

EPIDEMIOLOGIA DELLA STEATOSI EPATICA NON- ALCOLICA: LO STUDIO DI BAGNACAVALLO

Giorgio Bedogni

www.giorgiobedogni.it

Obiettivo

- Discutere risultati dello «Studio di Bagnacavallo» (BCV) sulla steatosi epatica

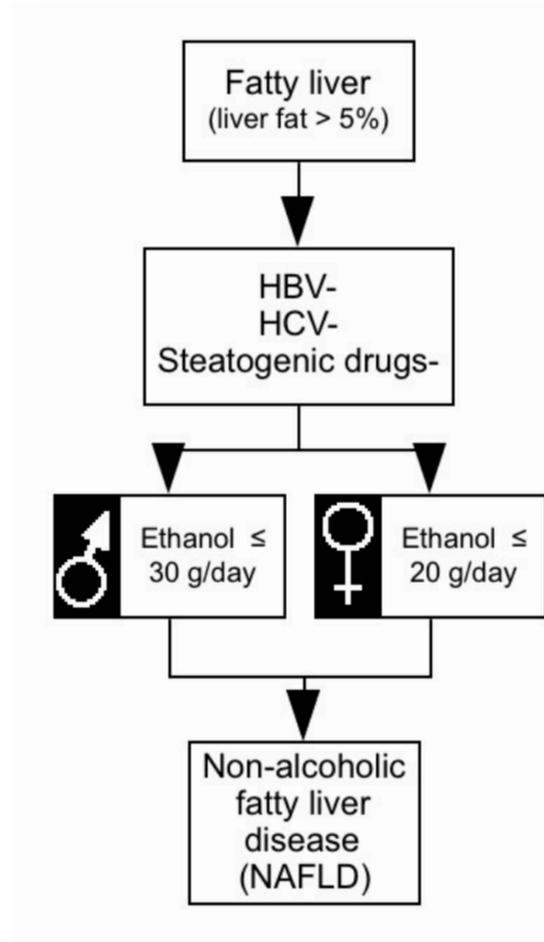
Programma

- Background
- Obiettivo
- Metodi
- Risultati
- Discussione

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Background



Background

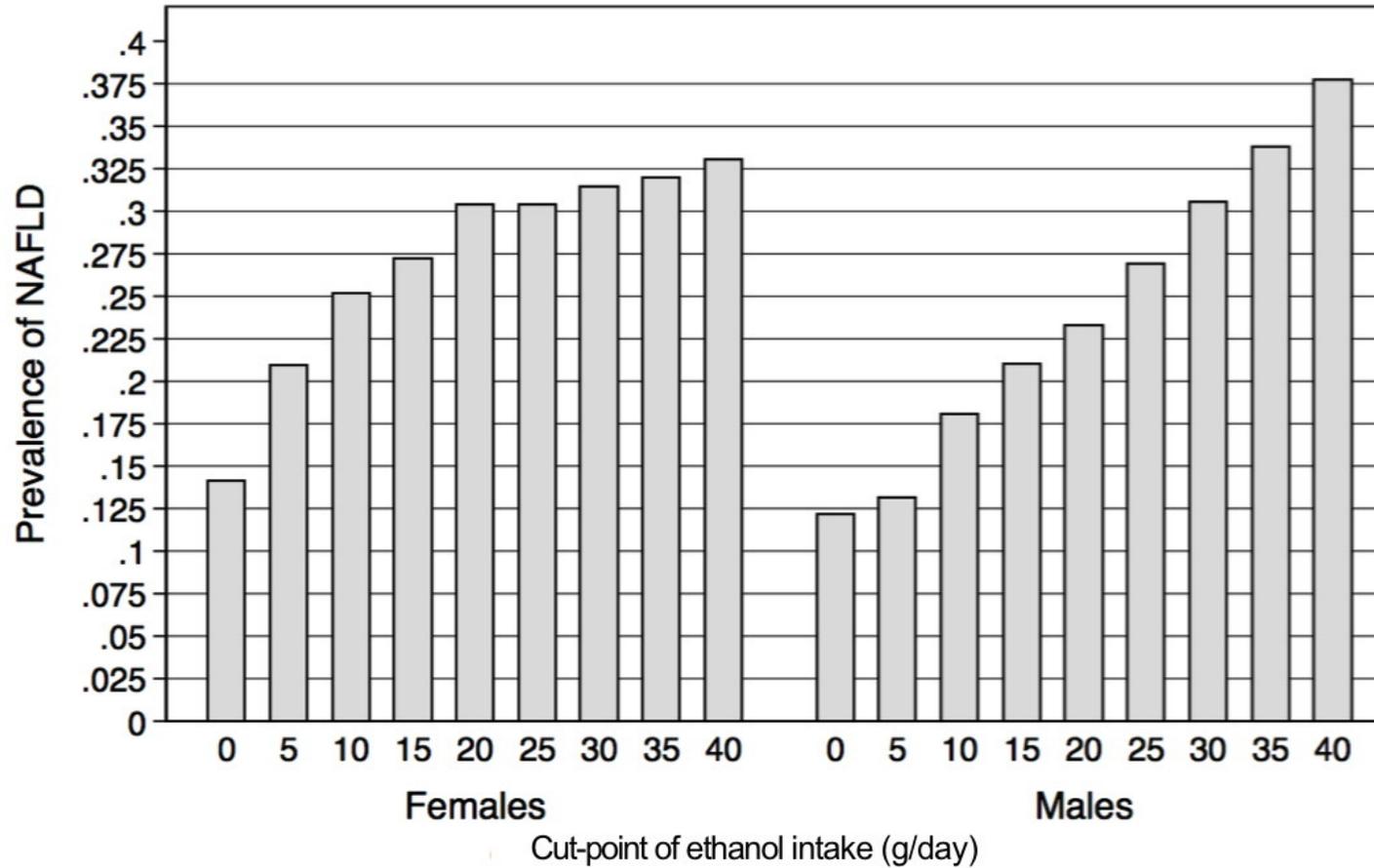
- La dicotomizzazione NAFLD vs. AFLD è utile nella pratica clinica perché l'etanolo non è per lo più tossico a quantità ≤ 30 g/die
- Nasconde però il fatto che l'introito di etanolo e l'obesità interagiscono nel determinare la prevalenza di epatopatia cronica nella popolazione generale

EASL-EASD-EASO J Hepatol. 2016;64:1388.

Hart CL et al. BMJ. 2010;340:c1240.

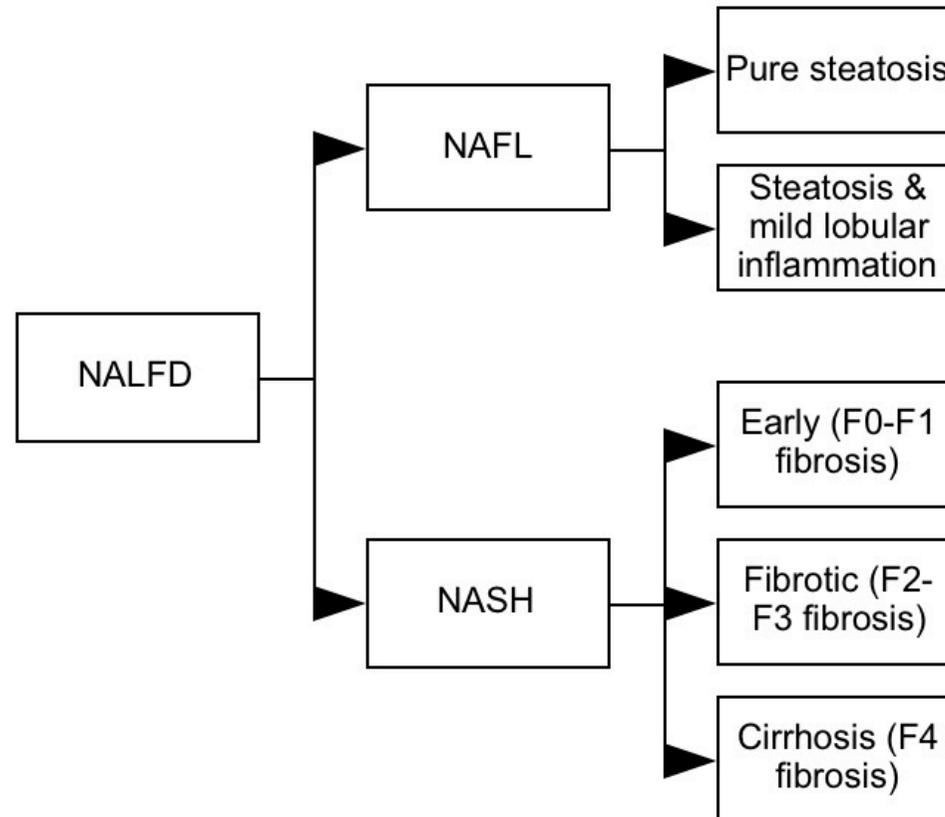
Bellentani S et al. Ann Intern Med. 2000;132:112.

Background



Calculated from Bedogni G. Hepatology. 2005;42:44

Background



Background

	N	Studies	Fibrosis progression (years to progress 1 stage, mean [95%CI])
NAFLD	366	11	7.7 [5.5 to 14.8]
NAFL	133	6	14.3 [9.1 to 50.0]
NASH	116	7	7.1 [4.8 to 14.3]

Singh S Clin Gastroenterol Hepatol 2015;13:643
(systematic review & metanalysis)

Background

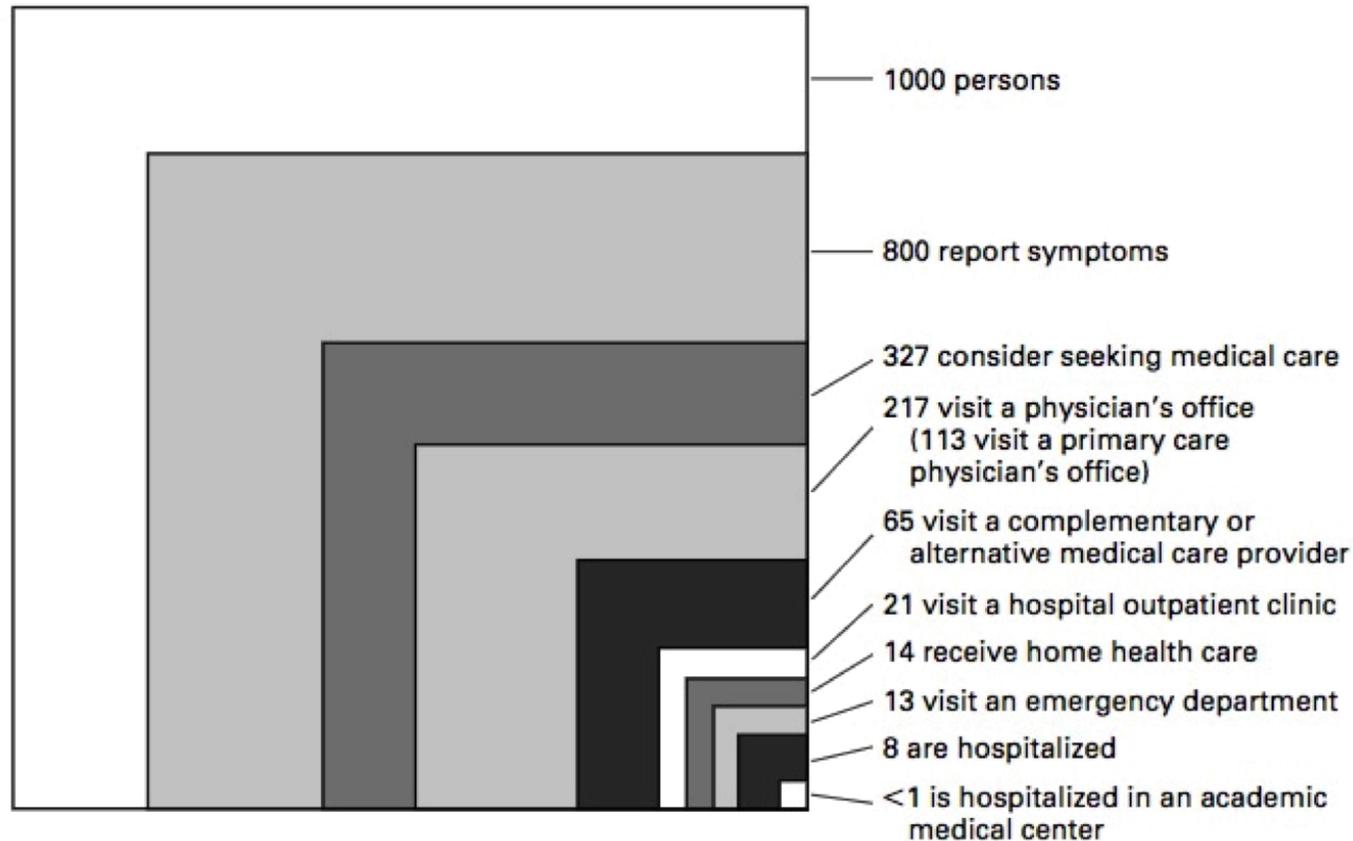


Figure 2. Results of a Reanalysis of the Monthly Prevalence of Illness in the Community and the Roles of Various Sources of Health Care.

Each box represents a subgroup of the largest box, which comprises 1000 persons. Data are for persons of all ages.

Goldberg W et al. N Engl J Med. 2001;345:1211

Background

- La prevalenza mondiale di NAFLD è attualmente stimata pari al 25% (intervallo di confidenza al 95% [95%CI] da 22 to 28%).

Younossi ZM et al. Hepatology. 2016;64:73
(systematic review & metanalysis).

- Pochi dati continuano ad essere disponibili nella popolazione generale

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Obiettivo

PREVALENCE OF AND RISK FACTORS FOR FATTY LIVER IN THE GENERAL POPULATION OF NORTHERN ITALY: THE BAGNACAVALLO STUDY

Francesco Giuseppe FOSCHI ^{1*}, Giorgio BEDOGNI ^{2*}, Marco DOMENICALI ³, Pierluigi GIACOMONI ⁴, Anna Chiara DALL'AGLIO, Francesca DAZZANI, Arianna LANZI, Fabio CONTI, Sara SAVINI, Gaia SAINI, Mauro BERNARDI, Pietro ANDREONE, Amalia GASTALDELLI, Andrea CASADEI GARDINI, Claudio TIRIBELLI ^{2*}, Stefano BELLENTANI, Giuseppe Francesco STEFANINI

* These Authors contributed equally to the present work.

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Metodi

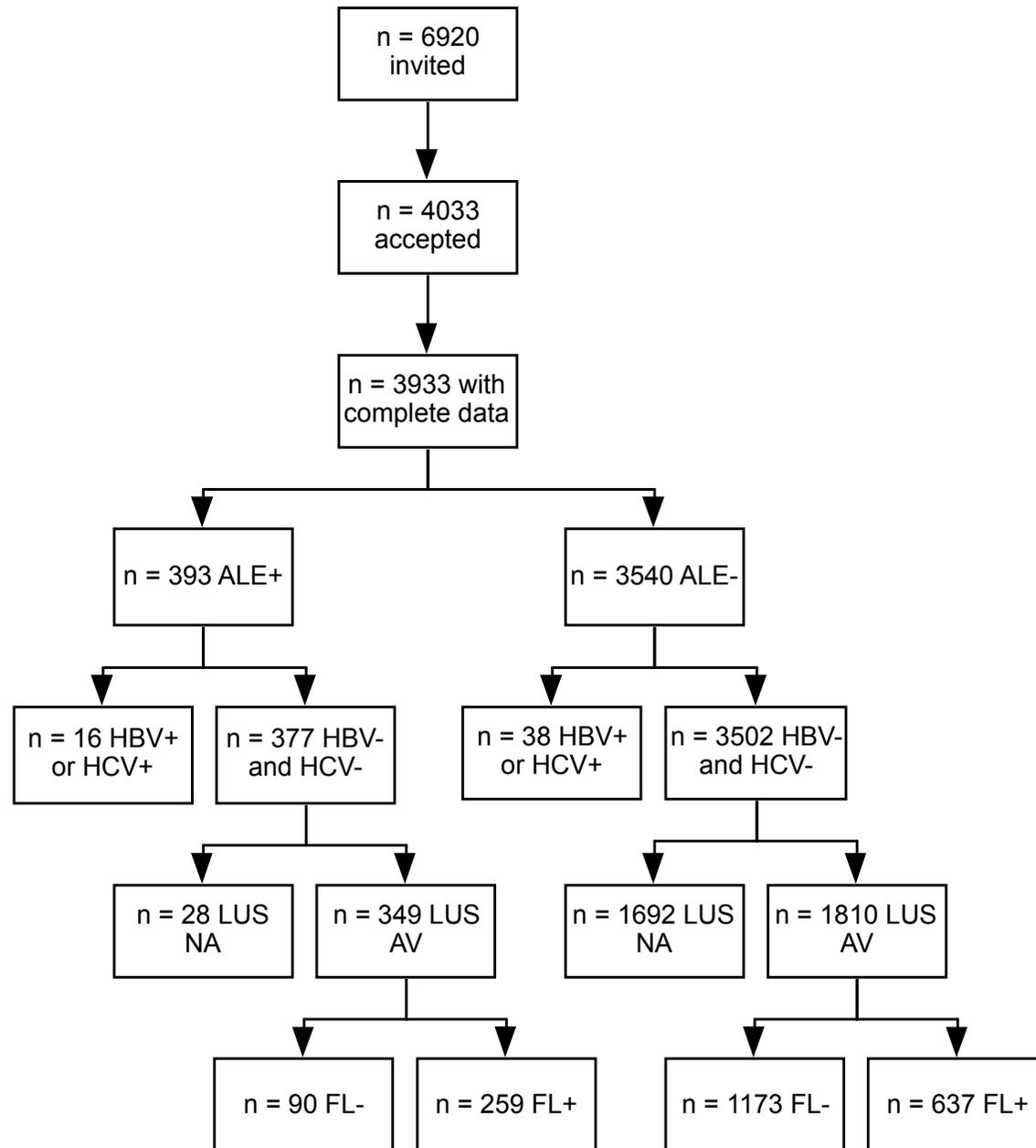
- Studio trasversale condotto tra Ottobre 2005 e Marzo 2009
- Tutti i cittadini di Bagnacavallo (Ravenna) che avevano da 30 a 60 anni di età a gennaio 2005 erano eleggibili per lo studio

Metodi

- “Altered liver enzymes (ALE)” è stato definito come come ALT > 40 U/l e/o AST > 37 U/l
- Il protocollo specificava che tutti i pazienti ALE+ e almeno il 50% degli ALE- dovevano effettuare un’ecografia epatica (LUS, liver ultranography)

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	ALE+ n = 349	ALE- n = 1810	p-value*
Male sex	267 (76.5%)	812 (44.9%)	<0.001
Age (years)	47 (40-55)	49 (41-56)	0.03
Weight (kg)	84.0 (74.0-95.0)	72.0 (61.0-82.0)	<0.001
Height (m)	1.73 (1.67-1.79)	1.68 (1.60-1.74)	<0.001
BMI (kg/m ²)	27.9 (25.4-30.9)	25.1 (22.6-28.1)	<0.001
BMI class (NIH)			<0.001
Underweight	0 (0.0%)	19 (1.0%)	
Normal	66 (18.9%)	871 (48.1%)	
Overweight	170 (48.7%)	607 (33.5%)	
Obesity class 1	81 (23.2%)	230 (12.7%)	
Obesity class 2	28 (8.0%)	65 (3.6%)	
Obesity class 3	4 (1.1%)	18 (1.0%)	
Fatty liver	259 (74.2%)	637 (35.2%)	<0.001
Fatty liver degree			<0.001
Light	105 (40.9%)	413 (66.4%)	
Moderate	102 (39.7%)	151 (24.3%)	
Severe	50 (19.5%)	58 (9.3%)	
Waist circumference (cm)	105.0 (100.0-113.0)	100.0 (93.0-107.0)	<0.001
Large waist circumference	259 (74.2%)	1236 (68.3%)	0.028
Glucose (mg/dl)	93 (87-102)	89 (83-96)	<0.001
High fasting glucose	109 (31.2%)	307 (17.0%)	<0.001
Triglycerides (mg/dl)	138 (98-206)	97 (68-139)	<0.001
High triglycerides	159 (45.6%)	405 (22.4%)	<0.001
Total cholesterol (mg/dl)	215 (192-240)	207 (184-234)	0.005
HDL cholesterol (mg/dl)	50 (44-61)	61 (51-73)	<0.001
Low HDL	64 (18.3%)	219 (12.1%)	0.002
LDL cholesterol (mg/dl)	138 (117-159)	126 (104-150)	<0.001
Systolic blood pressure (mm Hg)	130 (120-140)	125 (120-140)	<0.001
Diastolic blood pressure (mm Hg)	85 (80-90)	80 (80-90)	<0.001
High blood pressure	270 (77.4%)	1053 (58.2%)	<0.001
Metabolic syndrome	171 (49.0%)	444 (24.5%)	<0.001
Metabolic syndrome score			<0.001
0	19 (5.4%)	216 (11.9%)	
1	59 (16.9%)	595 (32.9%)	
2	100 (28.7%)	555 (30.7%)	
3	97 (27.8%)	294 (16.2%)	
4	59 (16.9%)	117 (6.5%)	
5	15 (4.3%)	33 (1.8%)	
ALT (U/l)	50 (44-63)	20 (15-26)	<0.001
AST (U/l)	33 (29-41)	20 (18-24)	<0.001
GGT (U/l)	42 (27-69)	17 (12-26)	<0.001
Total bilirubin (mg/dl)	0.6 (0.5-0.9)	0.6 (0.4-0.8)	0.003
Alcohol intake (units/day)	3 (1-5)	2 (0-4)	<0.001

Values are given as median (interquartile range) for continuous variables and as number (proportion) for discrete variables

*Median regression for continuous variables and Pearson's Chi-square test for discrete categorical variables.

Table 1

Comparison of citizens with and without altered liver enzymes.

Abbreviations: ALE = altered liver enzymes; BMI = body mass index; NIH = National Institutes of Health; HDL = high-density lipoprotein; LDL = low-density lipoprotein; ALT = alanine transaminase; AST = aspartate transaminase; GGT = gamma-glutamyl transferase.

	M1	M2	M3	M4	M5	M6
ALE	5.3** [4.1 to 6.9]	5.1** [3.9 to 6.7]	3.9** [2.9 to 5.2]	4.0** [3.0 to 5.4]	4.2** [3.2 to 5.6]	3.7** [2.8 to 5.0]
Male	—	2.1** [1.7 to 2.5]	2.0** [1.6 to 2.5]	2.1** [1.7 to 2.6]	2.0** [1.6 to 2.5]	2.4** [1.9 to 3.1]
Age (years) / 10	—	1.8** [1.6 to 2.0]	1.6** [1.4 to 1.8]	1.5** [1.4 to 1.7]	1.5** [1.4 to 1.7]	1.4** [1.3 to 1.6]
BMI (kg/m ²) / 5	—	—	3.9** [3.3 to 4.5]	—	—	—
Alcohol intake (units)	—	—	1.0 [0.9 to 1.0]	1.0 [1.0 to 1.1]	1.0 [0.9 to 1.0]	1.0 [0.9 to 1.0]
Waist circumference (cm) / 10	—	—	—	2.5** [2.3 to 2.8]	—	—
Metabolic syndrome	—	—	—	—	5.1** [4.1 to 6.3]	—
Large waist circumference	—	—	—	—	—	2.9** [2.3 to 3.8]
High triglycerides	—	—	—	—	—	3.1** [2.4 to 3.9]
Low HDL	—	—	—	—	—	1.6* [1.2 to 2.2]
High blood pressure	—	—	—	—	—	1.9** [1.5 to 2.3]
High glucose	—	—	—	—	—	2.0** [1.5 to 2.6]
<i>n</i>	2159	2159	2159	2159	2159	2159
AIC	2750	2595	2131	2244	2376	2266
BIC	2762	2618	2165	2278	2405	2317
ROC-AUC	0.61	0.72	0.83	0.81	0.79	0.81
Pseudo-R ² (Nagelkerke)	0.11	0.20	0.42	0.37	0.31	0.36

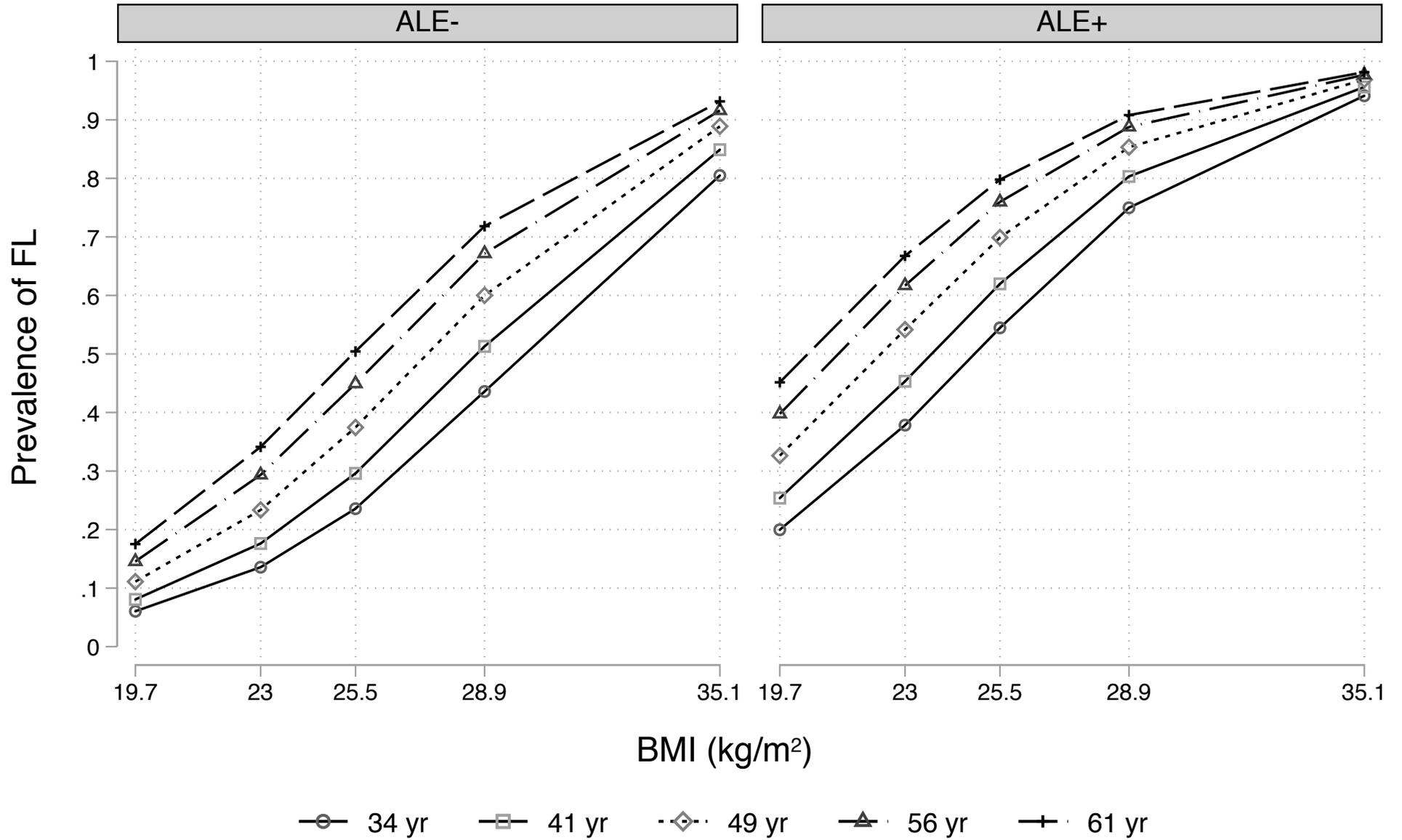
* $p < 0.01$; ** $p < 0.001$

Table 2

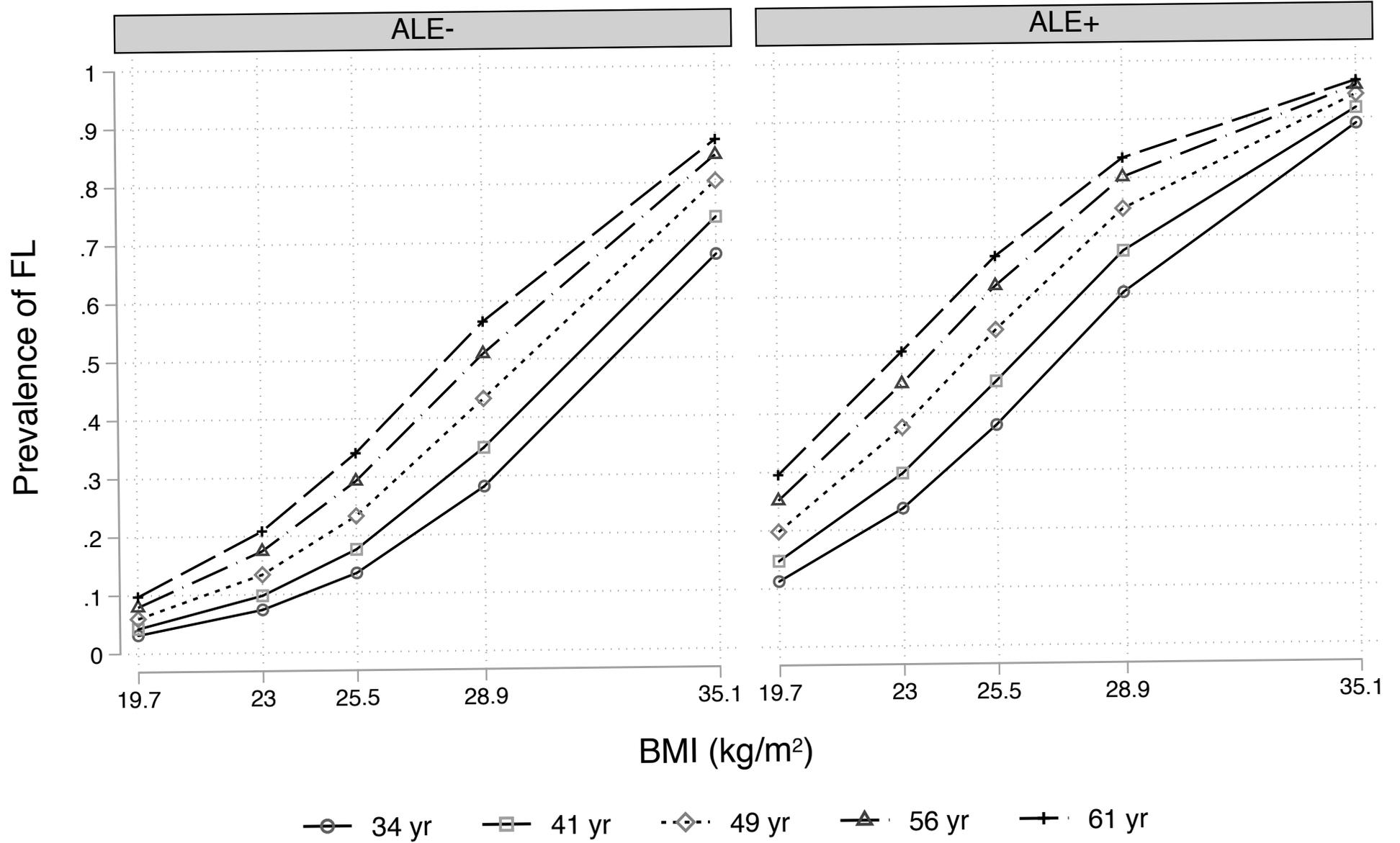
Logistic regression models used to investigate the association between fatty liver and potential risk factors. Values are odds ratios and 95% confidence intervals.

Abbreviations: M# = model number; ALE = altered liver enzymes; BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein; AIC = Akaike information criterion; BIC = Bayesian information criterion; ROC-AUC = area under the ROC curve; R² = squared R for logistic regression.

Men



Women



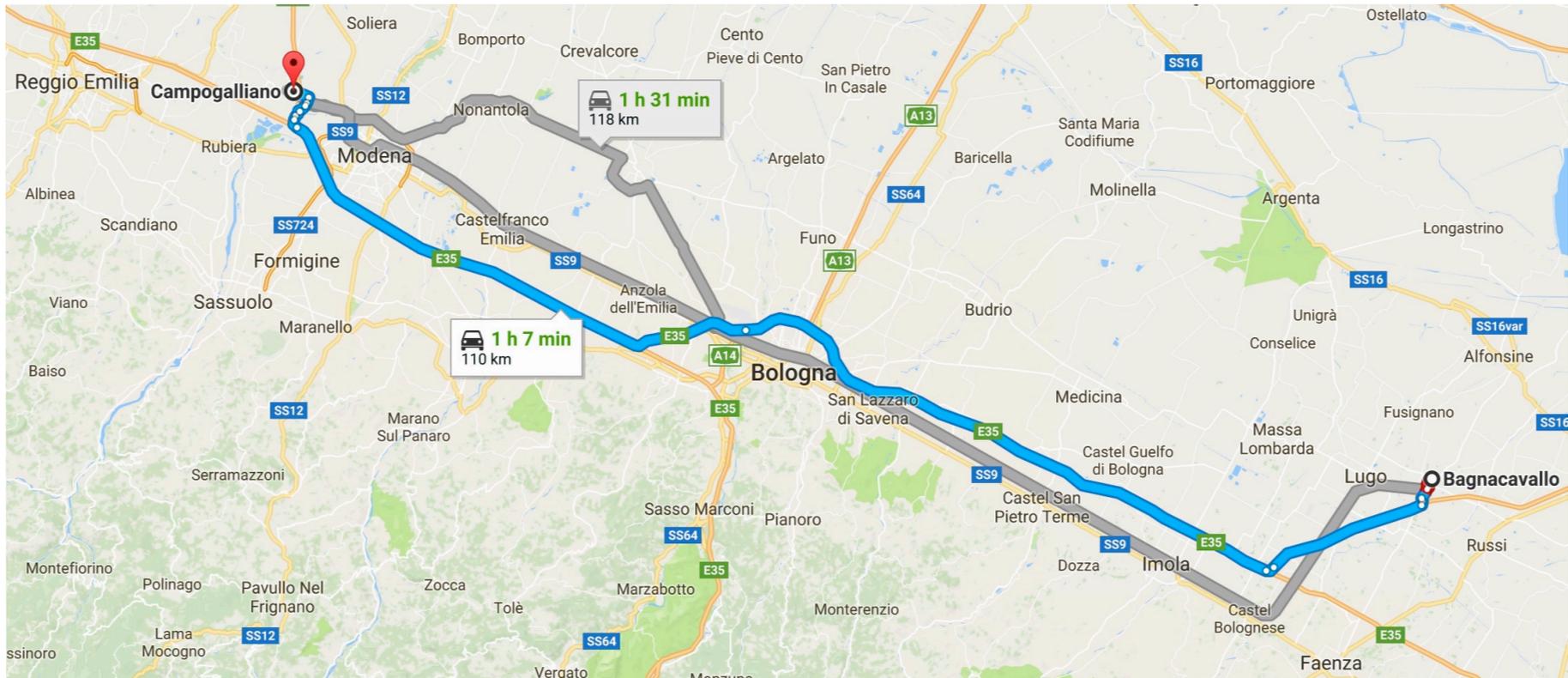
	ALE+	ALE-
Normal liver	0.26 (0.21 to 0.31)	0.65 (0.63 to 0.67)
NAFLD	0.46 (0.41 to 0.51)	0.22 (0.21 to 0.24)
ALFD	0.28 (0.24 to 0.33)	0.13 (0.11 to 0.14)

Prevalence of normal liver, NAFLD and AFLD. Values are proportions and 95% confidence intervals.

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Discussione



Discussione

- La prevalenza di NAFLD era 46% nei cittadini BCV ALE+ e 22% negli ALE-
- I dati corrispondenti per i soggetti con “suspected liver disease” (SLD) dello studio Dionysos Nutrition & Liver (DNL) erano 25% e 20%

Bedogni G et al. Hepatology. 2005;42:44.

Discussione

- Le stime degli studi BCV e DNL non sono confrontabili perché:
 - ALE e SLD non sono sinonimi
 - Il cut-point di etanolo usato per diagnosticare la NAFLD è diverso
 - La valutazione dell'introito di etanolo è stata fatta con un diario dei 7 giorni nello studio DNL e con un recall settimanale nello studio BCV

Discussione

- Due risultati particolarmente interessanti

Discussione

- L'introito di etanolo non era un predittore indipendente di steatosi epatica nella popolazione generale
- Lo studio DNL ha fornito un risultato analogo anche se il confronto diretto dei due studi non è possibile per i motivi sopra specificati

Bedogni G et al. BMC Gastroenterol. 2006;6:33.

Discussione

- Tutte le componenti della sindrome metabolica (MS) erano associate alla steatosi epatica indipendentemente da ALE, sesso, età e introito di etanolo
- Inoltre, tutte le componenti della MS identificavano la presenza della steatosi epatica meglio della sindrome metabolica stessa

Discussione

- La dicotomizzazione implicita nel concetto di MS è stata criticata da metodologi della ricerca sia sulla base di ragioni cliniche che statistiche

Bedogni G et al. World J Gastroenterol. 2014;20:9050-9054.

- Lo studio BCV offre un ulteriore argomento empirico per preferire l'uso delle singole componenti della MS alla MS per lo studio dell'associazione della steatosi epatica coi fattori di rischio cardio-metabolico

Conclusione

- La steatosi epatica era piuttosto comune a Bagnacavallo nel 2005/9 ed era più frequente tra i cittadini con enzimi epatici alterati
- Non era associata con l'introito di etanolo ma era fortemente associata con l'antropometria e le componenti della MS

Conclusione

- I dati trasversali presentati in questa relazione rappresenteranno la base per lo studio della coorte BCV che speriamo possa offrire dati nuovi e rilevanti sul “burden” attribuibile alla steatosi epatica nella popolazione generale

Grazie!

Backup slides

Clinical assessment

- All the citizens underwent a detailed clinical history and physical examination following the model of the Dionysos Study

Bedogni G et al. Hepatology. 2005;42:44-52.

Bellentani S et al. Hepatology. 1994;20:1442-1449.

Alcohol intake

- Current alcohol intake was assessed retrospectively by trained interviewers by measuring the quantity (grams) of beer, wine and liquor drunk in the week prior to the enrollment.
- Such quantity was divided by 7 to obtain a daily estimate and converted into alcohol units with rounding to the next integer.
- The conversion was done using an alcohol unit corresponding to 10 g of ethanol.

Anthropometry

- Weight and height were measured following international guidelines.
- Body mass index (BMI) was calculated and classified following the NIH guidelines.
- Waist circumference (WC) was measured at the midpoint between the last rib and the iliac crest.

Laboratory assessment

- 1) glucose;
- 2) triglycerides;
- 3) total cholesterol;
- 4) high-density lipoprotein (HDL) cholesterol;
- 5) low-density lipoprotein (LDL) cholesterol;
- 6) ALT;
- 7) AST;
- 8) gamma-glutamyl-transferase (GGT);
- 9) bilirubin;
- 10) hepatitis B surface antigen (HBsAg);
- 11) antibodies against hepatitis C virus.

Metabolic syndrome

- The metabolic syndrome (MS) was diagnosed using the harmonized international definition.

Alberti KG et al. Circulation. 2009;120:1640-1645.

Metabolic syndrome

- ≥ 3 of the following
 - Large WC : WC ≥ 102 cm in men or ≥ 88 cm in women;
 - High triglycerides: triglycerides ≥ 150 mg/dl or use of triglyceride-lowering drugs;
 - Low HDL: HDL < 40 mg/dl in men or < 50 mg/dl in women or use of HDL-increasing drugs;
 - High blood pressure: systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg or use of blood pressure-lowering drugs;
 - High glucose: glucose ≥ 100 mg/dl or use of glucose lowering drugs.

Liver ultrasonography

- LUS was performed by five experienced physicians following international guidelines and using the same methodology of the Dionysos Nutrition and Liver Study (DNL).
- Normal liver / light FL / moderate FL / severe FL