

Developing a non-invasive algorithm for the diagnosis of steatotic liver disease in primary healthcare

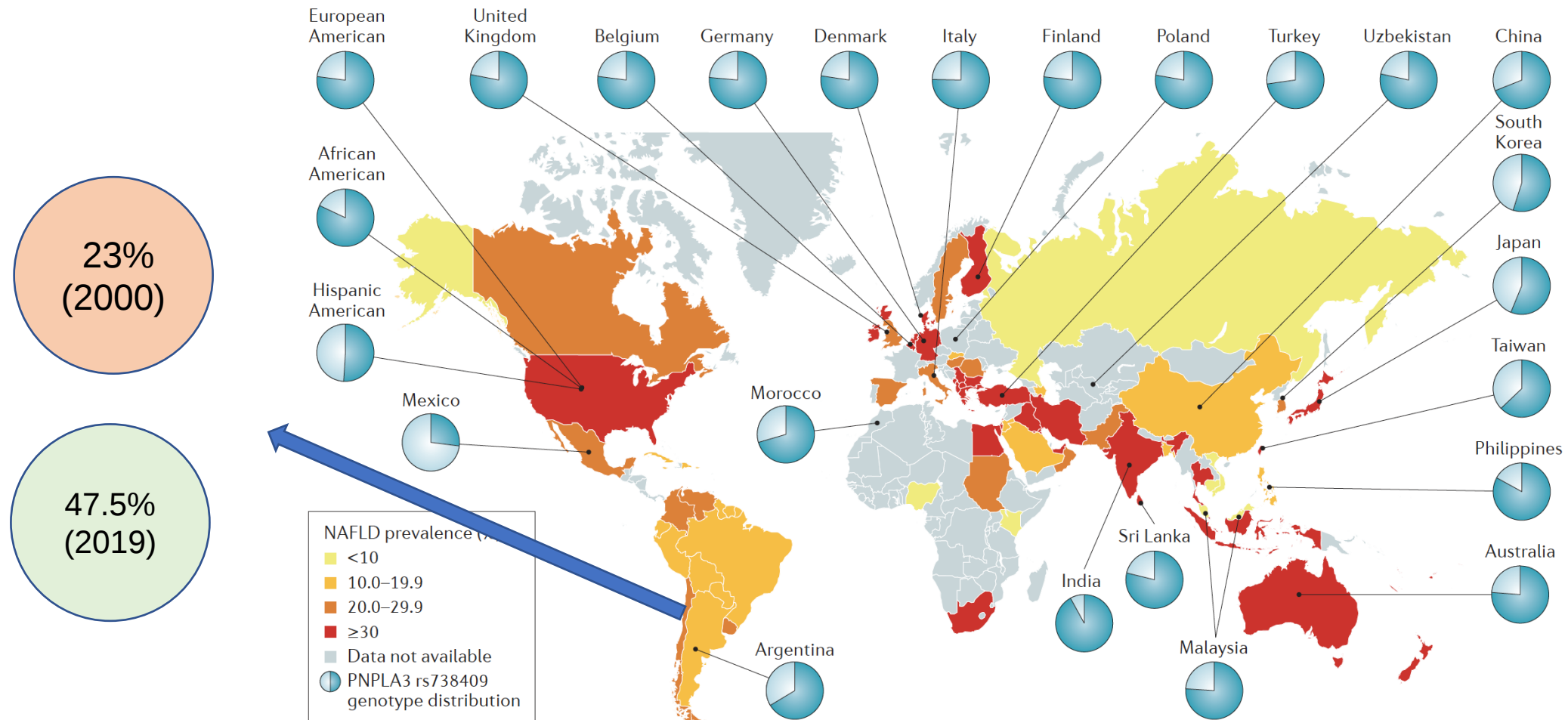
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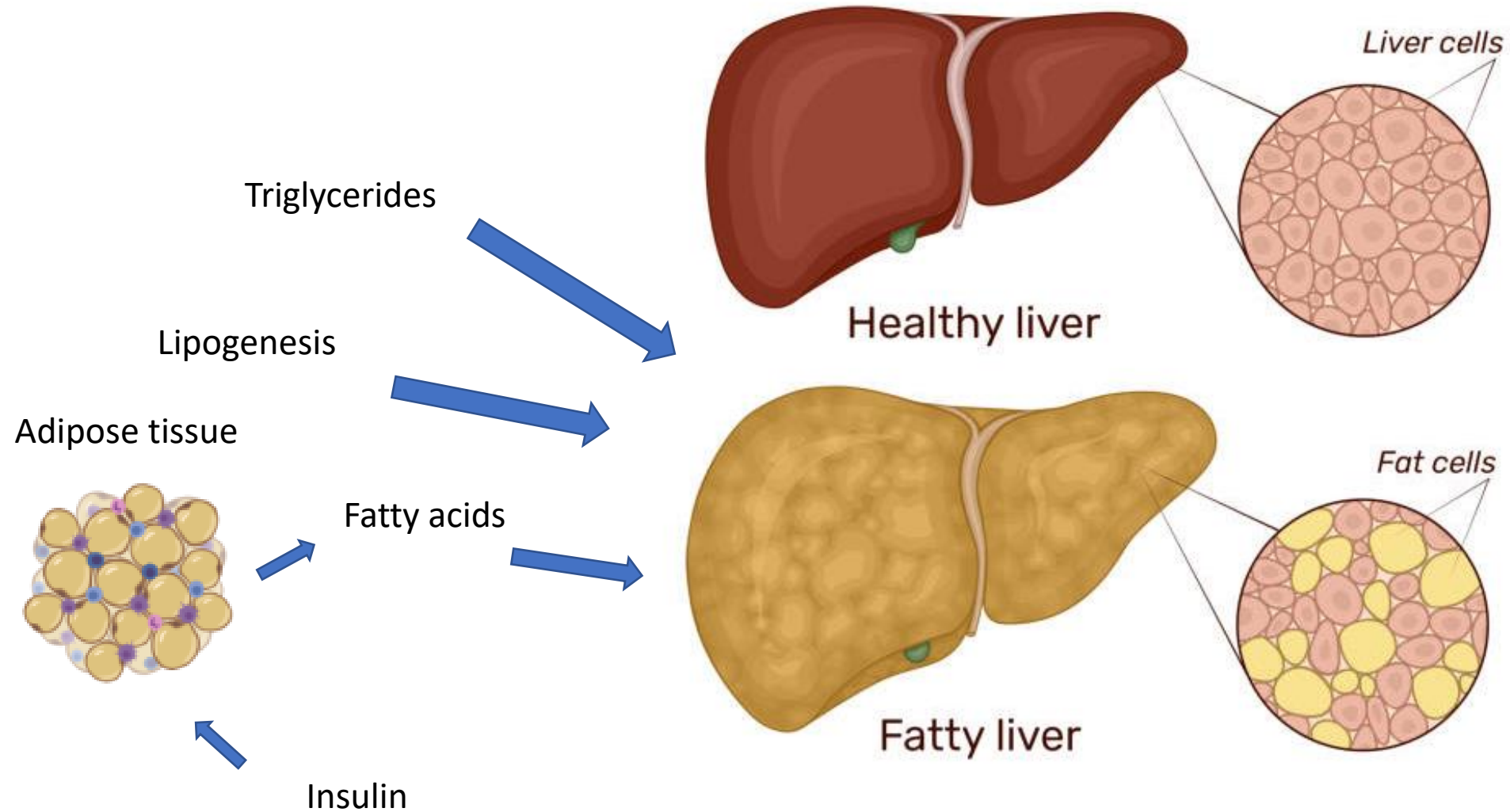
Chilean demographic changes

- Even though life expectancy has increased, chronic diseases and risk factors have risen, implying poor quality of life for the extra years.
- Tobacco consumption (39,8% 2009-2010 to 33,3% 2016-2017)
- Alcohol consumption (12,7% to 11,7%)
- Sedentary lifestyle (88,6% to 86,7%)
- Obesity (22,9% to 31,2%)
- Hypertension (26,5% to 27,6%)
- Diabetes (9% to 12,3%)

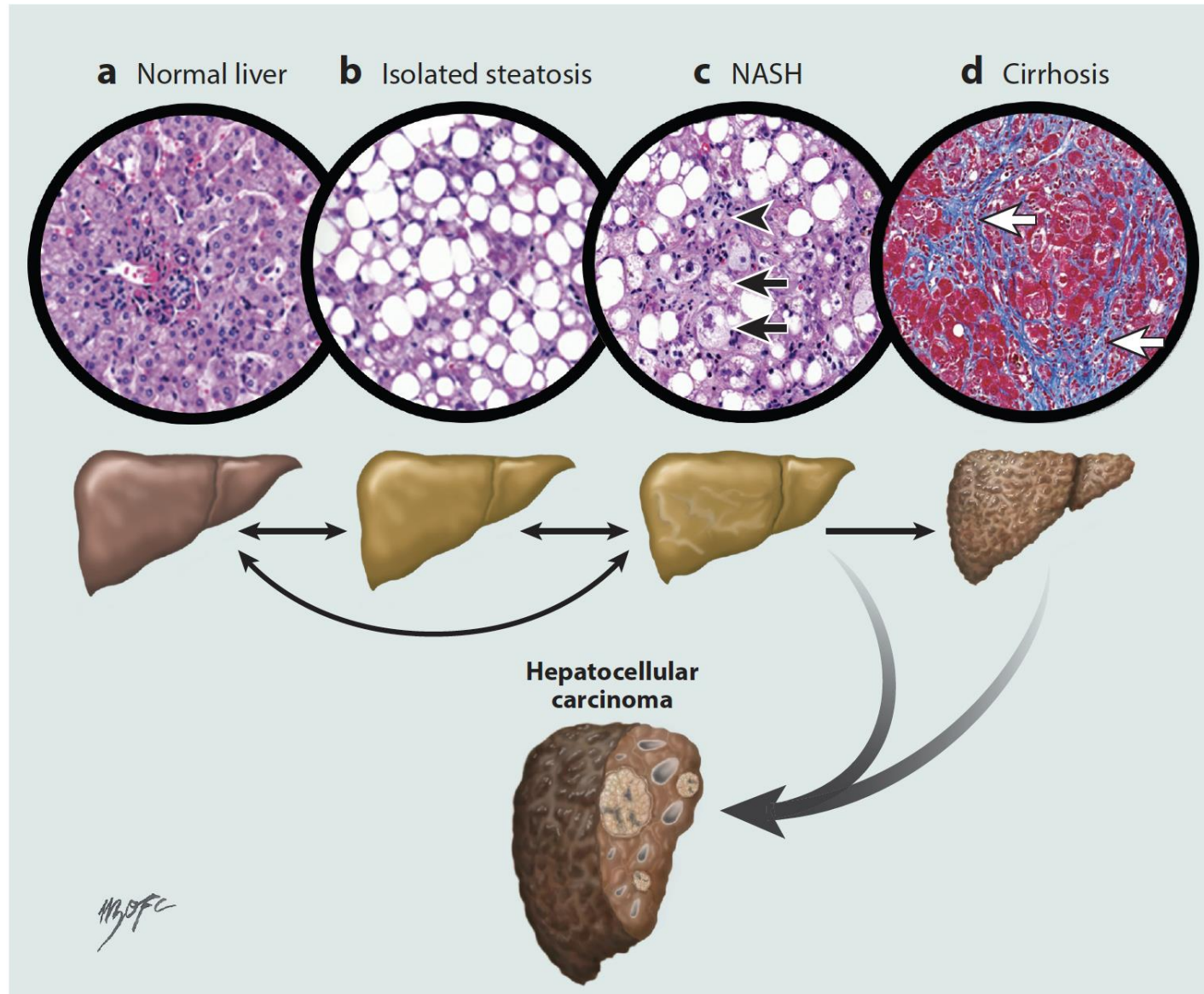
Steatoc liver disease (SLD) prevalence (NAFLD)



Steatotic Liver Disease (SLD)

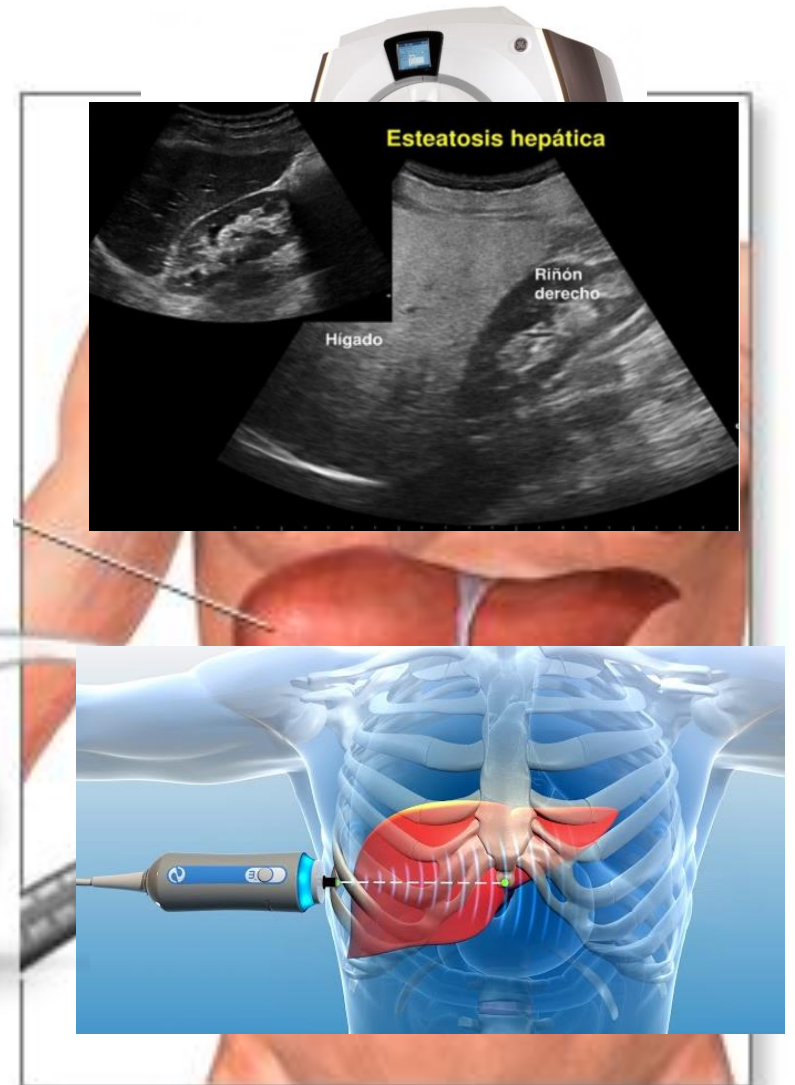


SLD stages



Diagnostic techniques for steatosis detection

- Histological
- Imagological
- ~~Serological~~



Why is early detection of SLD is important?

- Diagnosing is associated with accidental discoveries.
- Non-invasive intervention in early stages
 - Exercise
 - Diet
- Which becomes challenging in advanced stages of the disease.
 - $\geq 10\%$ of their body weight, but usually only 10-20% achieve it.

Algorithms

- Highly used in the primary health care
- To optimize diagnostics
- Helps in the patient classification
- Mostly used in health care
 - Decision tree
 - Scores



Scores for fatty liver disease

Fibrosis 4 (Fib4)	Fibrosis	AST (U/L) ALT (U/L) Platelets (mm3) Age (years)	<1.45 1.45-3.25 >3.25	F0-F1 F2-F3 F4-F6
Fibrosis scale for NAFLD	Fibrosis	AST (U/L) ALT (U/L) Platelets (10*9/L) Age (years) Weight (kg) Height (cm) Albumin (g/L)	< -1.455 -1.455 – 0.675 > 0.675	F0-F2 Indeterminate F3-F4
BARD	Fibrosis	BMI ≥ 40 (yes/no) AST (U/L) ALT (U/L)	0-1 2-4	Low High
		GGT (U/L) Triglycerides (mmol/L)	≥60	High

Our study proposition

To contribute to the early diagnosis of Steatotic Liver Disease in the Chilean population, based on available technology to apply in the primary health care system.

Maule cohort (MAUCO)

- High burden of chronic diseases and risk factors
- Overall mortality rate 10.5%
- Since 2014
- Women and men ages 30 to 70 years
- 9,462 participants



MAUCO +

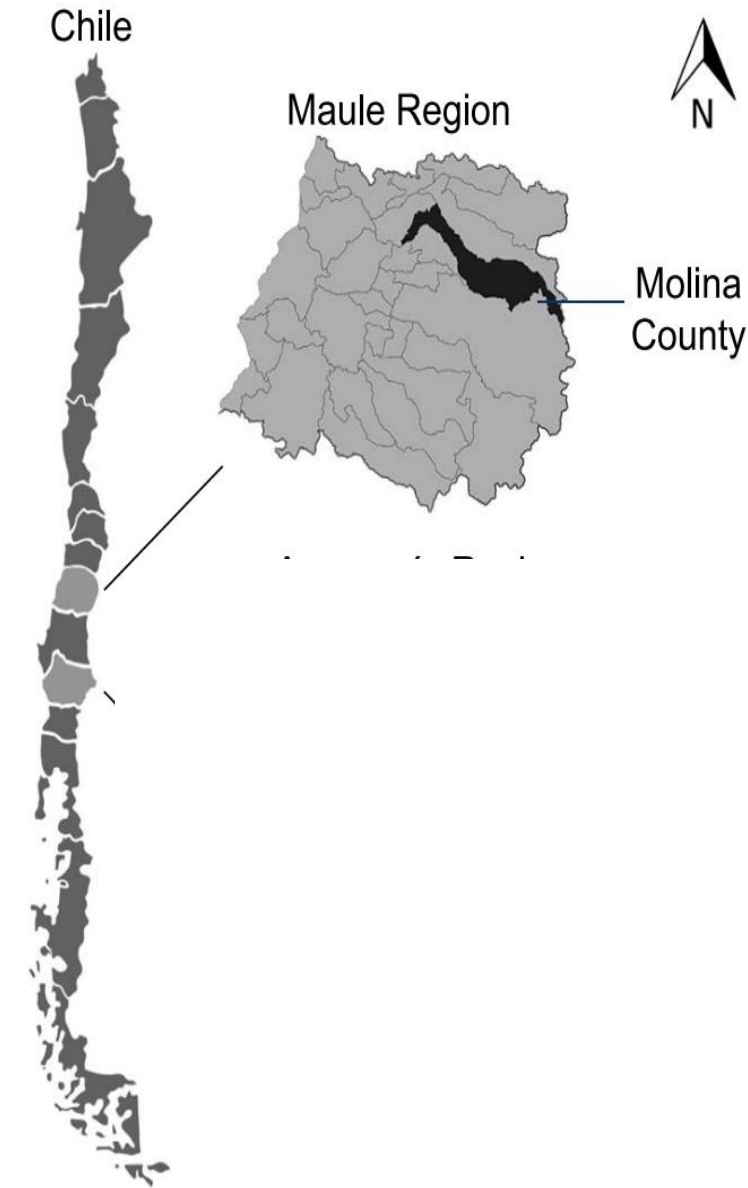
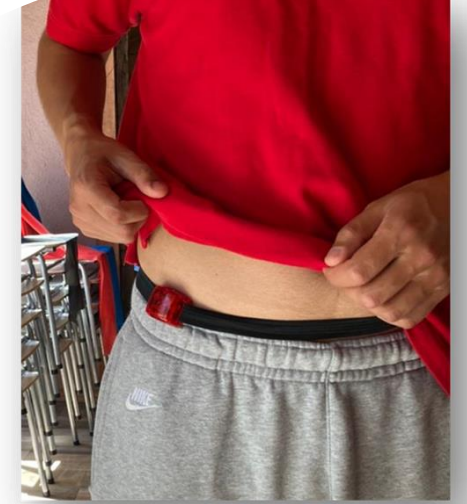


Figure adapted from Koshiol et al. Am J Epidemiol 2021

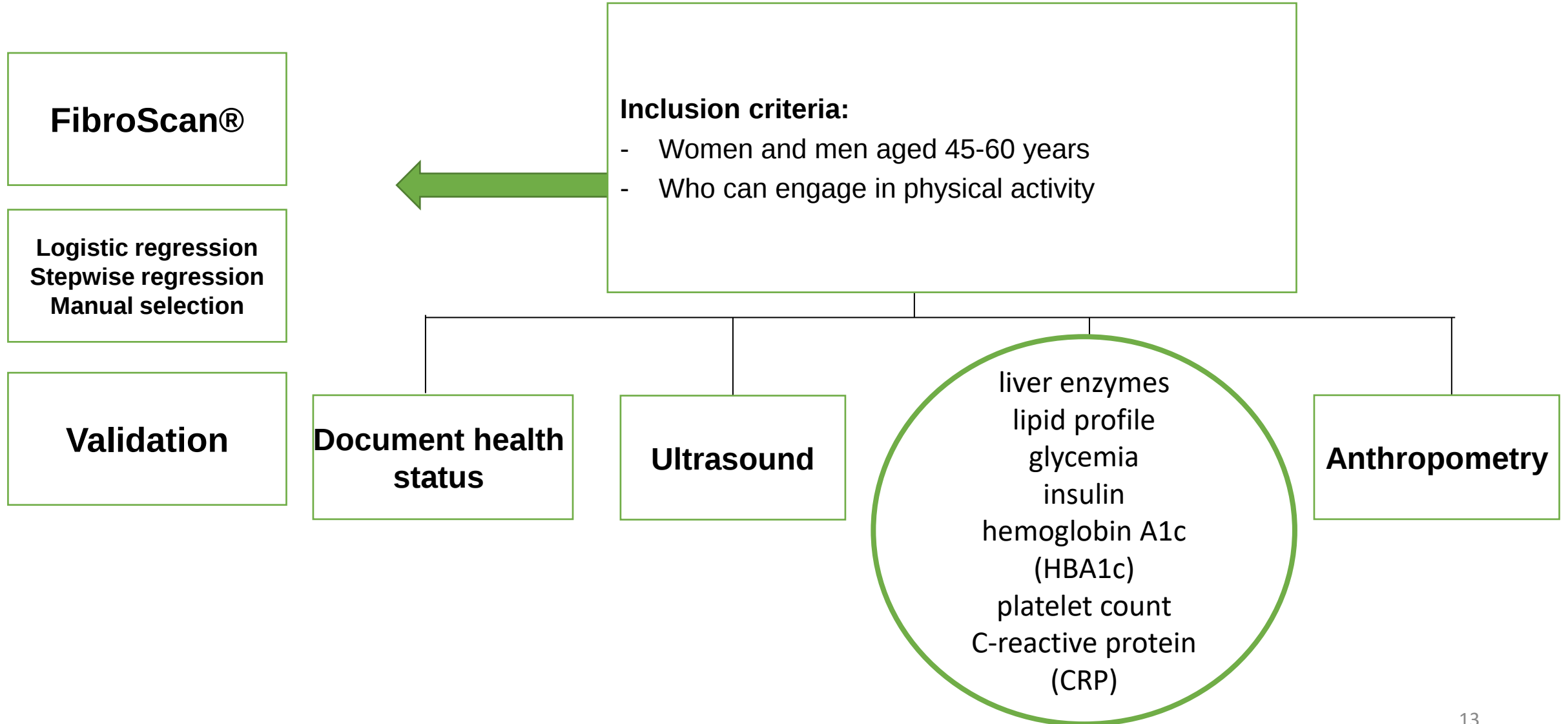
ClinicalTrials.gov Identifier: NCT05618626

MAUCO +



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Score development



Score development

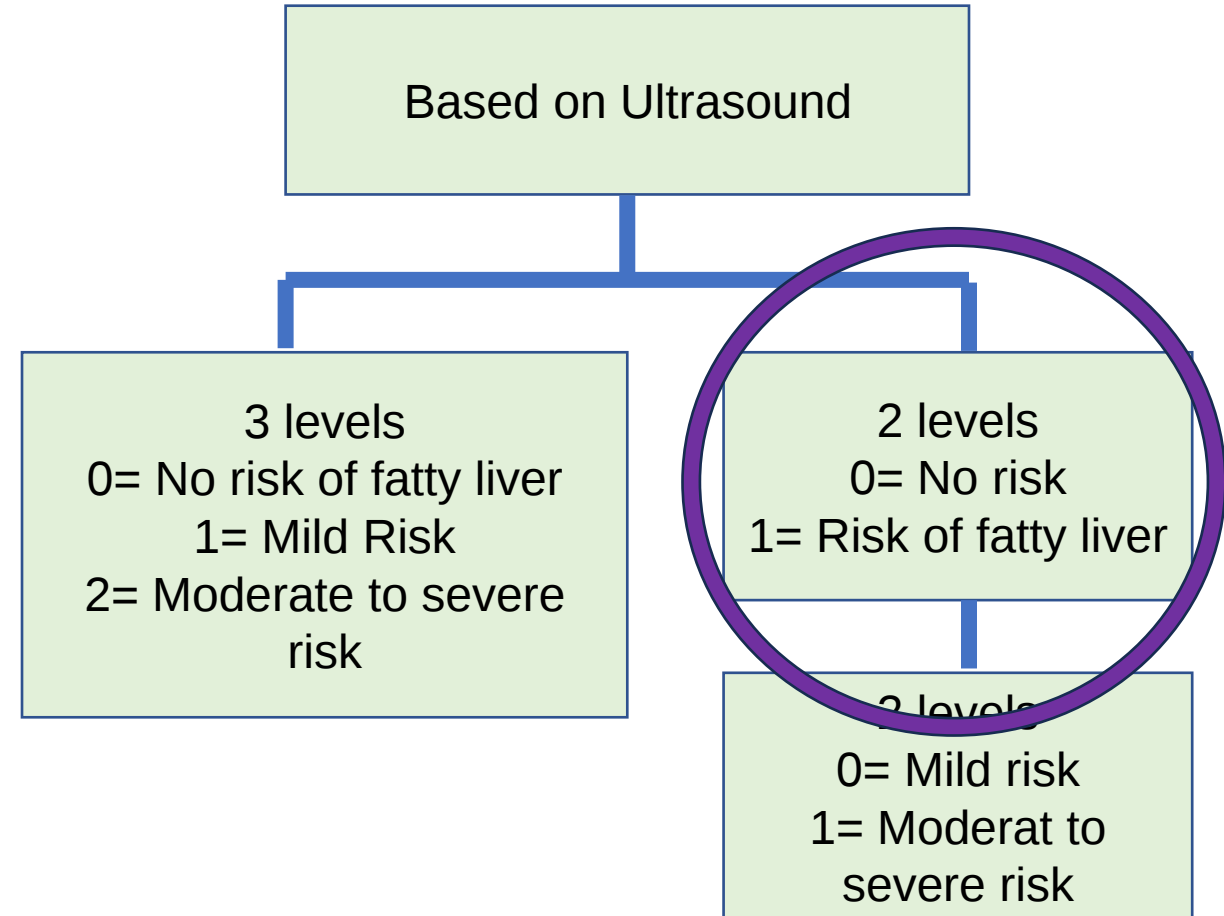
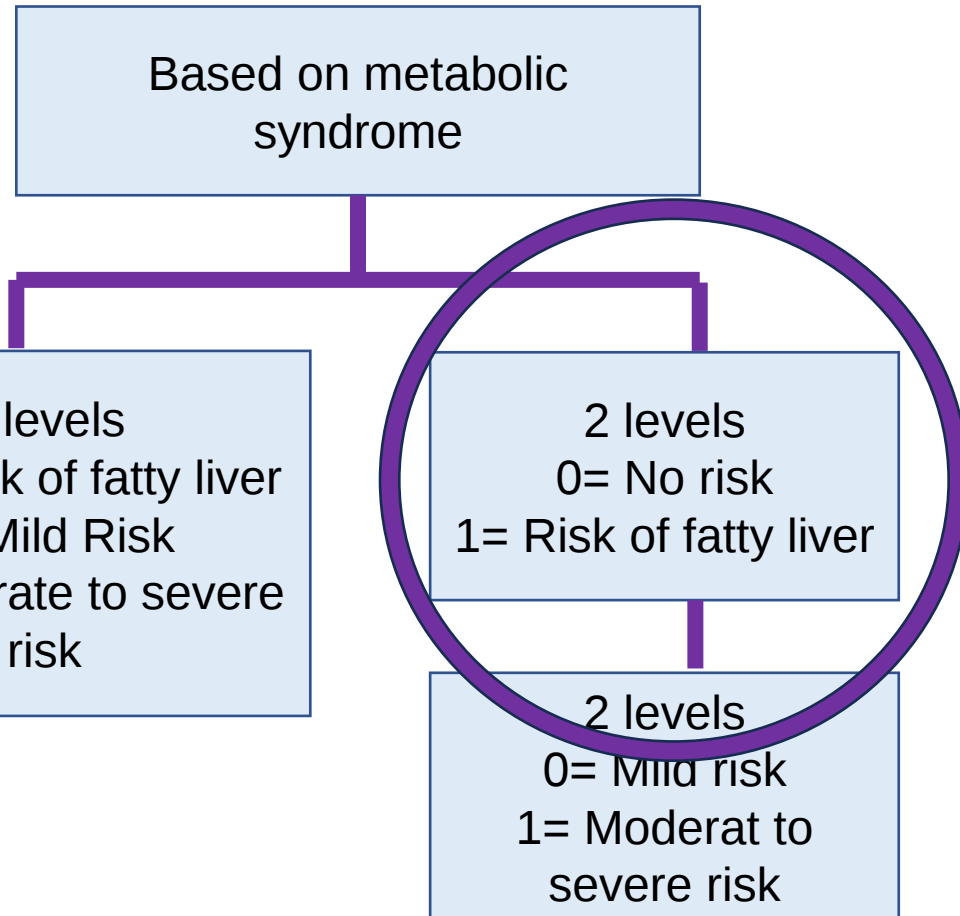


Table 1. MAUCO + participants with whole clinical profile (n=826)

Health profile		None (n=418)	Mild (n=190)	Moderate (n=111)	Severe (n=107)
Age, mean (SD)		54.1 (4.3)	54.3 (4.3)	54.1 (4.1)	53.7 (4.5)
Sex	Men	102 (24.4)	69 (36.6)	49 (44.1)	52 (48.6)
	Women	316 (75.6)	121 (63.7)	62 (55.9)	55 (51.4)
Weight, mean (SD)		74.4 (13.3)	83.0 (12.6)	86.8 (15.4)	93.9 (18.8)
Height, mean (SD)		159.3 (8.3)	161.3 (8.5)	161.8 (8.4)	162.2 (9.5)
Body fat percentage, mean (SD)		39.4 (8.7)	39.9 (9.8)	40.6 (10.0)	41.7 (8.9)
BMI, mean (SD)		29.3 (4.5)	31.9 (4.2)	33.1 (5.3)	35.5 (5.3)
BMI	<25 kg/m ²	65 (15.6)	4 (2.1)	3 (2.7)	1 (0.9)
	≥25 kg/m ²	351 (84.4)	186 (97.9)	108 (97.3)	106 (99.1)
Waist circumference, mean (SD)		95.8 (10.9)	102.7 (11.1)	107.4 (11.2)	112.7 (12.5)
Waist circumference (≥88 cm women, ≥102 cm men)		267 (64.8)	148 (77.9)	95 (87.2)	95 (91.3)
Hip circumference, mean (SD)		105.0 (8.8)	109.1 (9.0)	110.8 (9.9)	114.2 (12.2)
Neck circumference, mean (SD)		74.3 (13.3)	82.6 (13.8)	86.8 (15.5)	94.0 (19.2)
Diabetes		17 (4.1)	24 (12.8)	18 (16.4)	47 (44.3)
Prediabetes		79 (20.1)	55 (33.7)	41 (44.6)	30 (50.8)
Glycemia, mean (SD)		96.4 (23.3)	106.5 (31.6)	112.0 (40.2)	139.0 (59.1)
Insulin, mean (SD)		10.3 (7.4)	15.8 (9.7)	18.7 (14.3)	23.6 (16.5)
HOMA (≥2.5), mean (SD)		5.8 (0.9)	6.1 (1.2)	6.1 (1.2)	7.3 (2.2)
AST/GPT, mean (SD)		24.4 (12.1)	26.8 (14.1)	33.1 (25.5)	37.0 (29.6)
ALT/GOT, mean (SD)		30.3 (22.2)	37.8 (28.2)	47.0 (34.9)	53.5 (45.0)
GGT, mean (SD)		34.0 (35.6)	31.7 (22.7)	43.9 (33.8)	63.7 (65.2)
HDL, mean (SD)		50.6 (12.8)	45.5 (10.0)	42.8 (9.0)	39.7 (9.7)
Low HDL (<50 mg/dL women, <40 mg/dL for men)		187 (45.5)	102 (54.8)	67 (60.9)	79 (74.5)
Triglycerides, mean (SD)		131.5 (71.3)	170.3 (134.4)	179.8 (136.8)	213.7 (153.8)
PCR, mean (SD)		0.3 (0.4)	0.3 (0.4)	0.4 (0.4)	0.5 (0.4)

Table 2. Parameters of predictive model for risk of SLD without ultrasound

Parameter	OR	CI (95%)	p-value
Intercept	0.008	0.0004 -0.14	<0.001*
Sex (ref. fem.)	0.804	0.52-1.25	0.322
Age	1.002	0.96- 1.05	0.919
BMI (≥ 25 kg/m ²) (ref <25 kg/m ²)	3.455	1.47- 9.37	<0.01*
Bilirubin direct (mg/dL)	21.46	1.23- 391.76	<0.05*
Bilirubin indirect (mg/dL)	0.905	0.34-2.38	0.838
Cholesterol total/HDL (mg/dL)	1.384	1.16-1.66	<0.001*
Insulin (mg/dL)	1.087	1.06- 1.12	<0.001*
C-RP ≥ 0.2 mg/dL (ref. <0.2 mg/dL)	1.815	1.22-2.71	<0.01*
GPT >31U/L (ref. ≤ 31 U/L)	1.812	1.24-2.65	<0.01*
Diabetes Glycemia >100 (mg/dL) (Ref)	-	-	-
Glycemia ≥ 100 - <126 (mg/dL)	1.904	1.24- 2.93	<0.001*
Glycemia ≥ 126 (mg/dL)	3.201	1.63- 6.54	<0.001*

**statistical significance.*

Table 3. Parameters of predictive model for risk of SLD with ultrasound

Parameter	OR	CI (95%)	p-value
Intercept	0.27	0.016-4.55	<0.05*
Sex (ref. fem.)	0.68	0.44- 1.06	0.09
Age	0.99	0.94-1.04	0.65
Ultrasound mild (ref. normal)	8.26	5.17- 13.47	<0.001*
Ultrasound moderate (ref. normal)	34.34	19.17- 64.06	<0.001*
Ultrasound severe (ref. normal)	41.51	7.36- 783.31	<0.001*
Insulin (mg/dL)	1.06	1.03 - 1.08	<0.001*

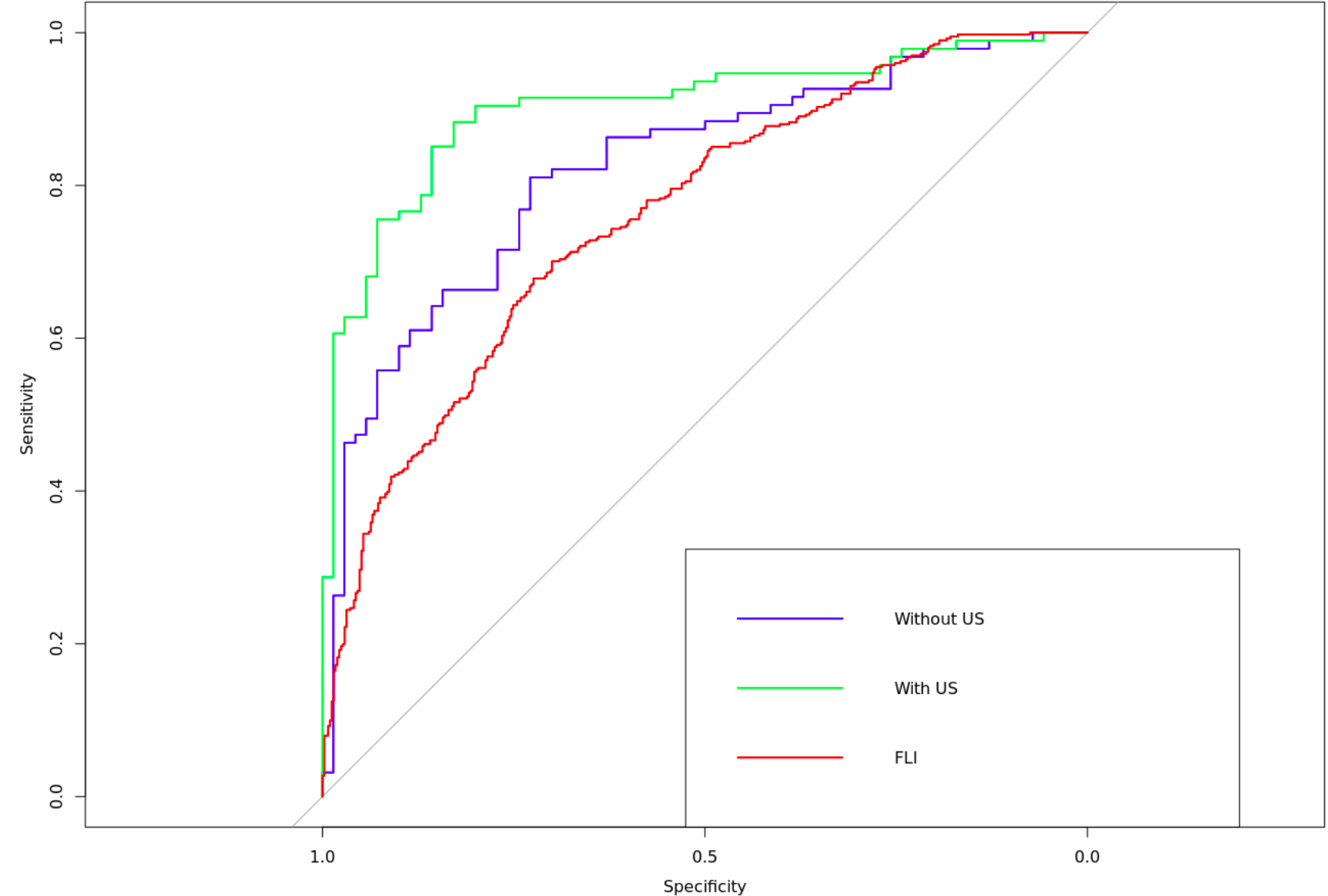
Abbreviations: β = regression coefficient. *statistical significance.

Table 4. Diagnostic accuracy of the predictive model for SLD

Predictive model	Sample	Sensitivity	Specificity	PPV	NPV
Risk of SLD without ultrasound	820	81.1% (71.7%- 88.4%)	70% (57.9%-80.4%)	78.6%	73.1%
Risk of SLD with ultrasound	820	91.5% (84%- 96.2%)	70% (57.9%-80.4%)	80.4%	86%
Fatty liver Index	814	80.3% (76.1%- 84.1%)	52.8% (47.8%-57.7%)	62.3%	73.4%

Abbreviations: PPV: positive predictive value, NPV: negative predictive value

Figure 1. Comparison of ROC Curves



Predictive model	AUC
Risk of SLD without ultrasound	0.822
Risk of SLD with ultrasound	0.903
Fatty liver Index	0.762

THANKS

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