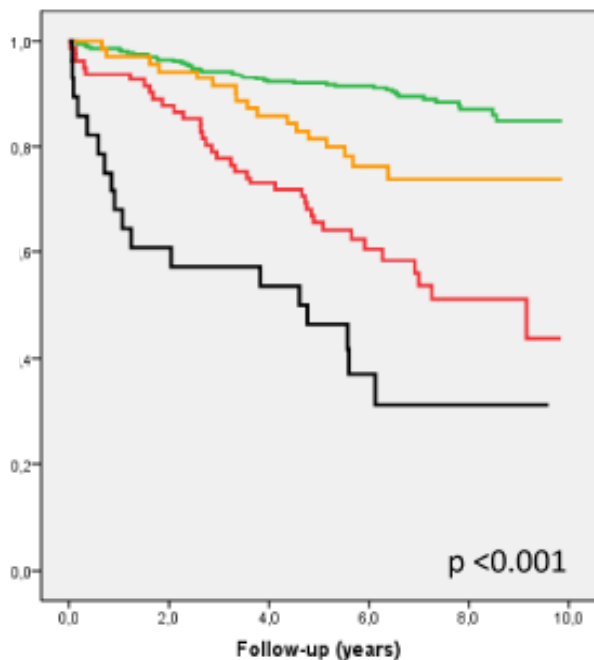
452 biopsy-proven NAFLD patients

From 2003 through 2014, median follow-up 6.4 years

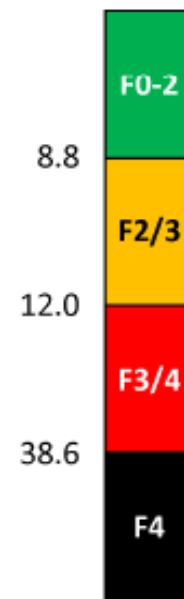
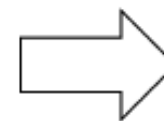
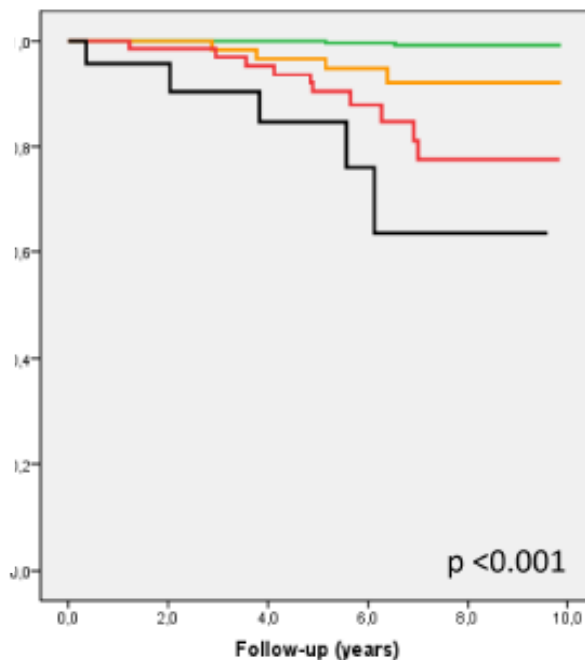
France (Bordeaux, Angers)

NAFLD: Liver stiffness determines outcomes

Overall Survival



Survival free of death from liver-related complication



Fibrosis Progression NAFL vs. NASH

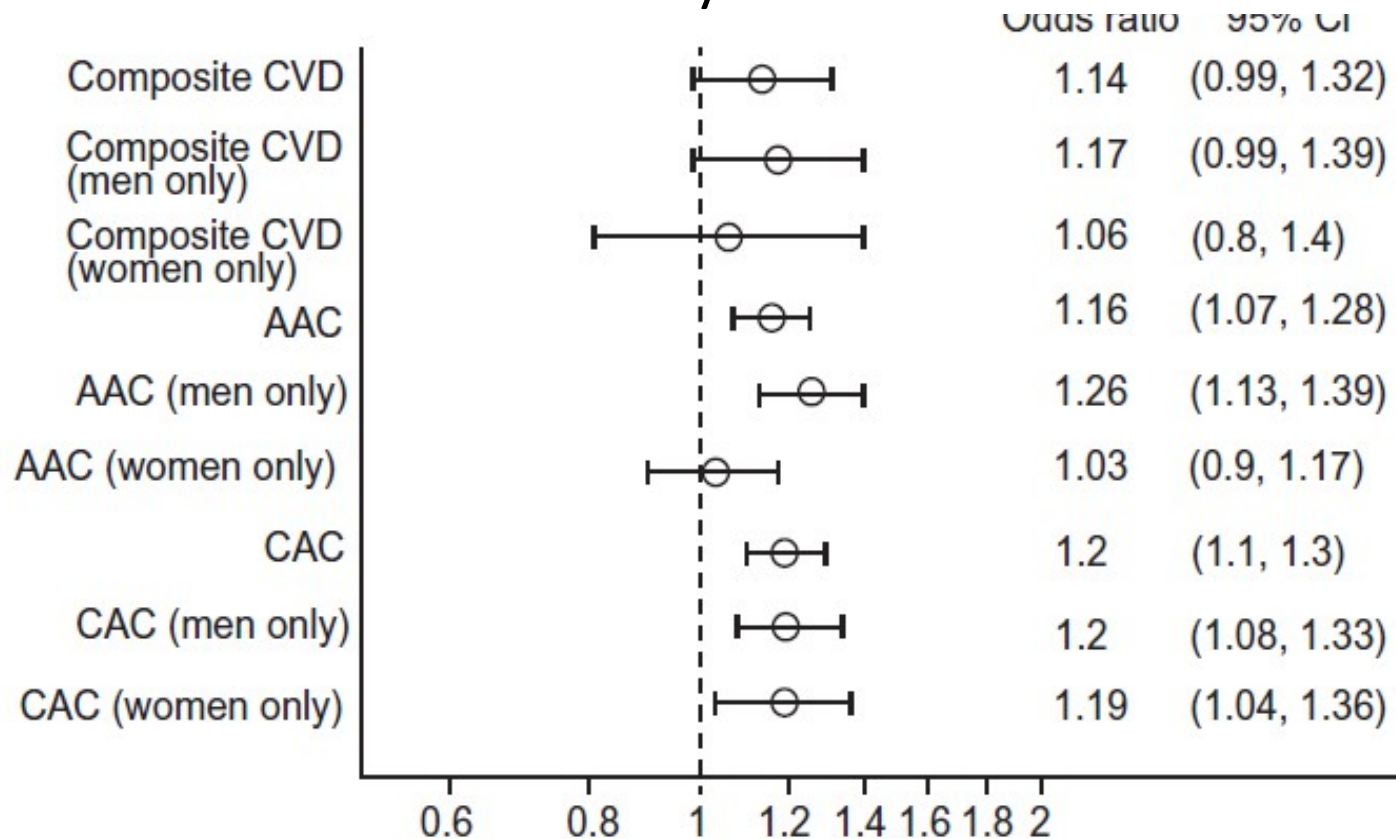
Progression	NAFL	NASH
F1 to F2	36%	18%
F2 to F3	15%	16%
F1 to F3	15%	10%
F2 to F4	8%	16%
F1 to F4	0%	2%
Any	41%	38%
Rapid progressors	17%	18%

NAFLD predictor of CVD events independently of obesity

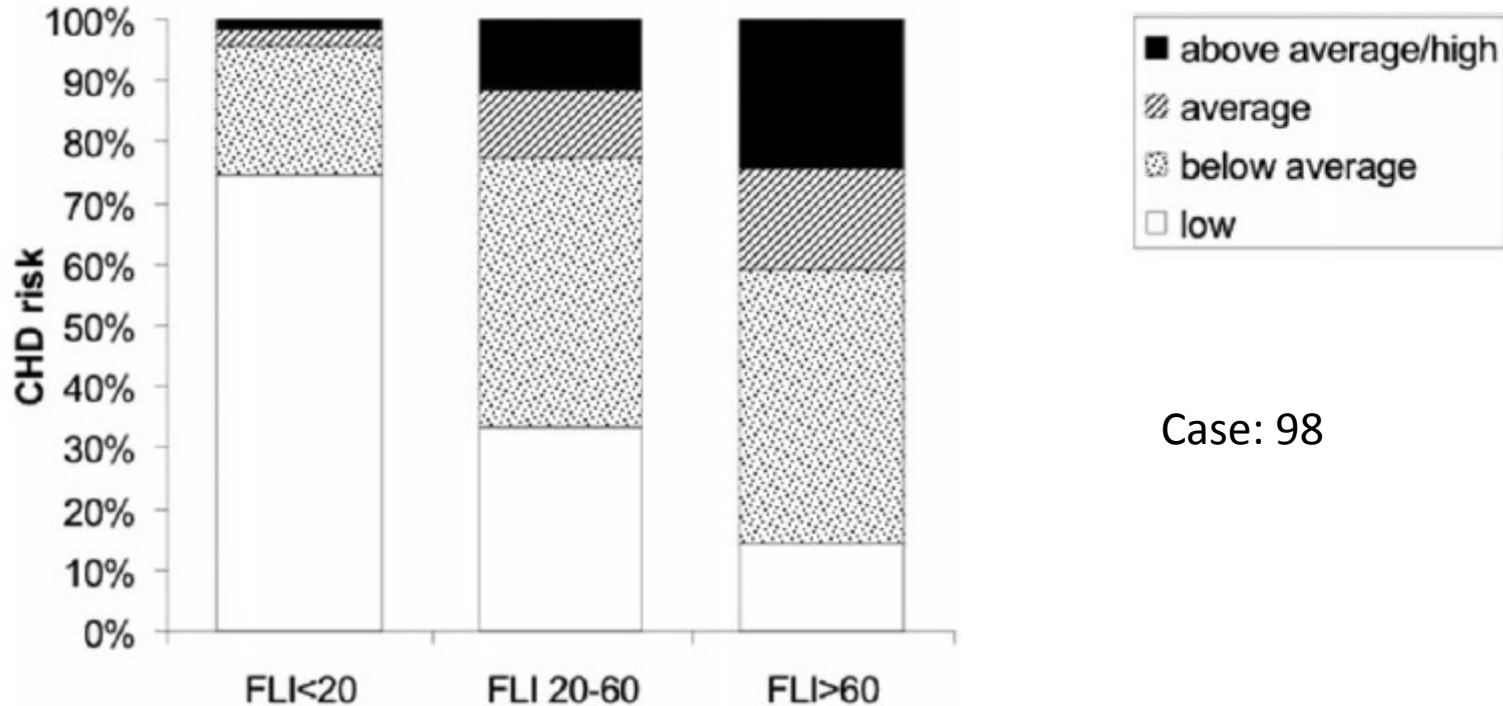
Author, Year	N	Yrs of follow-up	Predictor
Wannamethee 1995	7613	11.5	GGT
Ruttman 2005	163944	17	GGT
Lee 2006	28838	11.9	GGT
Schindheim 2007	1439	10	ALT
Lee 2007	3451	19	GGT
Targher 2007	2103	6.5	US
Hamaguchi 2007	1637	5	US
Stepanova 2012	11613	14	US
Loomba 2013	2364	13.7	GGT

Steatosis as predictor of CVD events

3529 participants of the Framingham study
Steatosis assessed by CT Scan



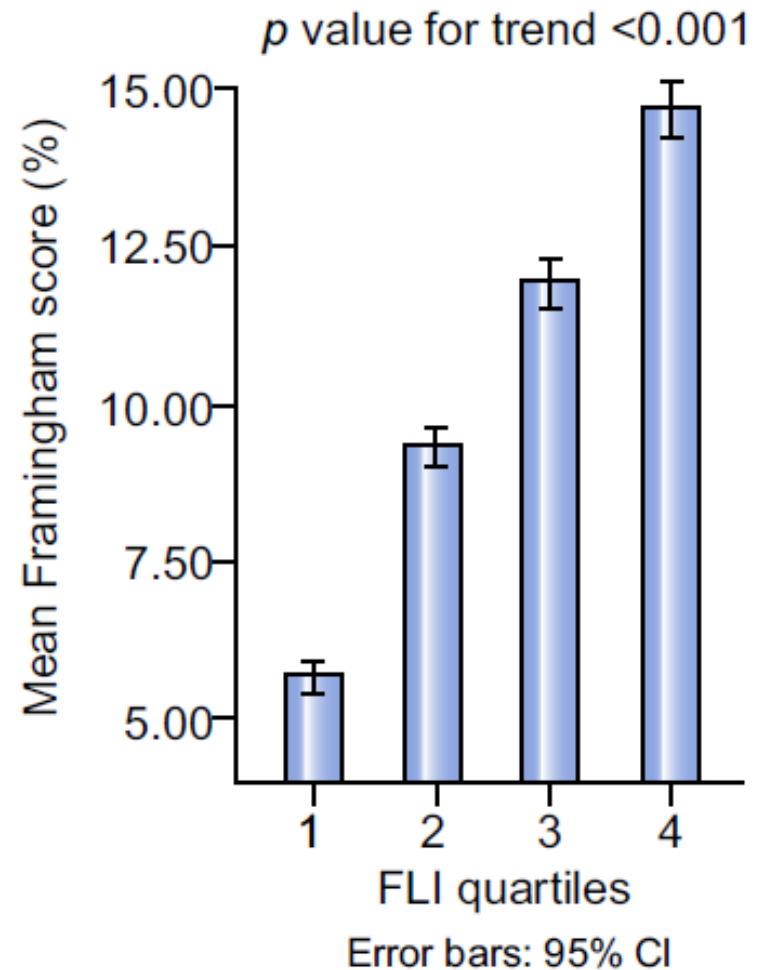
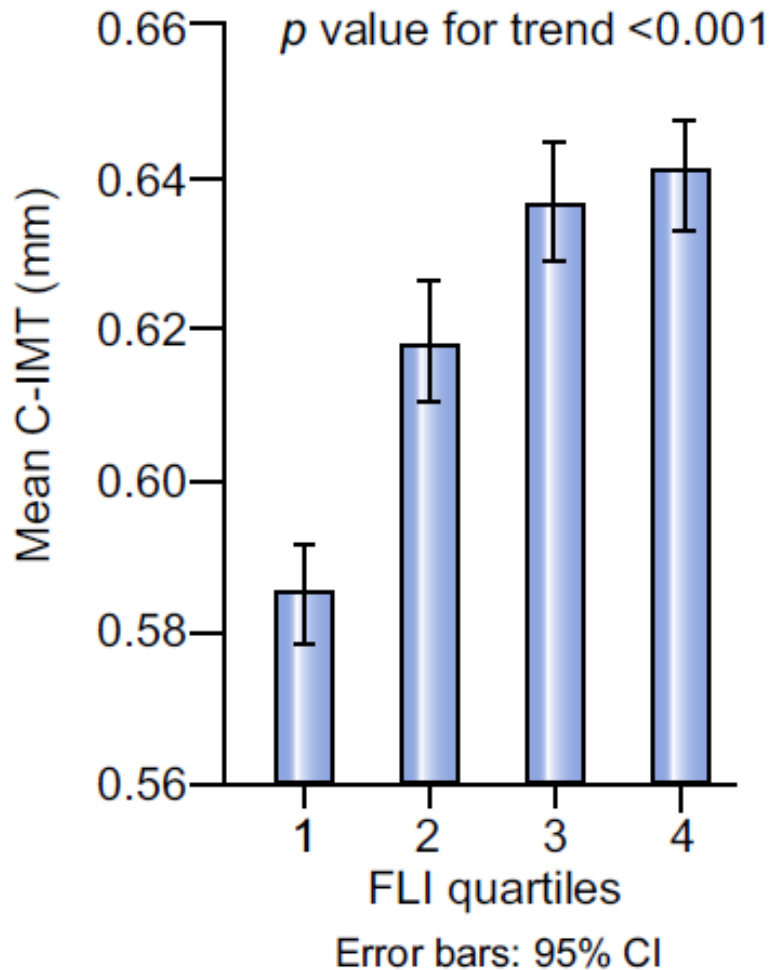
Steatosis as predictor of CVD events



Case: 98

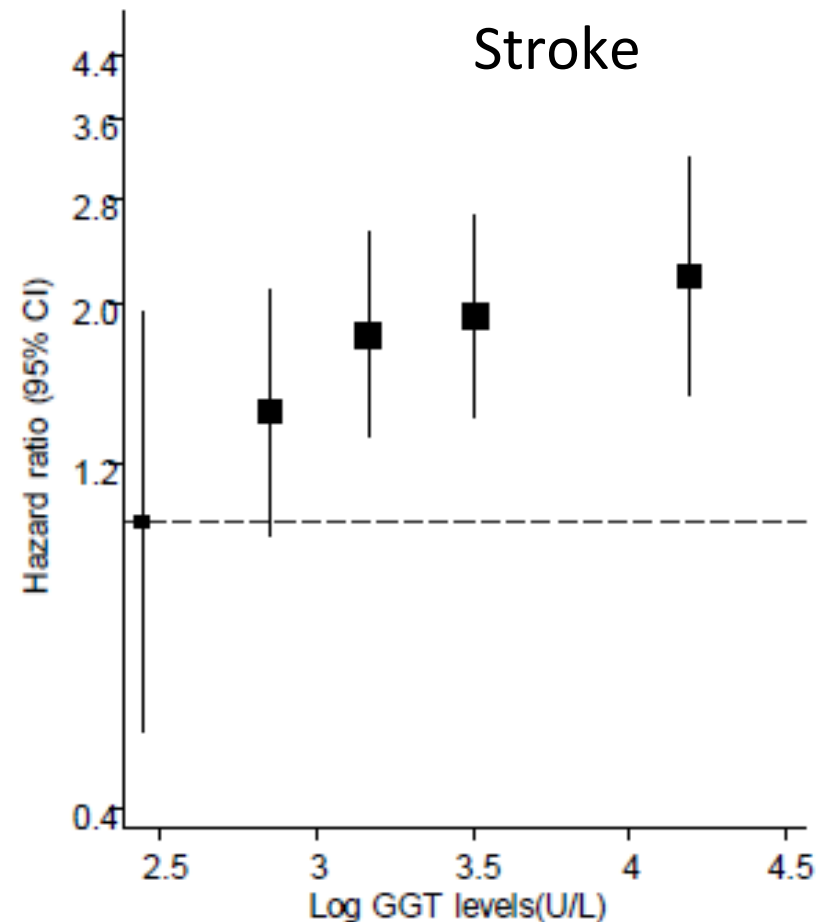
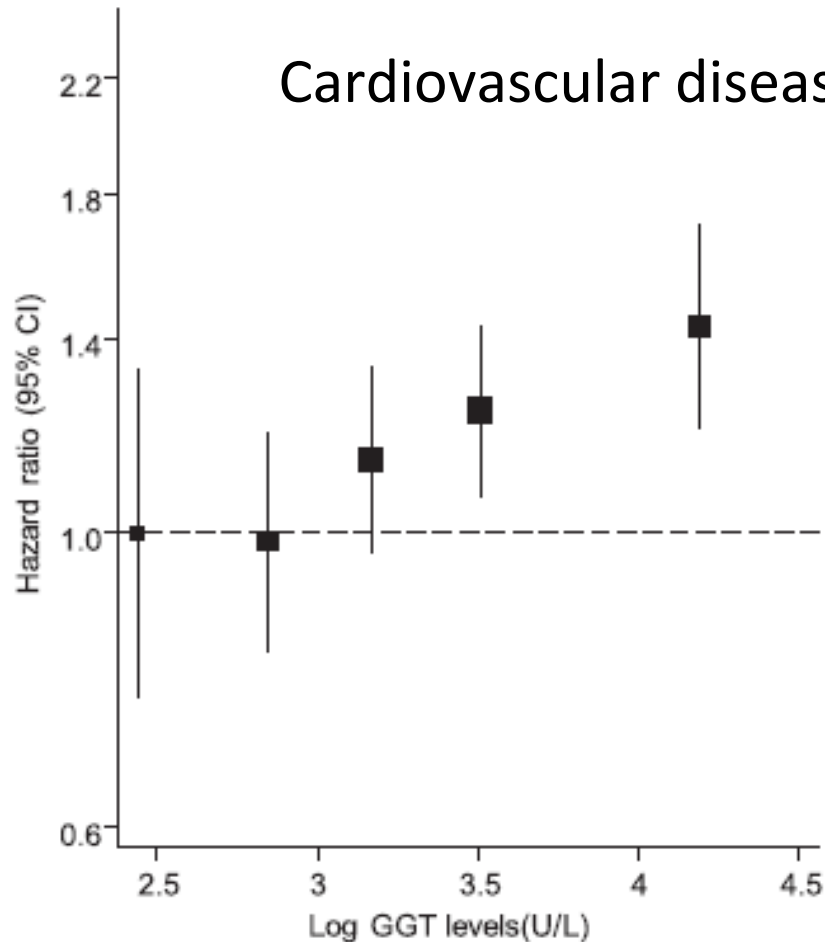
Coronary heart disease risk evaluated using the Framingham score in subjects with a low (FLI < 20), intermediate (FLI 20 to 60), and high (FLI > 60) likelihood of fatty liver

Steatosis as predictor of CVD events



GGT associates with cardiovascular disease

PREVEND cohort: 6969 participants, 10.5 yrs follow-up



Take home messages

NAFLD patients have increased overall mortality compared to matched controls without NAFLD.

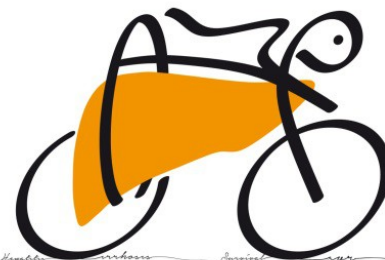
The most common cause of death in NAFLD patients is cardiovascular disease followed by cancers.

Fibrosis is associated with overall and liver-related mortality.

Non-invasive markers of fibrosis predict mortality.



Thank you.



Driven to care
www.swissliver.ch

Fibrosis determines outcomes

Retrospective cohort study of 646 biopsy-proven NAFLD patients.
Each case matched for age, sex and municipality to 10 controls.

Cause of death	NAFLD	Controls	P values
Cardiovascular	37%	39%	0.74
Extrahepatic Cancers	26%	29%	0.96
Respiratory disease	8%	6%	0.13
Liver-related	8%	1%	<0.001
Endocrine (incl. DM)	5%	3%	0.02

Scores predict outcomes

