

*Update Hepatologie, Ärztekammer Steiermark
Graz, 12. März 2008*

Nicht-alkoholische Fettleber und Steatohepatitis (NASH)

Michael Trauner

Klinische Abteilung für

Gastroenterologie und Hepatologie

Univ. Klinik für Innere Medizin



Spektrum der nicht-alkoholischen Fettlebererkrankung (NAFLE / NAFLD)

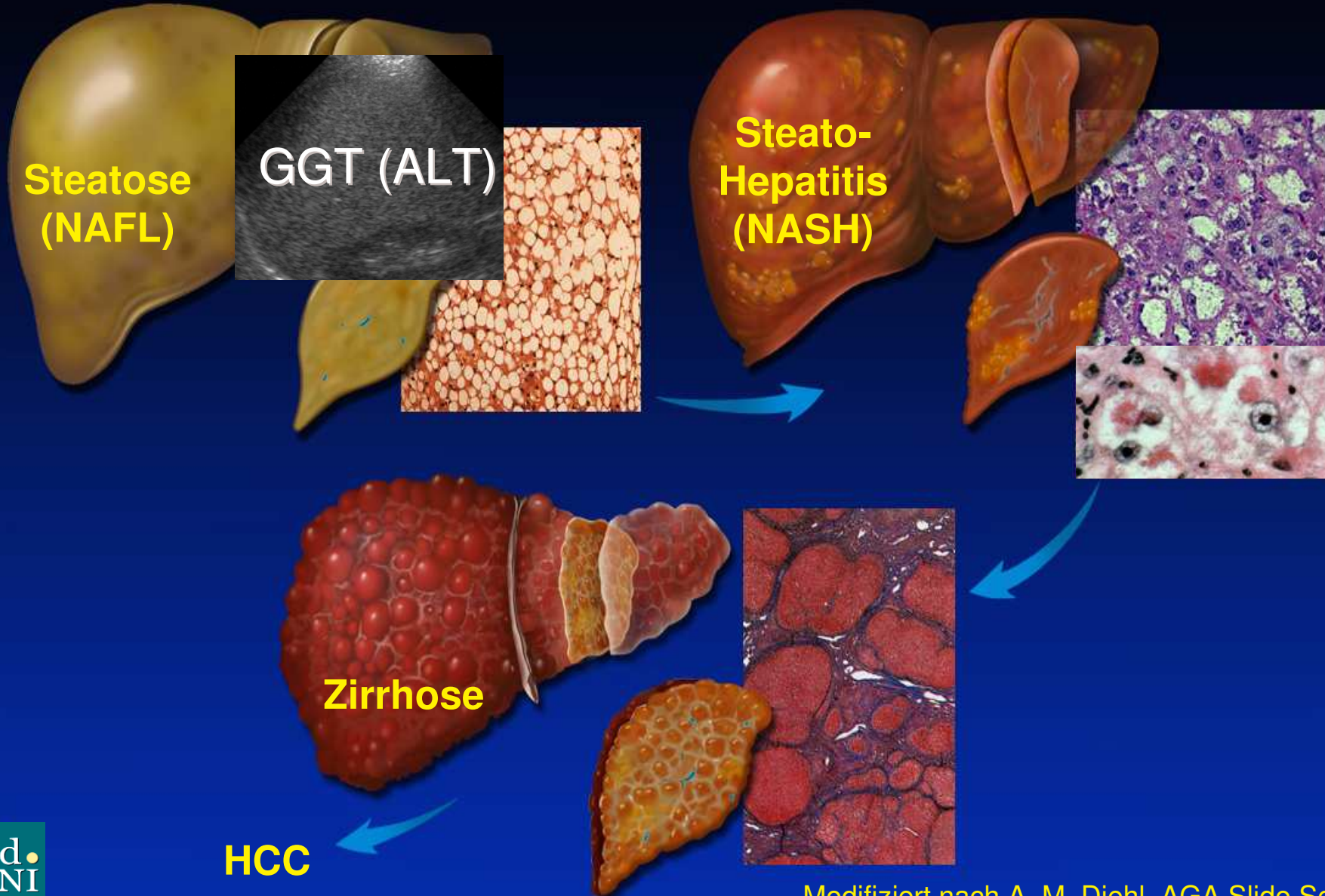
Steatose
(NAFL)

GGT (ALT)

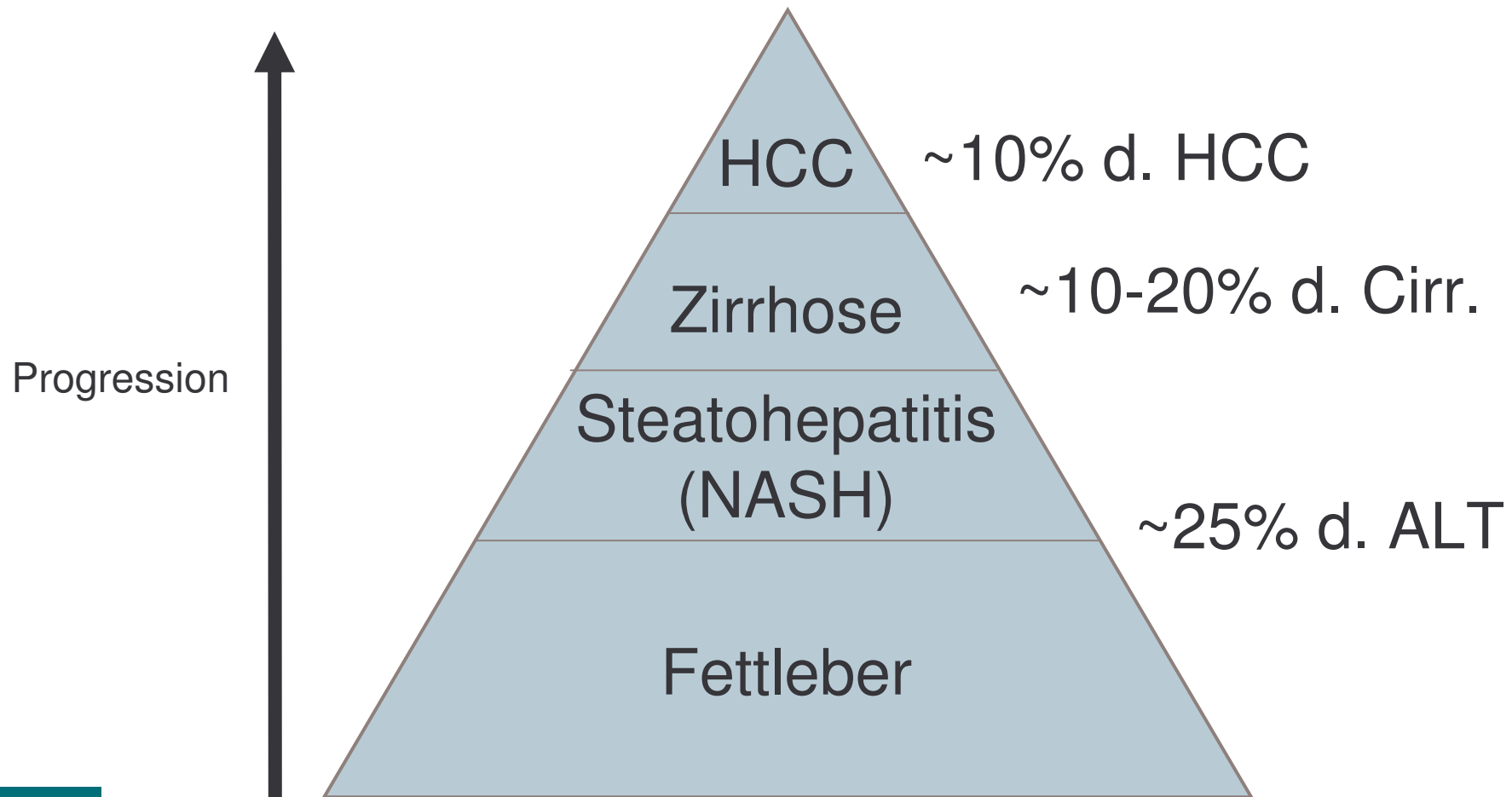
Steato-
Hepatitis
(NASH)

Zirrhose

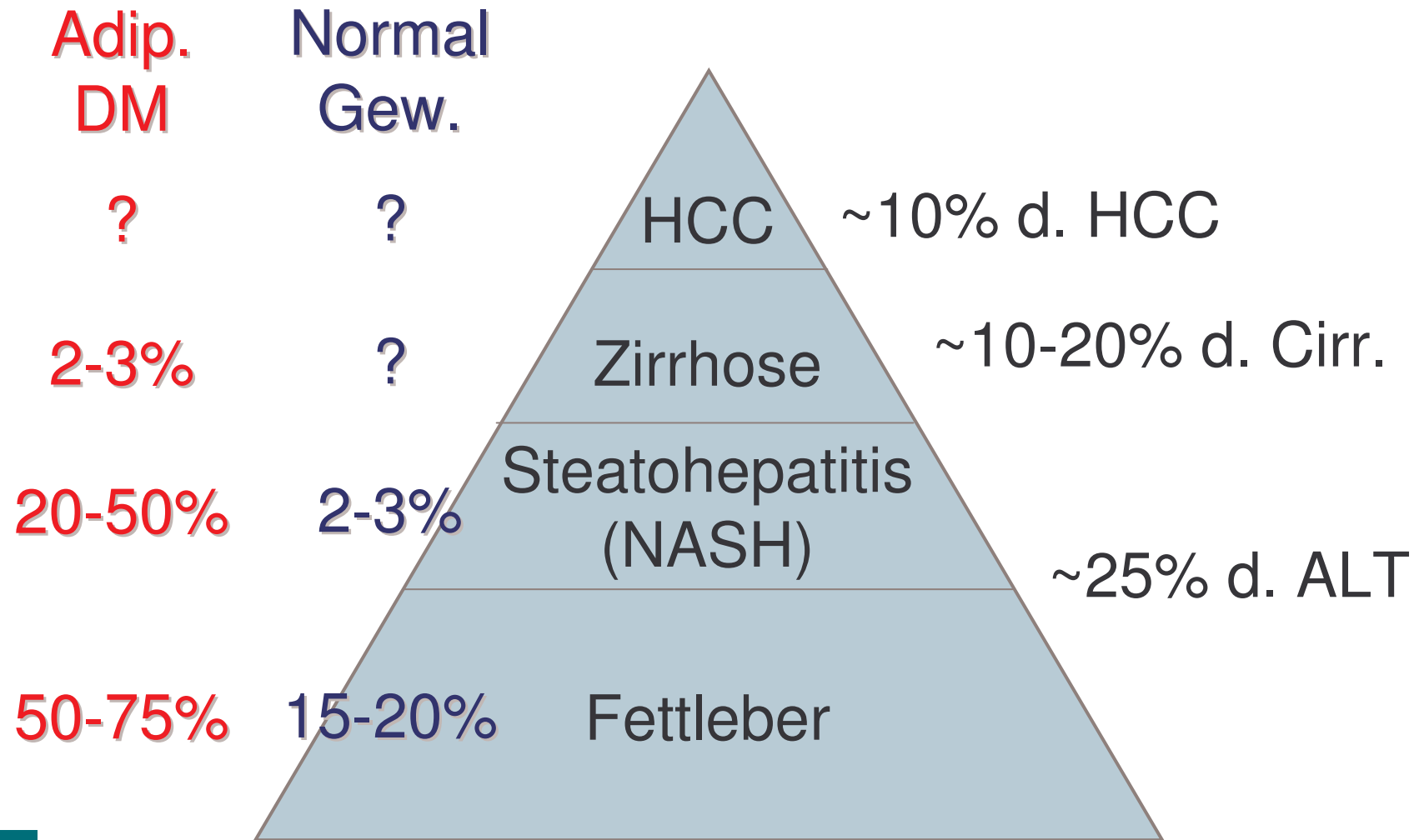
HCC



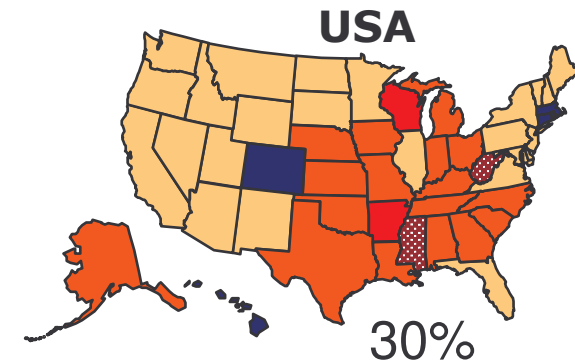
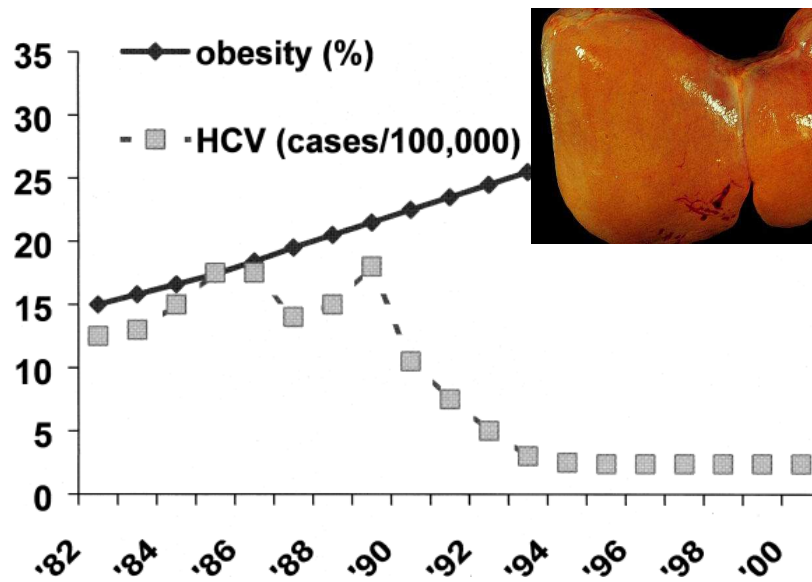
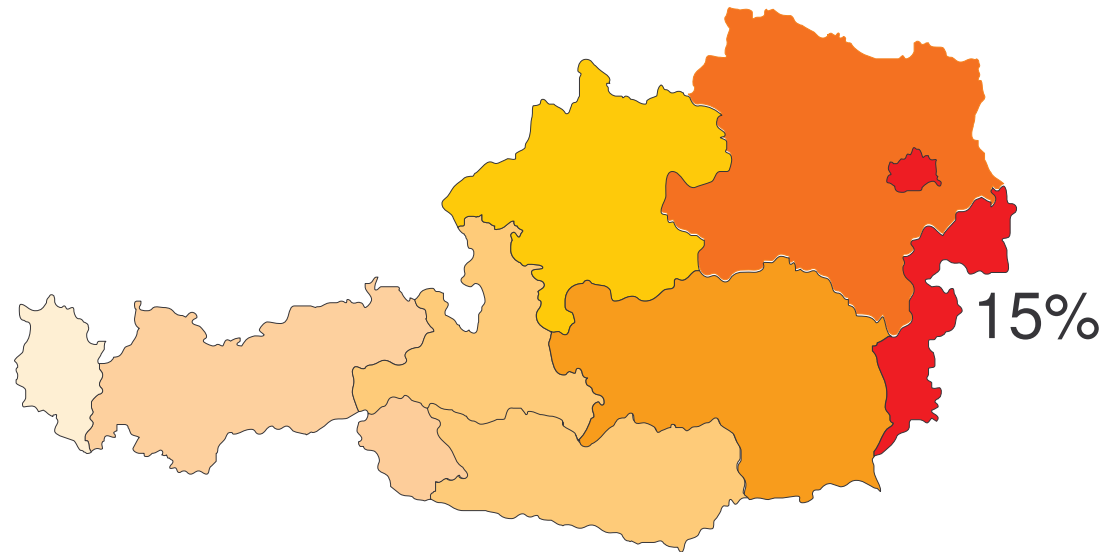
Nicht-alkoholische Fettleber-Erkrankung (NAFLE): Spektrum



Nicht-alkoholische Fettleber-Erkrankung (NAFLE): „Volkskrankheit“



Adipositas in Österreich



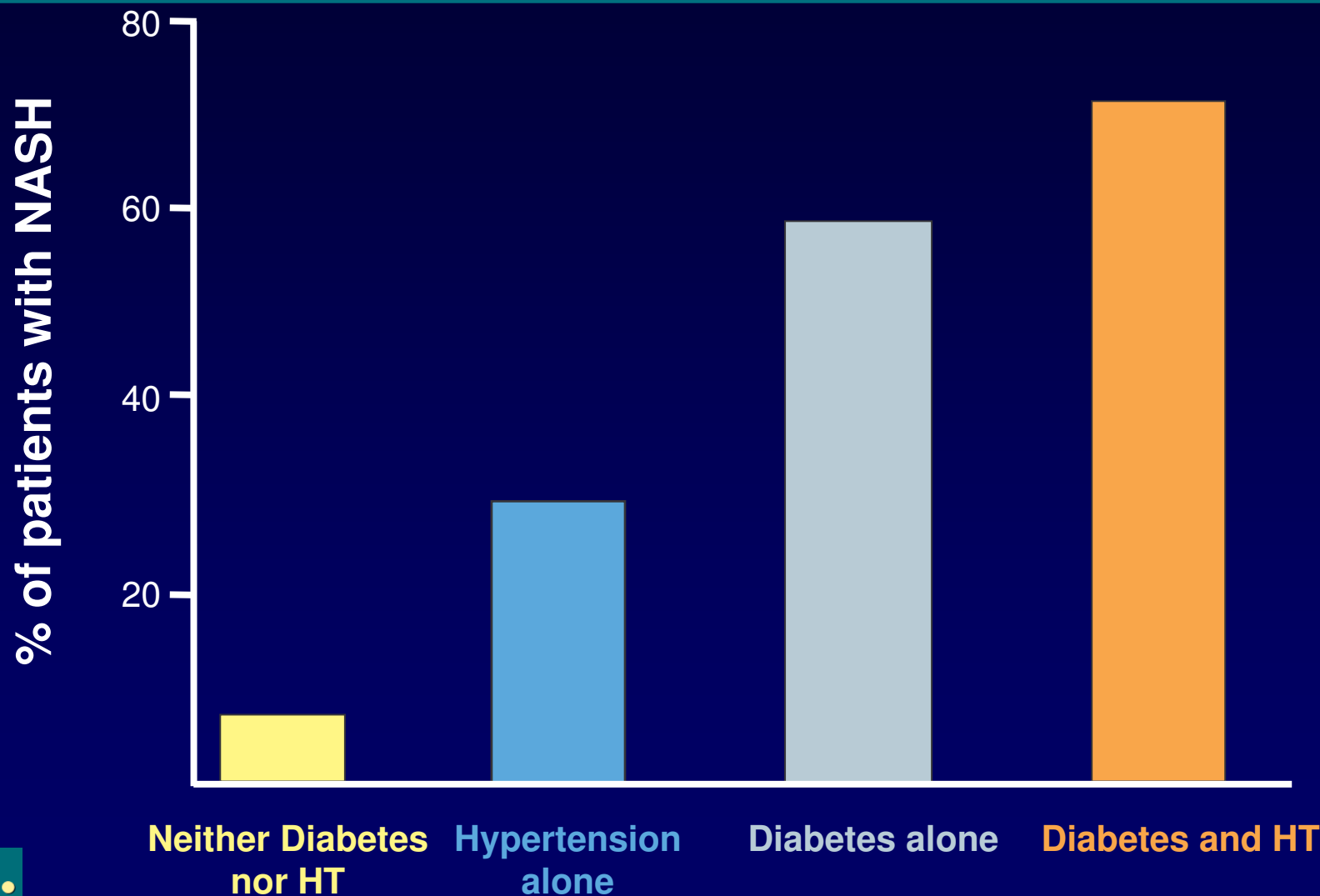
NAFLE & NASH - Hepatische Manifestation des Metabolischen Syndroms



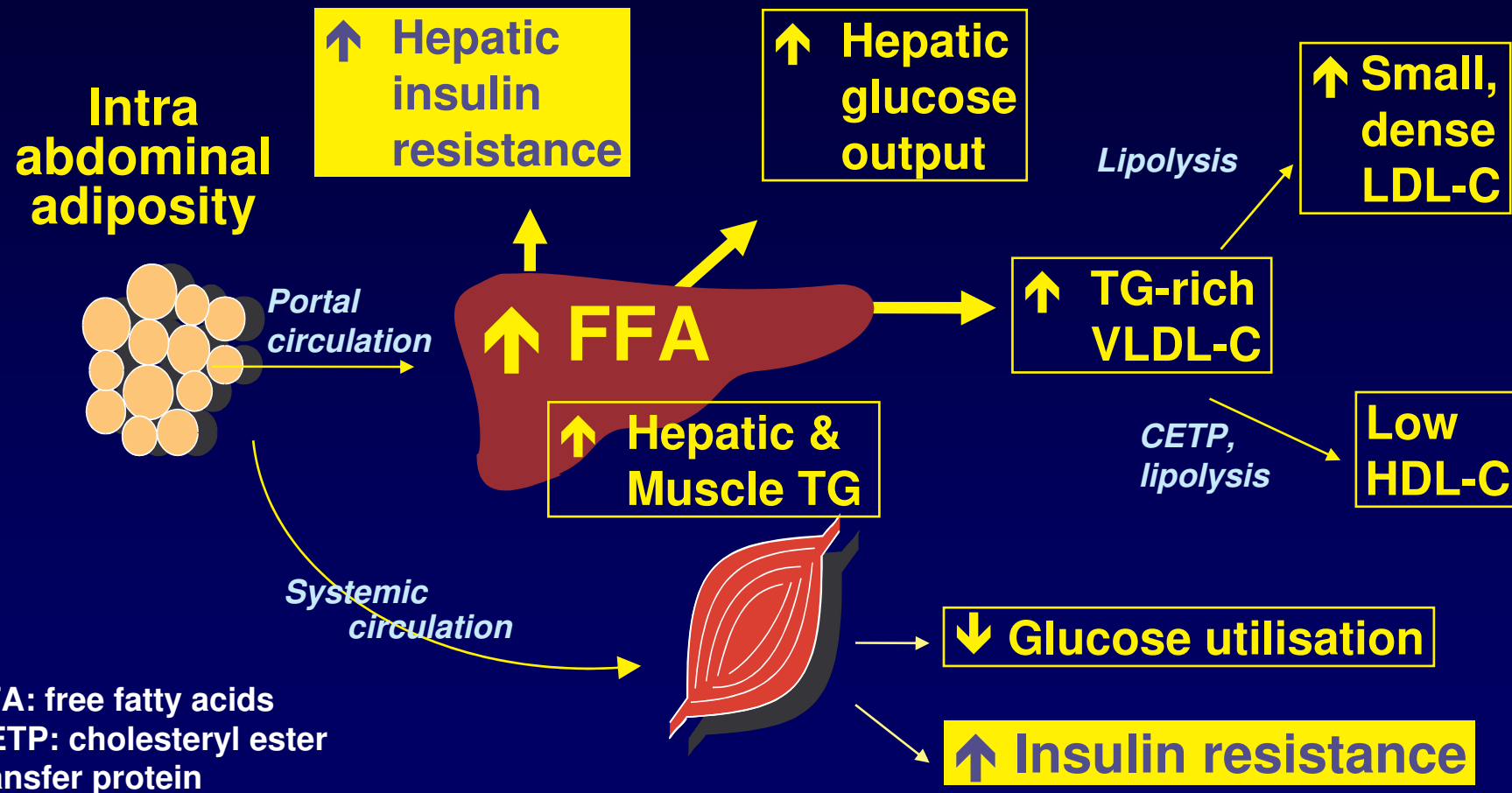
- Adipositas (40-100%)
- DM II (20-75%)
- Dyslipidämie (20-80%)
- Art. Hypertonus
- Insulinresistenz

Andere Ursachen (2°):
Med., TPE, Bact. Overgrowth

Association between NASH, Diabetes and Hypertension in Severely Obese Subjects



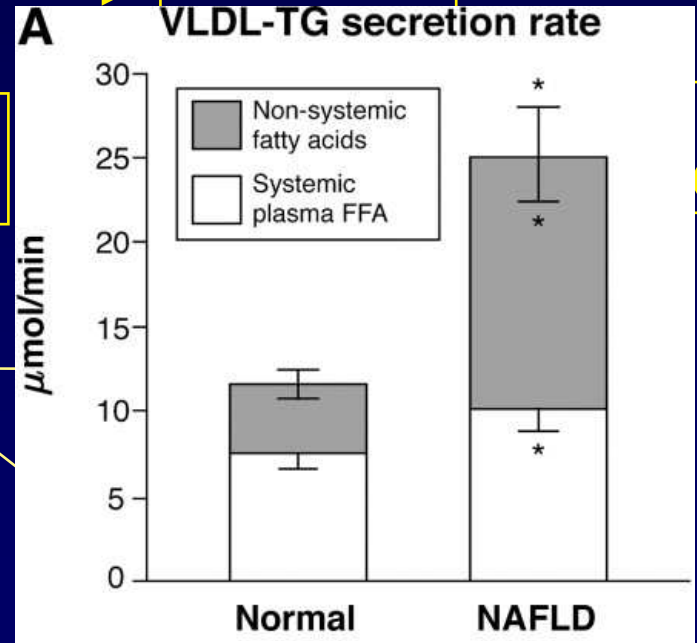
Suggested Role of Intra-abdominal Adiposity and FFA in Insulin Resistance



Suggested Role of Intra-abdominal Adiposity and FFA in Insulin Resistance



FFA: free fatty acids
 CETP: cholesteryl ester transfer protein

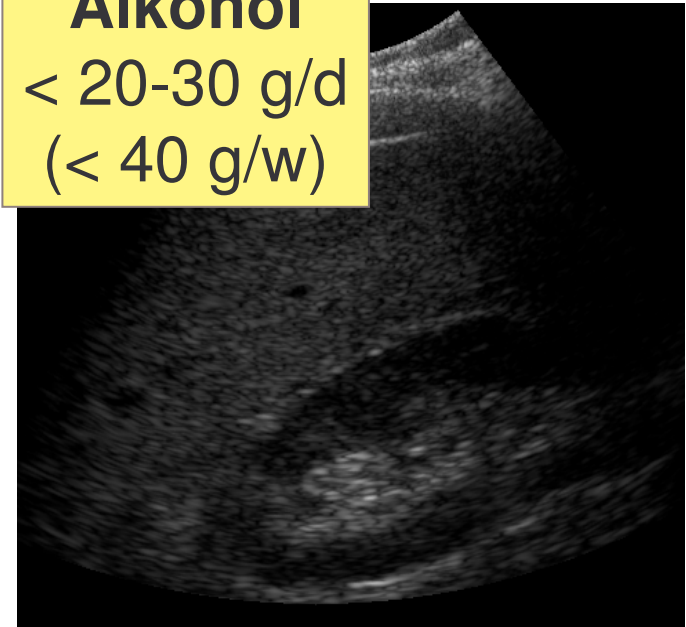


Lam et al. 2005; Fabbrini et al., *Gastro* 2008; 134: 424

Fettleber - Wichtige Ursachen

- Alkoholisch
- Nicht-alkoholisch (NAFL)
- Medikamente
- HCV (Genotyp 3)
- Hämochromatose
- Mb. Wilson

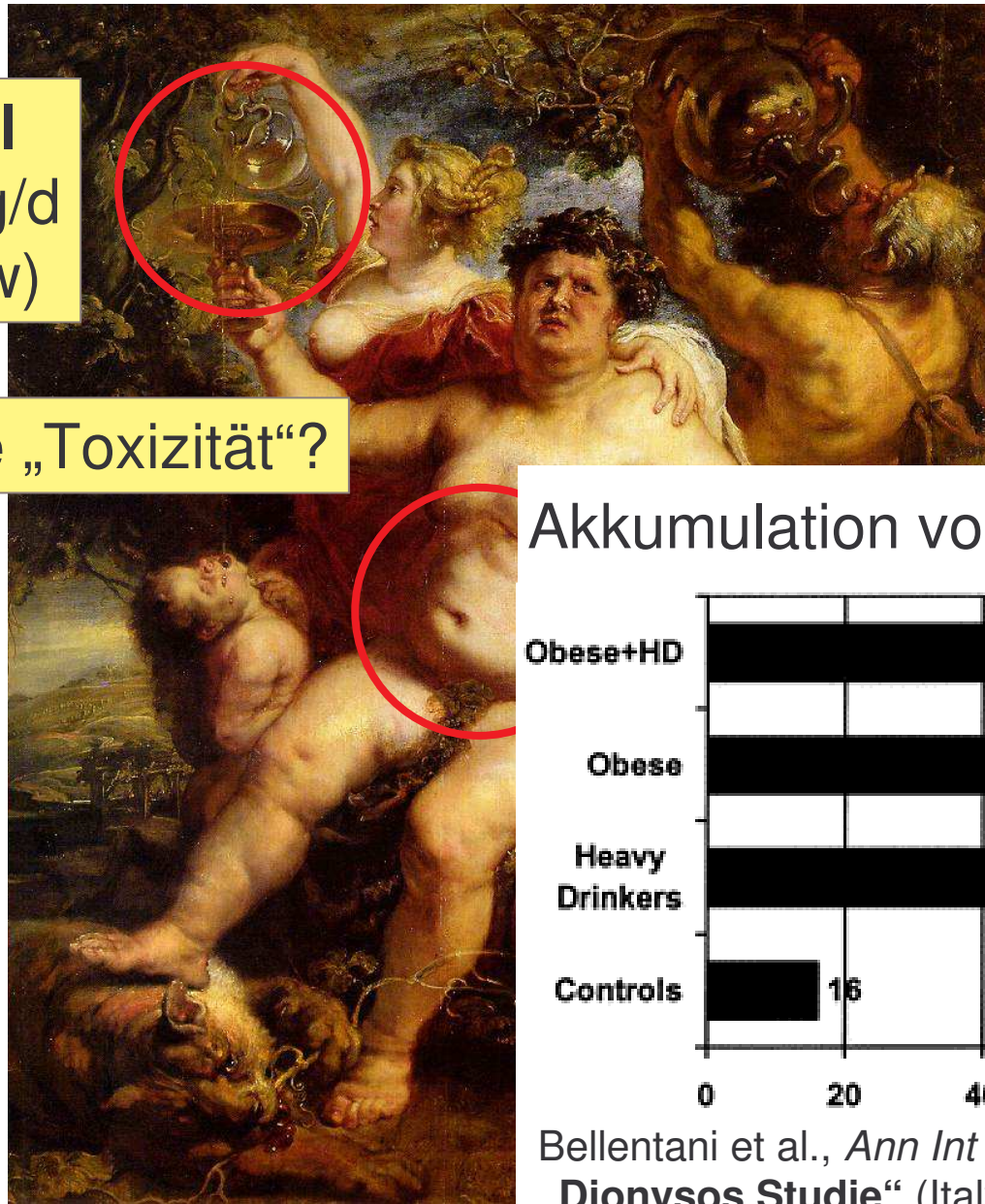
Alkohol
< 20-30 g/d
(< 40 g/w)



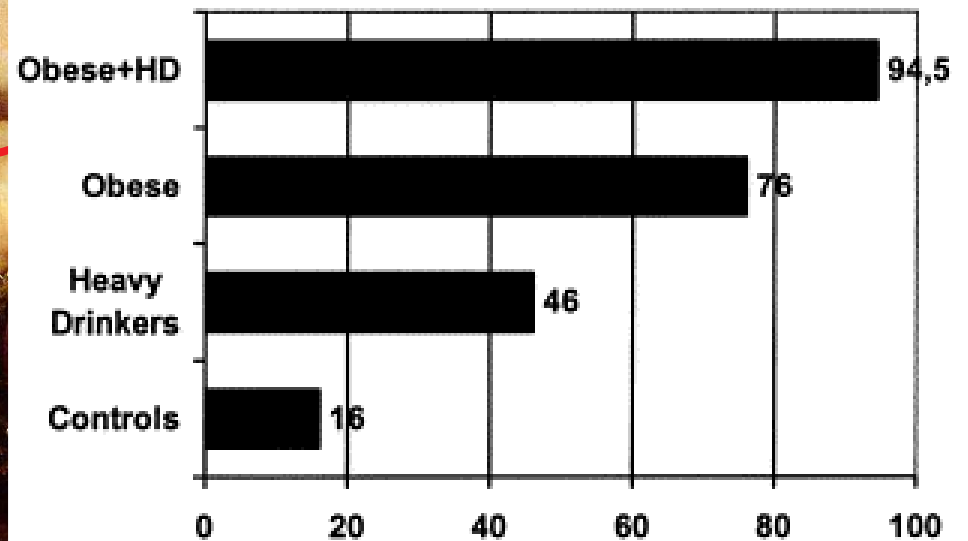
Nicht-alkoholische Fettlebererkrankung

Alkohol
< 20-30 g/d
(< 40 g/w)

Erhöhte „Toxizität“?

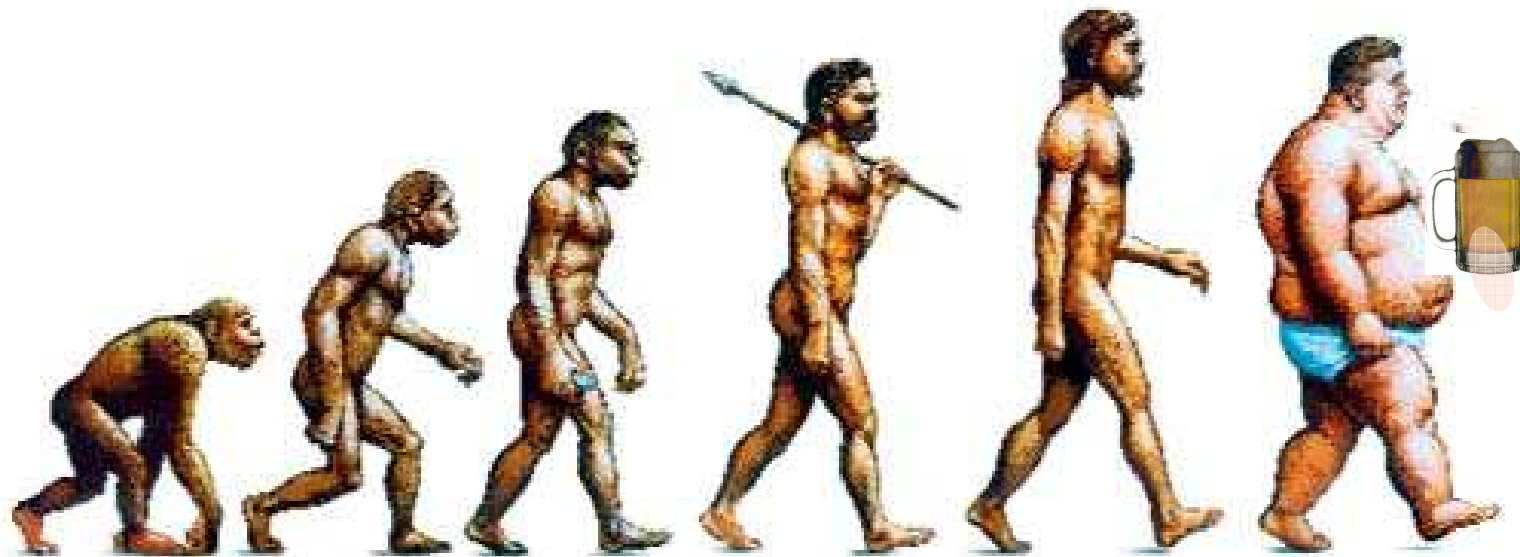


Akkumulation von Risikofaktoren

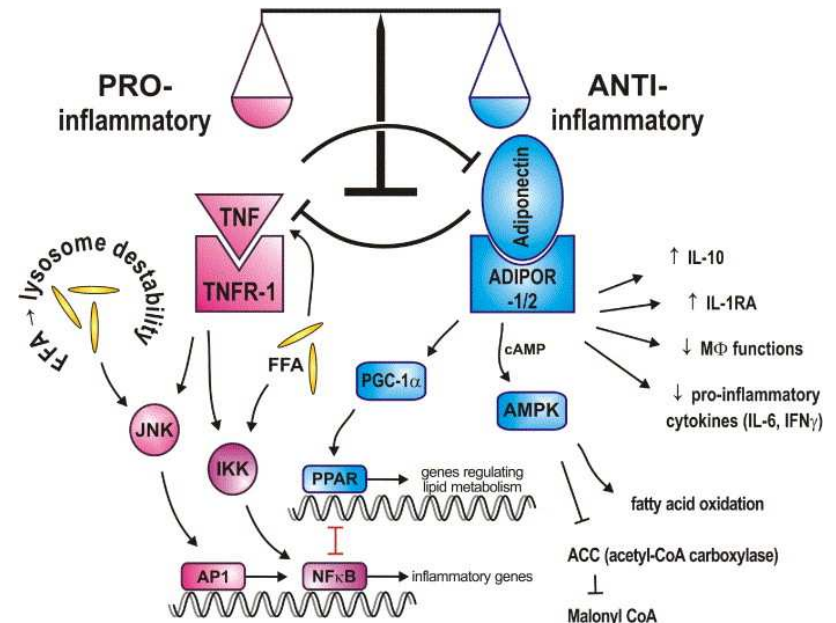
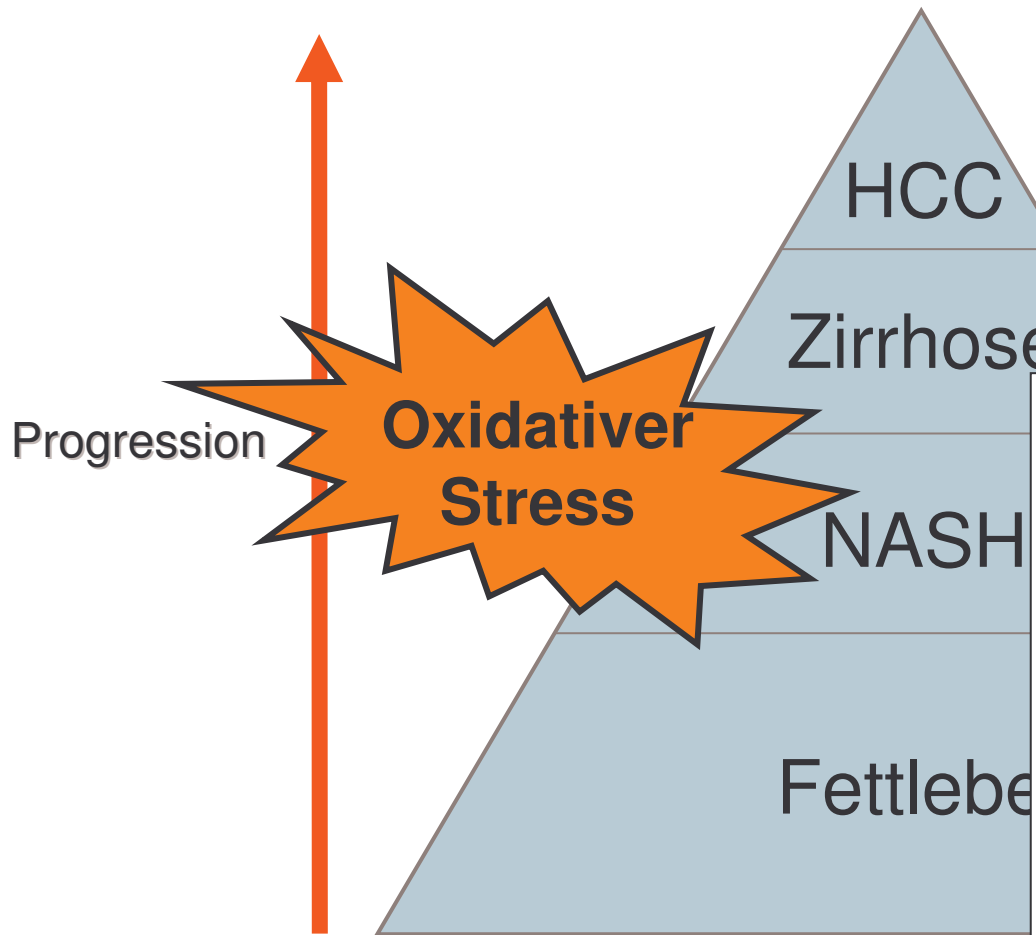


Bellentani et al., *Ann Int Med* 2000; 132: 117
„Dionysos Studie“ (Italy): Steatosis on US

(Nicht)alkoholische Fettlebererkrankung

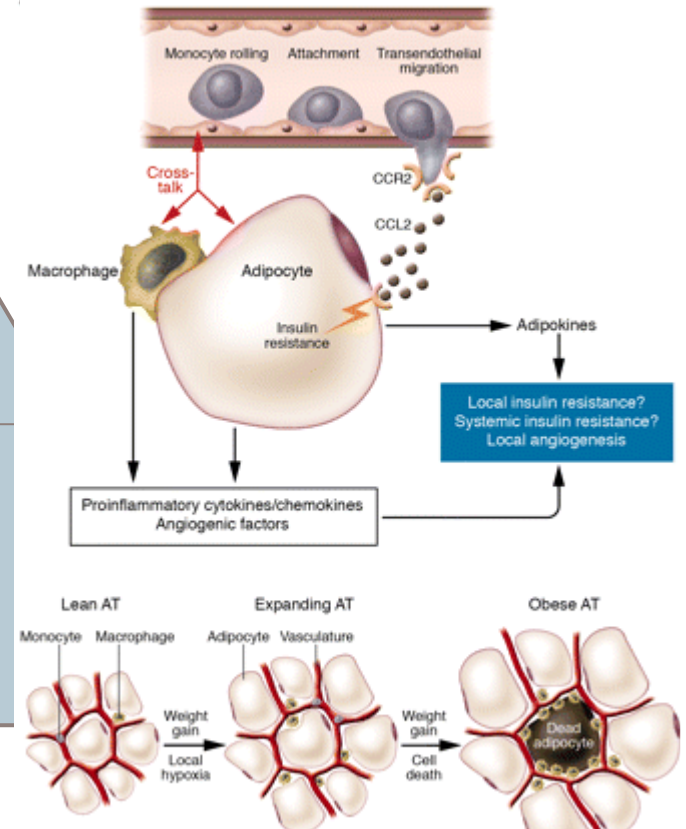
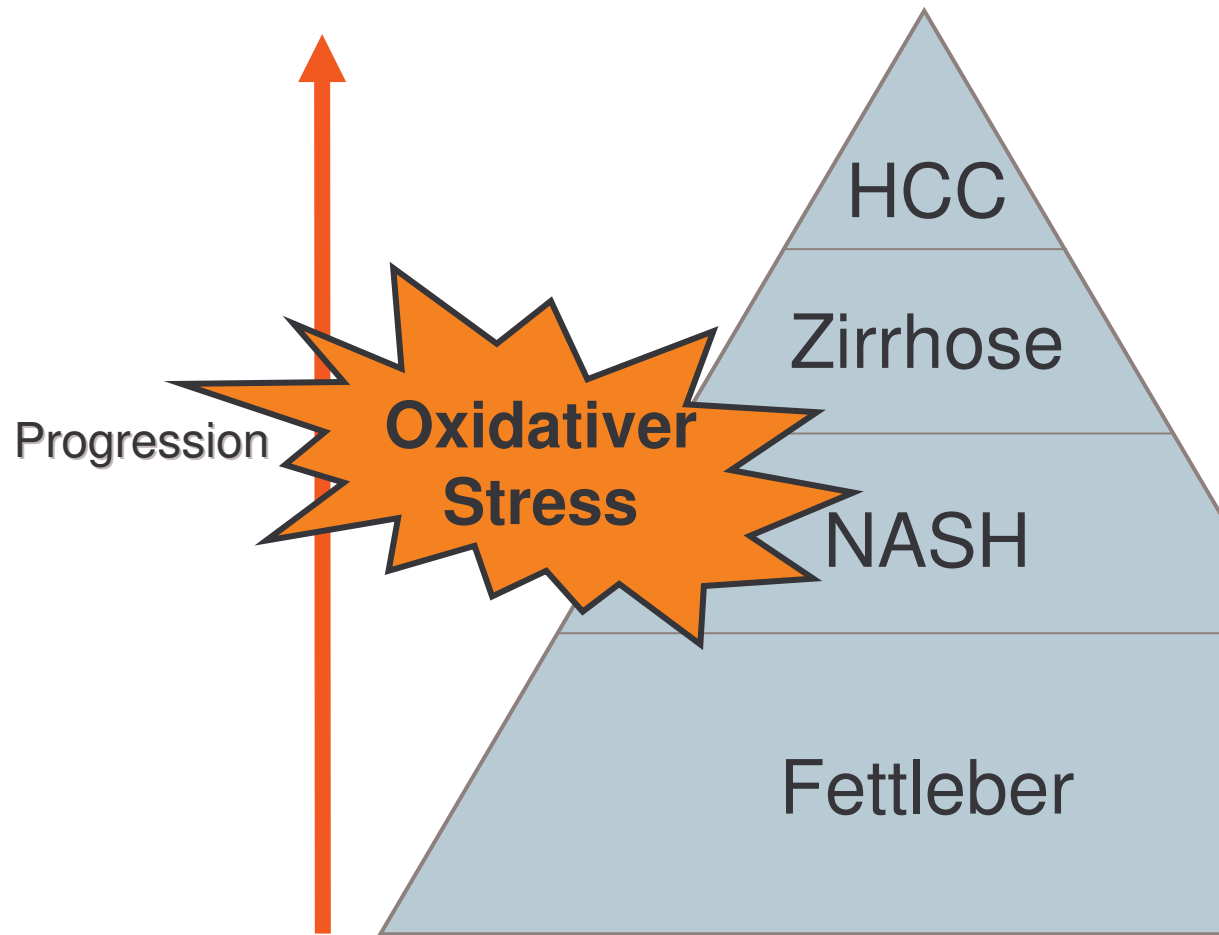


NAFLE: Natürlicher Verlauf & Prognose



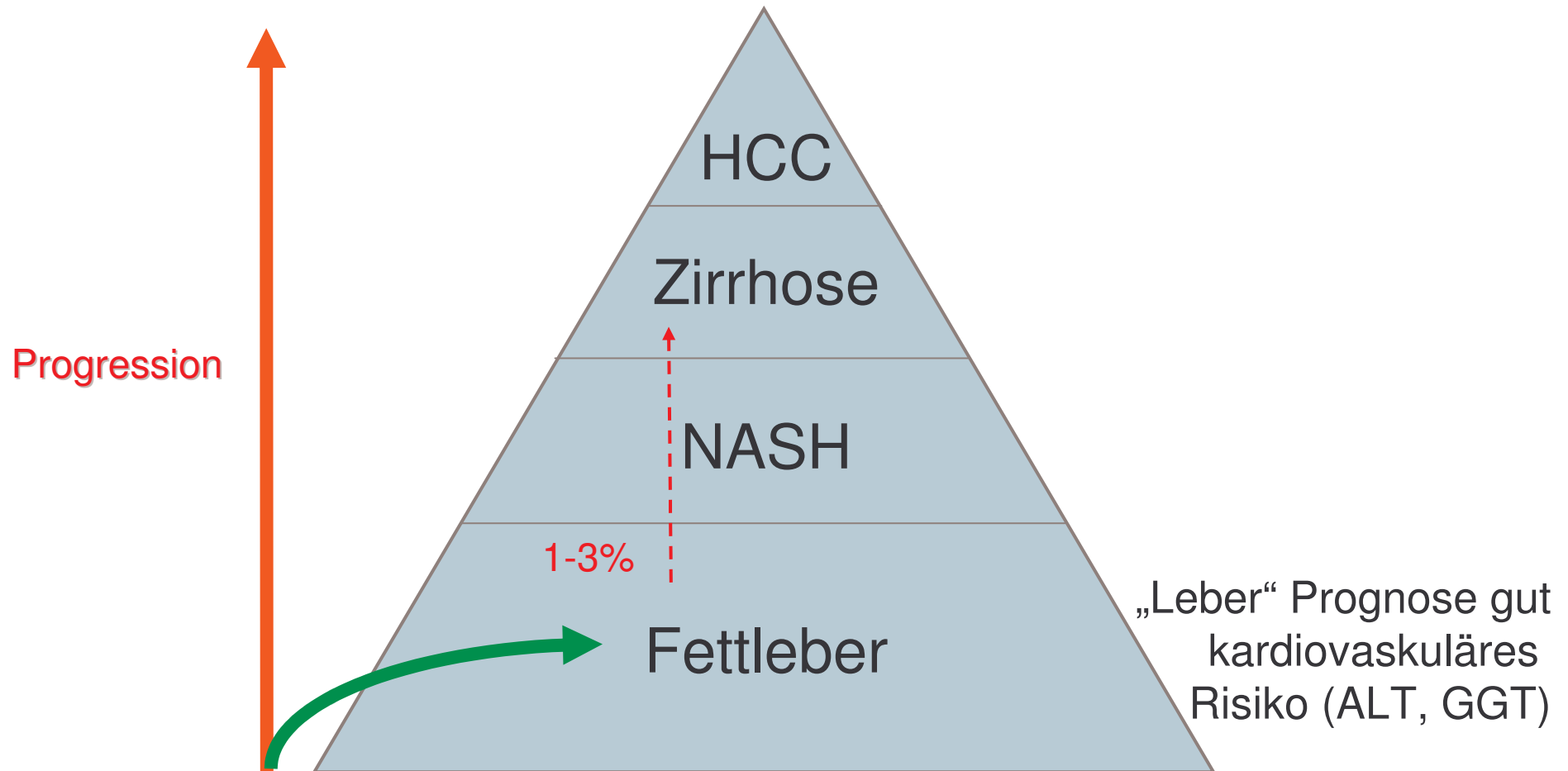
Tilg & Hotamisligil, *Gastro* 2006; 131: 934

NAFLE: Natürlicher Verlauf & Prognose

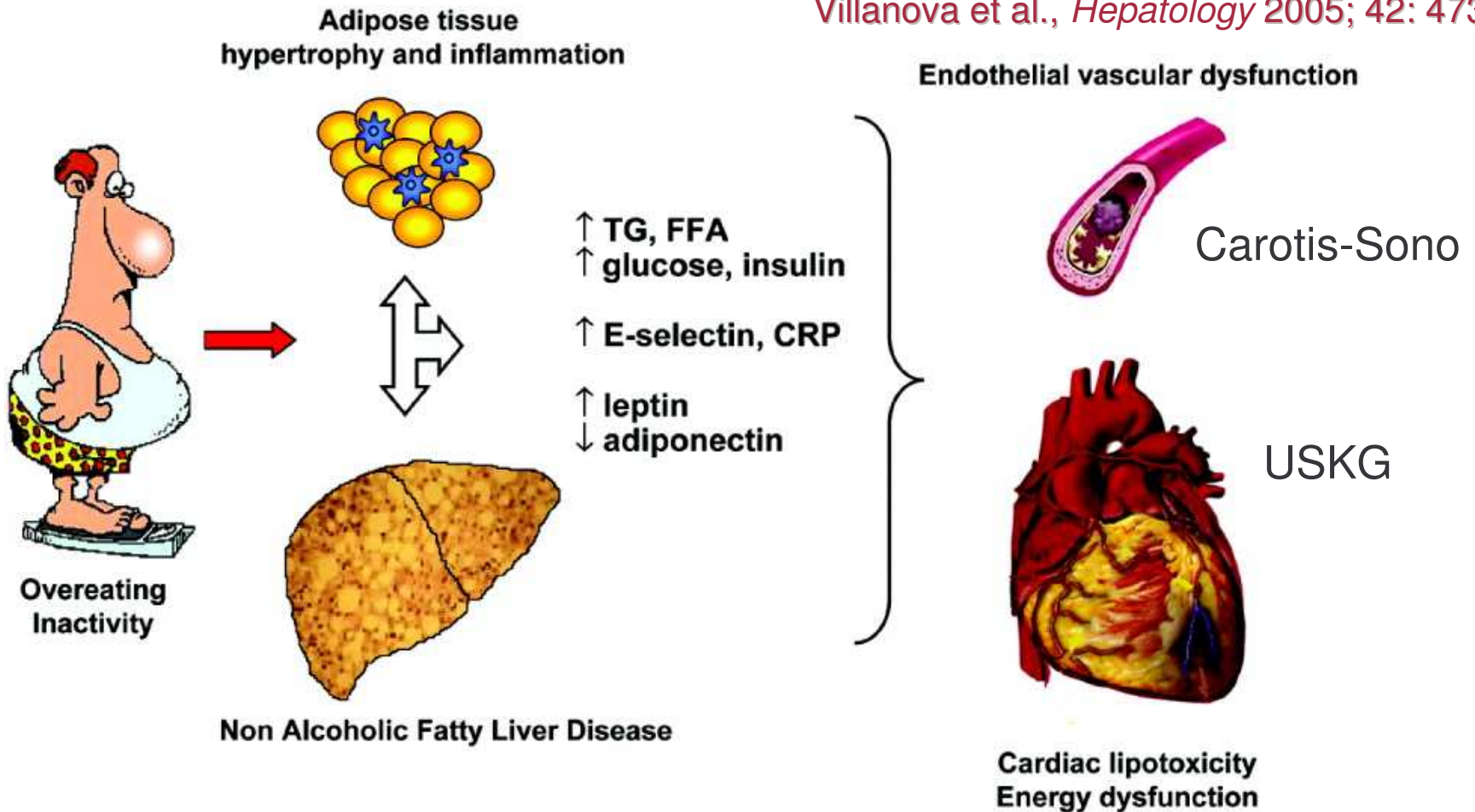


Neels & Olefsky *JCI* 2006; 116: 33

NAFLE: Natürlicher Verlauf & Prognose



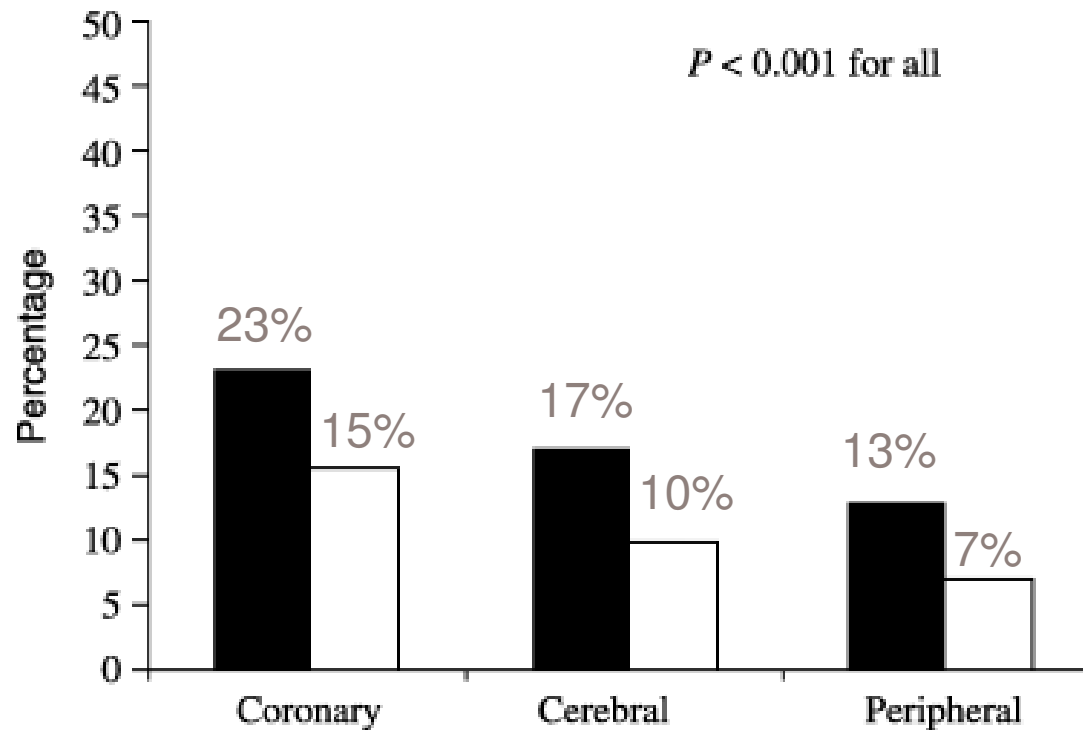
Kardiovaskuläres Risiko bei NAFLE



Perseghini et al., *Hepatology* 2008; 47: 51

Kardiovaskuläres Risiko bei NAFLE

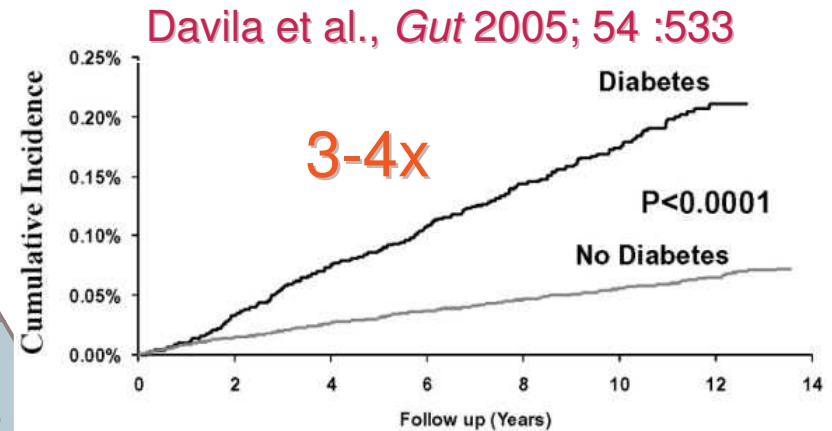
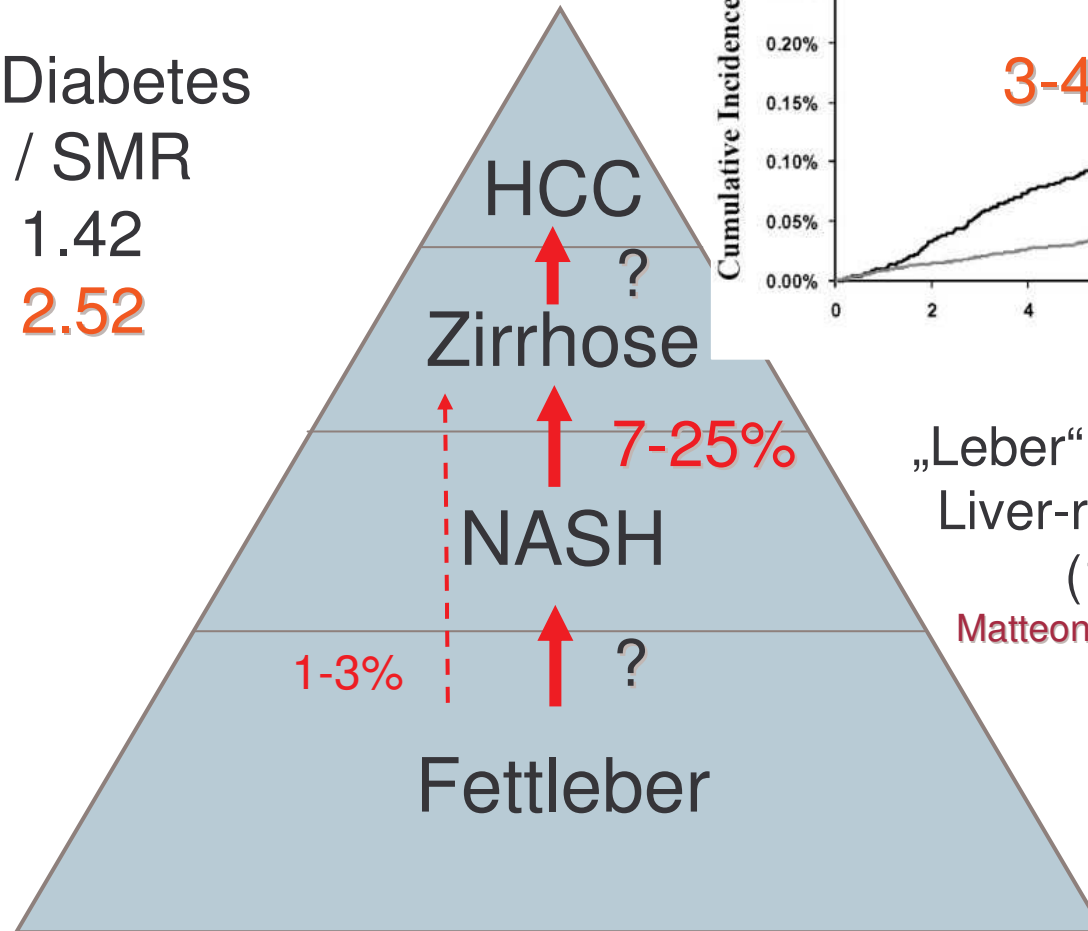
Prevalence of CVD in T2DM with vs. without NAFLD



Unabhängig von klass. Risikofaktoren & metabol. Syndrom!

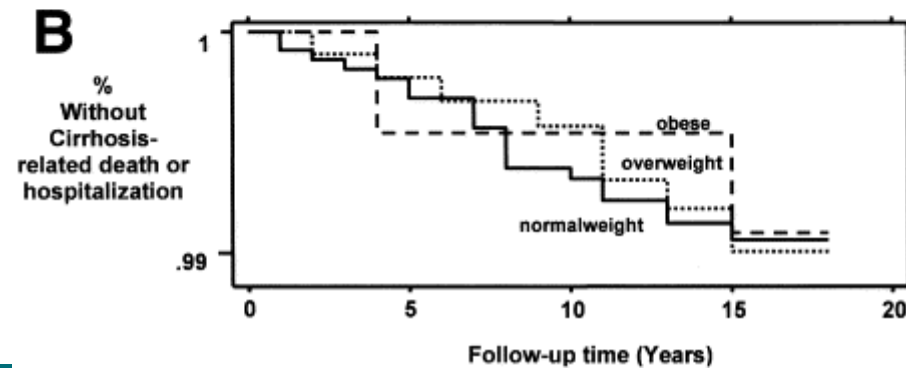
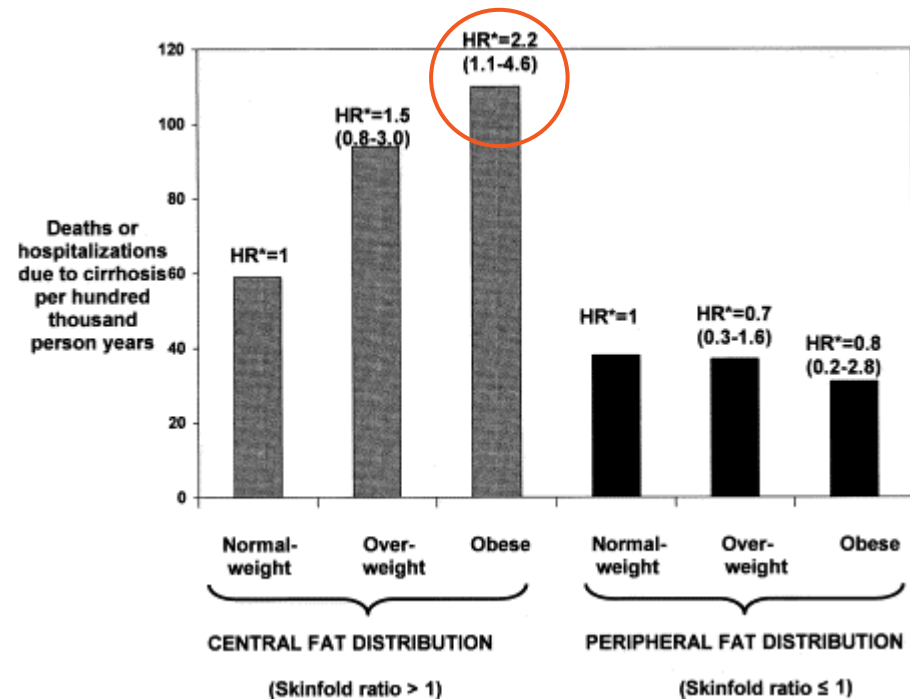
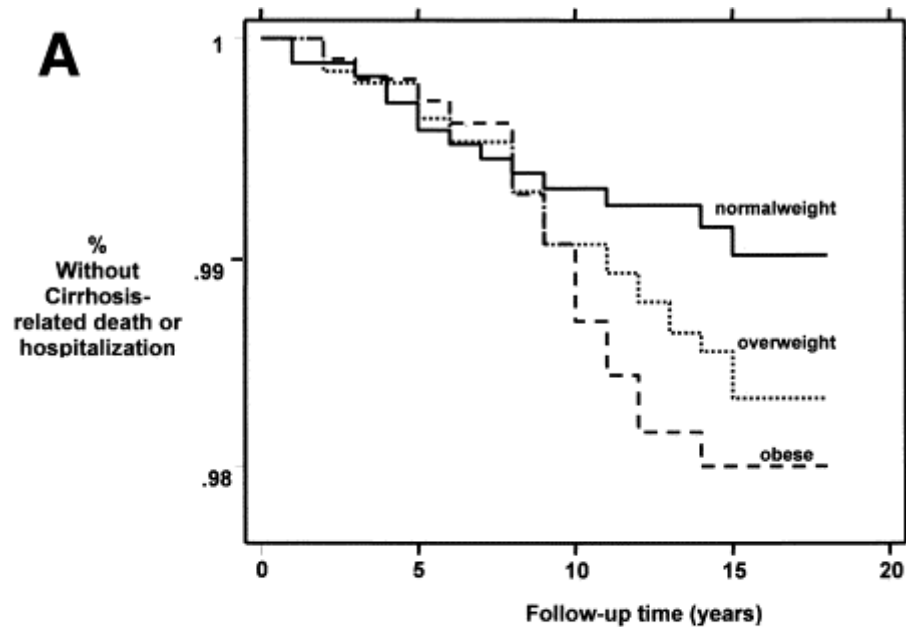
NAFLE: Natürlicher Verlauf & Prognose

Verona Diabetes
Study / SMR
CVD 1.42
Cirr. 2.52

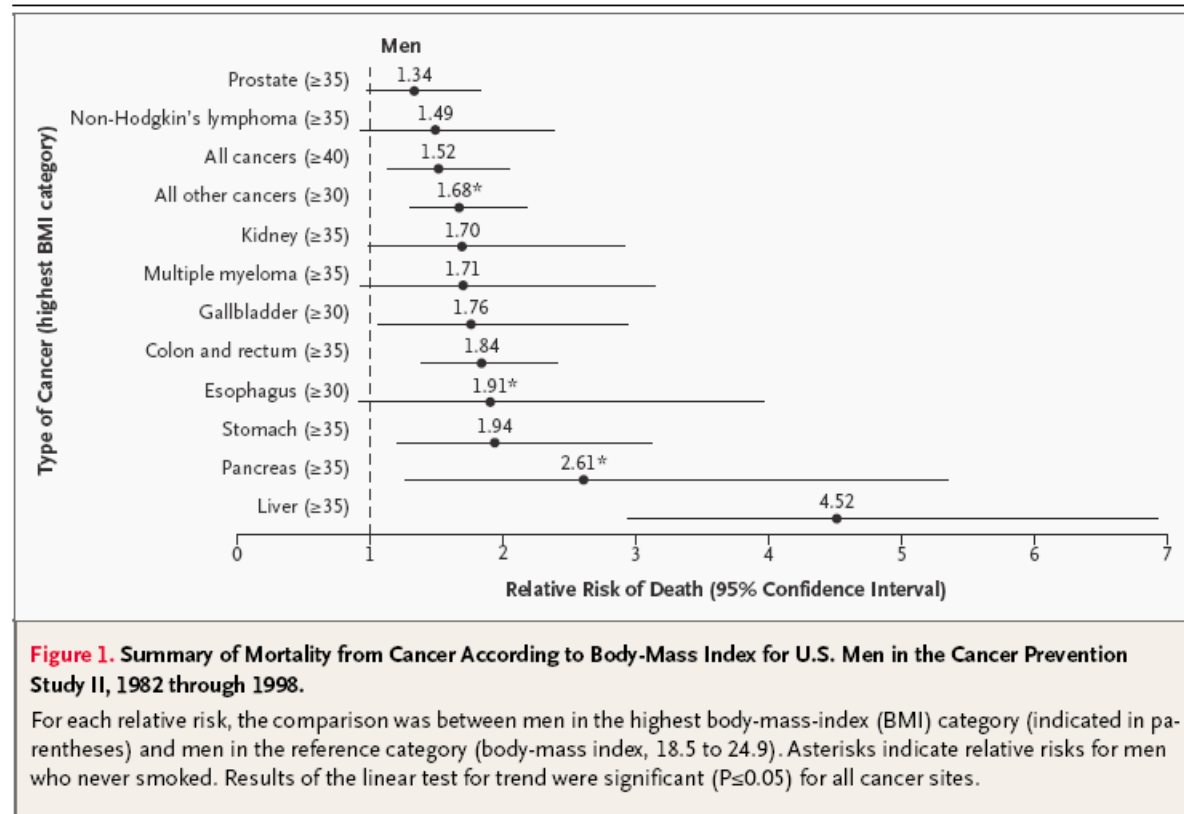


„Leber“ Prognose ernst
Liver-related Death
(11% / 8J)
Matteoni et al., *Gastro* 1999

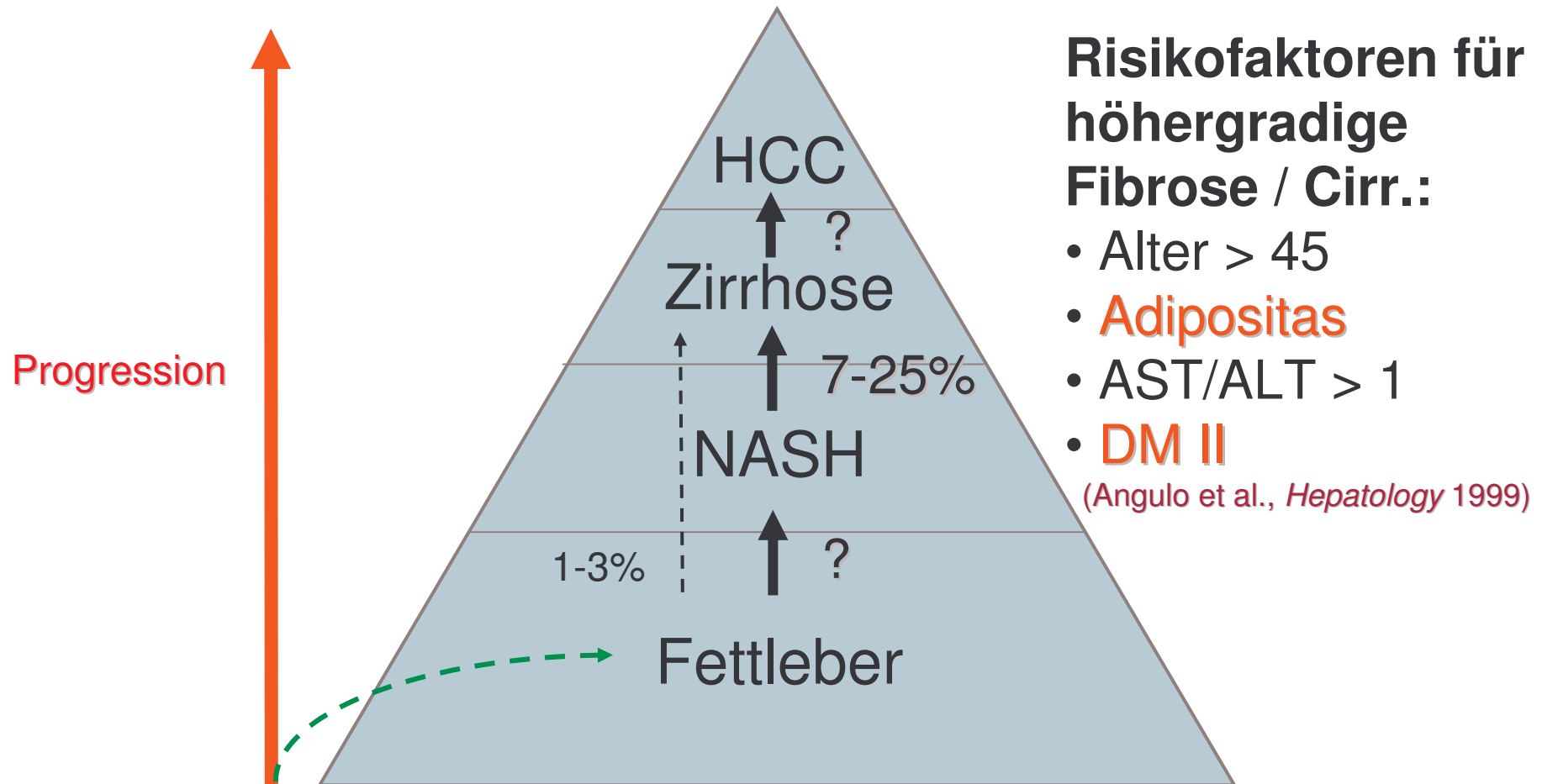
Cirrhosis-related Mortality in Obesity



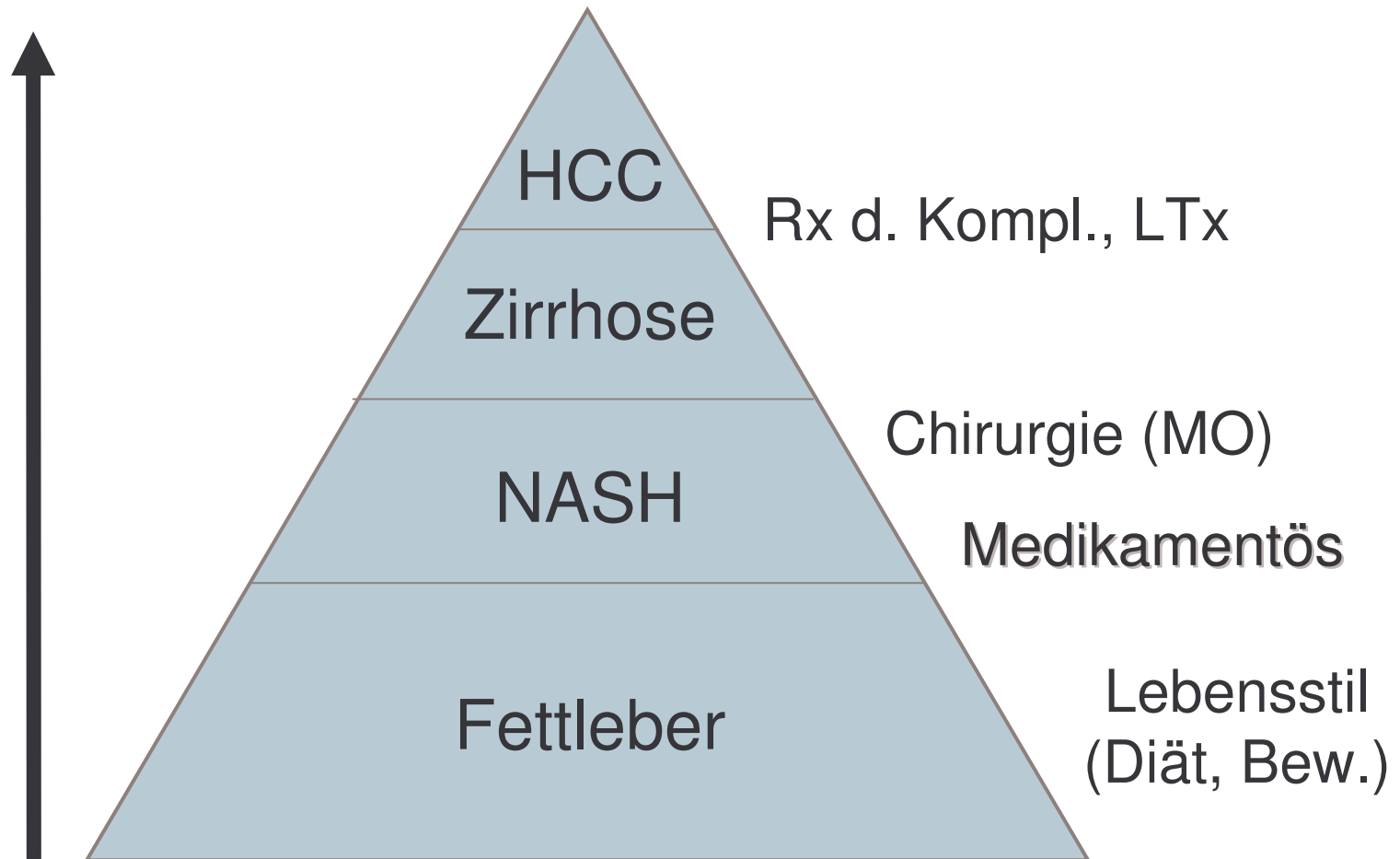
Cirrhosis-related Mortality in Obesity



NAFLE: Natürlicher Verlauf & Prognose

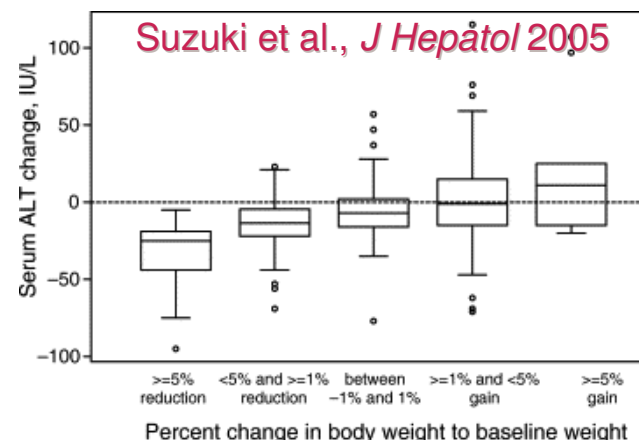


NAFLE: Stufen-Therapie



Therapieansätze bei NAFLE

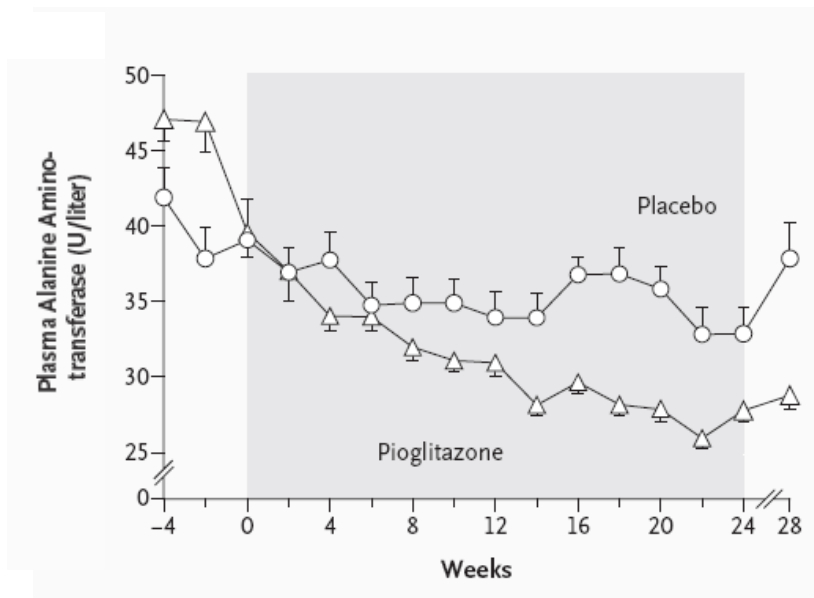
- Gewichtsreduktion (-5%, <1-1.5 kg/Wo)
 - – Lifestyle (Diät & Bewegung)
 - – Medikamentös (Orlistat, Sibutramin)
 - – Bariatrische Chirurgie
- Insulinresistenz
 - – Metformin, Glitazonen
- Andere Ansätze
 - – Oxidativer Stress, Zytoprotektion, ...



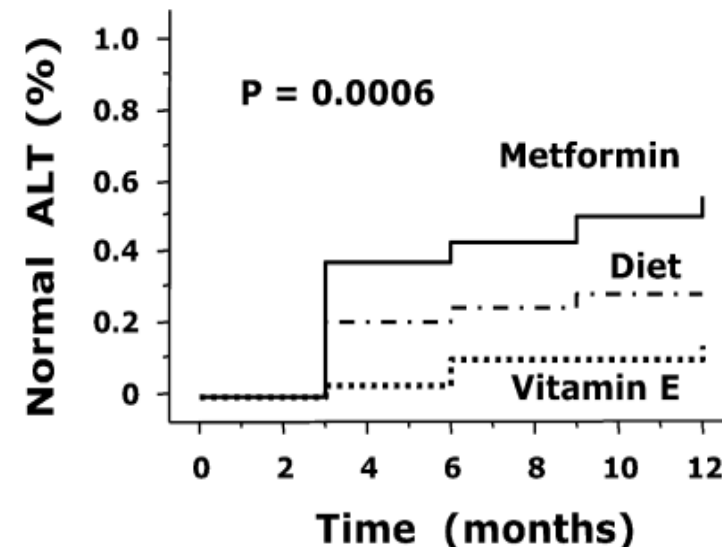
Effekte auf Fibrose generell (noch) fraglich bzw. unsicher

NASH: Medikamentöse Therapie

- Glitazone
 - Metformin
- } Insulinresistenz
Zytokine, Fibrose ↓

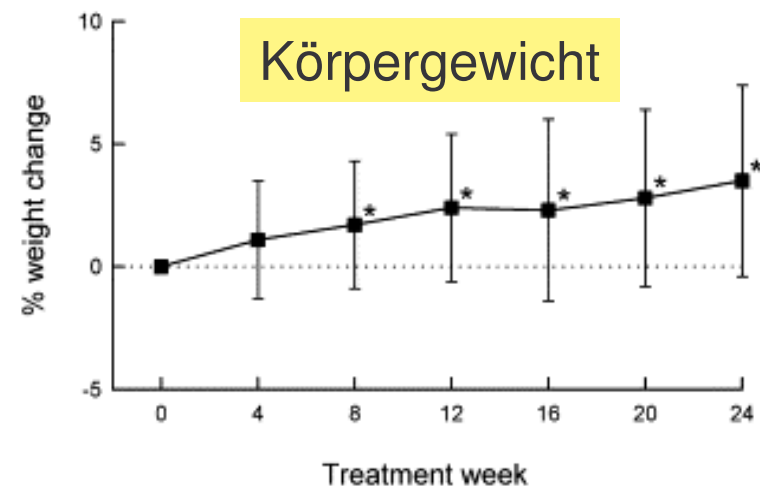
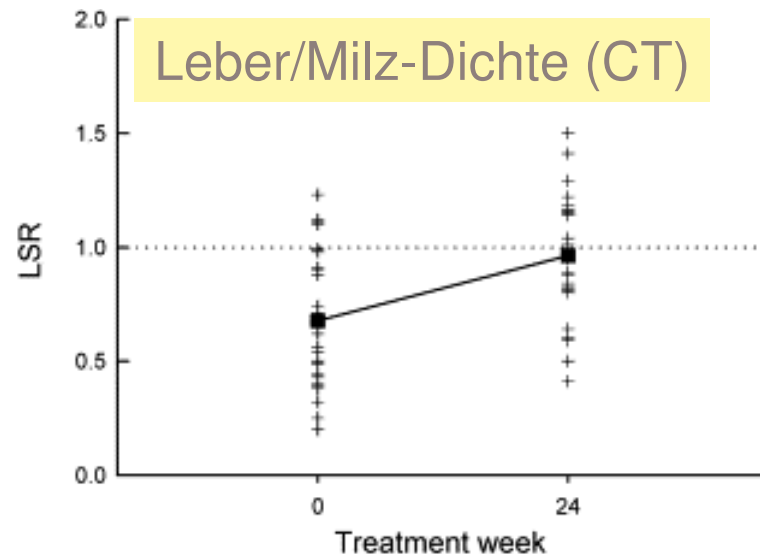
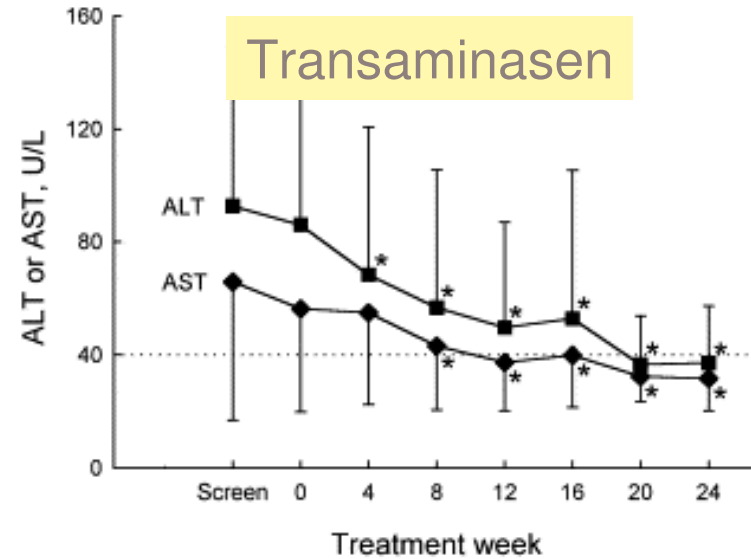
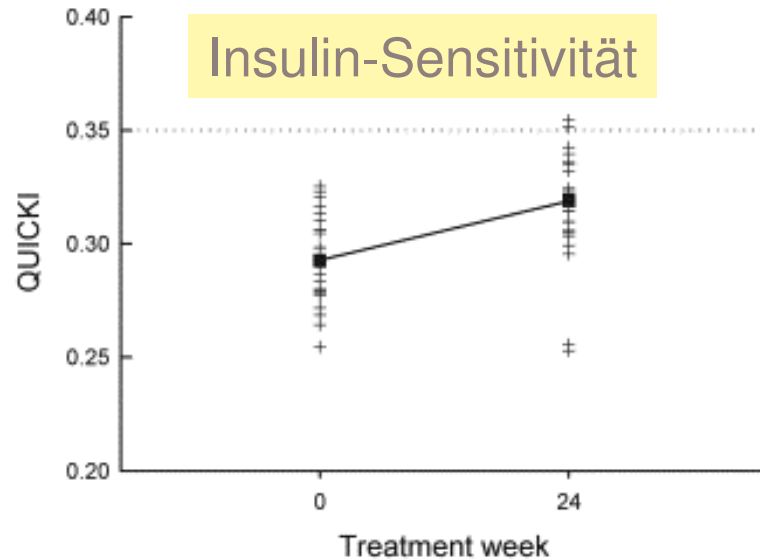


Belfort et al.,
New Engl J Med 2006; 355: 2297



Bugianesi et al.,
Am J Gastroenterol 2005; 100: 1082

Effekte von Rosiglitazon bei NASH



Wirkung der Thiazolidindione auf das Lipidprofil

The NEW ENGLAND
JOURNAL of MEDICINE

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Effect of Rosiglitazone on the Risk of Myocardial Infarction
and Death from Cardiovascular Causes

Steven E. Nissen, M.D., and Kathy Wolski, M.P.H.



- Troglitazon (600 mg 1xtgl.)
- Rosiglitazon (8 mg 2xtgl.)
- Pioglitazon (45 mg 1xtgl.)

NASH: Medikamentöse Therapie

- Glitazone
- Metformin
- Orlistat, Sibutramin
- Neuere Ansätze: Losartan, Pentoxifyllin
- Ohne (gesicherten) Nutzen:
 - Vitamin C, E
 - Ursodeoxycholsäure (UDCA)
 - Silymarin (Insulinresistenz?, keine Daten)
 - Lipidsenker (aber sicher)



Zusammenfassung

- Keine etablierte med. Rx der NASH (Fibrose!)
- Lebensstil-Änderung (wäre) beste Rx
- „Begleit“-KH nicht vergessen (Prognose!)
- DM: Glitazon (\pm) Metformin
- Art. HT: Losartan
- HLP: Statine erlaubt
- Zukunft: CB-1, GLP-1, TGR5, STORM?

Danke für Ihre
Aufmerksamkeit!

michael.trauner@meduni-graz.at