

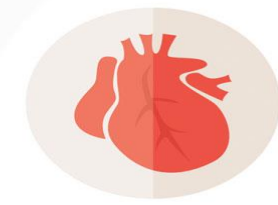
MASLD



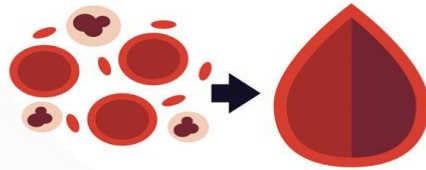
PRINCIPALES CAUSAS DE MORTALIDAD EN MÉXICO

FUENTE: INEGI, 2016

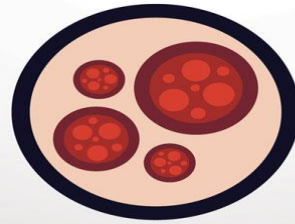
#1
19.9%
ENFERMEDADES
CARDÍACAS



#2
15.4%
DIABETES



#3
12.9%
TUMORES
MALIGNOS



BURDEN OF DISEASE IN MÈXICO

MORTALITY

	%
Cardiopatía Isquémica	15.4
Diabetes mellitus	9.6
Enf. Renal Crónica	9.4
Enf. Cerebrovascular	6.2
CIRRHOSIS	5.7
Enf. Pulmonar obs. Crónica	4.9
Enf. de Alzheimer	4.7
Infecc. Respiratoria baja	3.6
Acc. de vehículo de motor	2.4
Homicidios	2.3

YEARS LOST BY PREMATURE DEATH

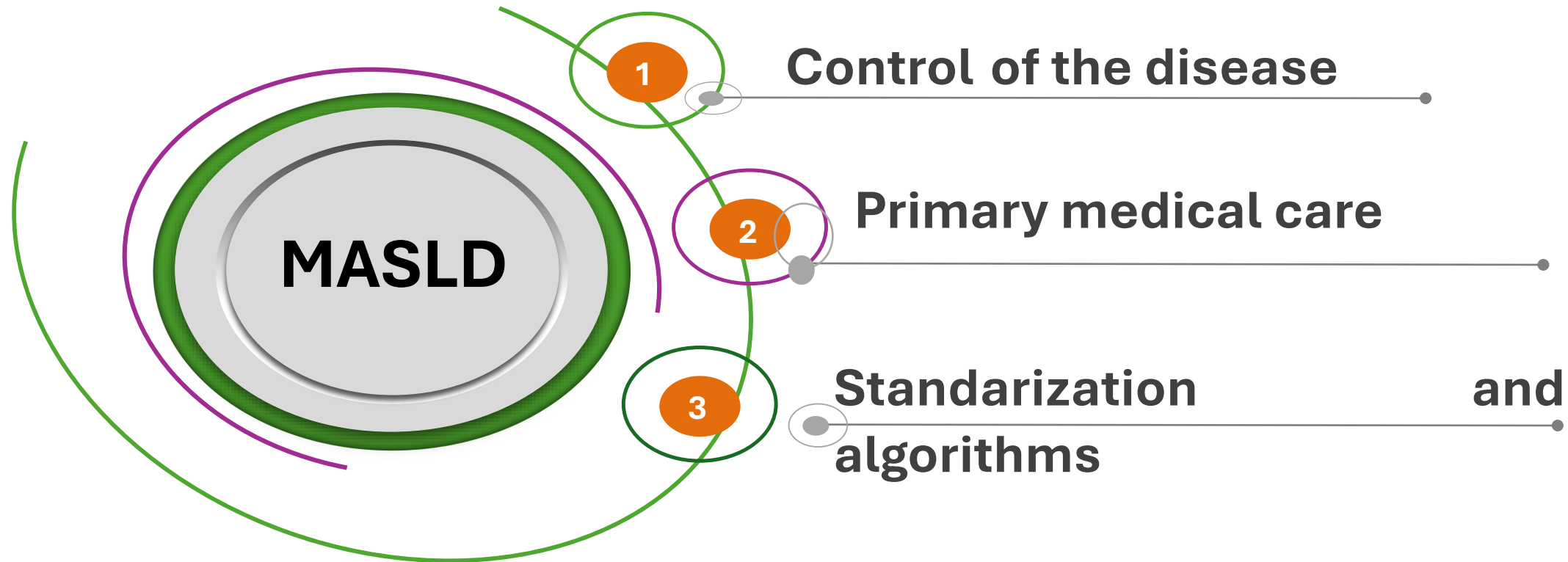
	%
Cardiopatía Isquémica	10.0
Enf. Renal Crónica	8.3
Diabetes mellitus	7.9
CIRRHOSIS	6.5
Homicidios	4.9
Acc. de vehículo de motor	4.7
Anomalías Congénitas	4.7
Enf. Cerebrovascular	4.2
Infecc. Respiratoria baja	3.7
R.N. pre-término	2.9

YEARS LOST BECAUSE OF DISCAPACITY

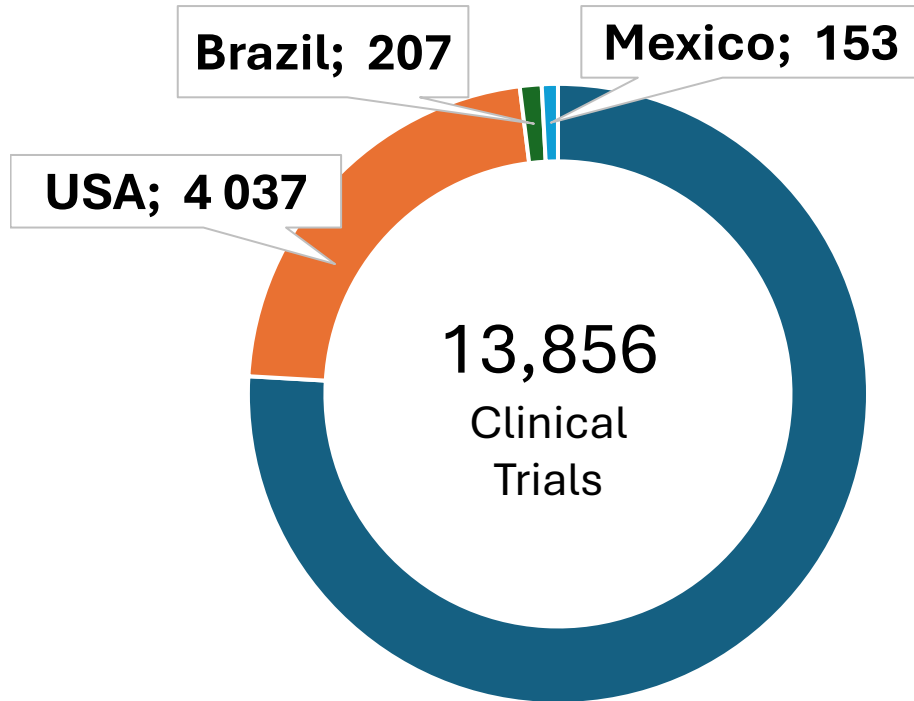
	%
Diabetes mellitus	10.0
Lumbalgia	6.6
Hipoacusia rel. con la edad	6.5
Depresión	5.7
Dolor de cuello	4.7
Migraña	4.5
Otras enf. Musculo esqueléticas	3.3
Ansiedad	3.2
Problemas visuales de refracción	2.5
Anemia ferroporiva	2.5

YEARS OF HEALTHY LIFE LOST

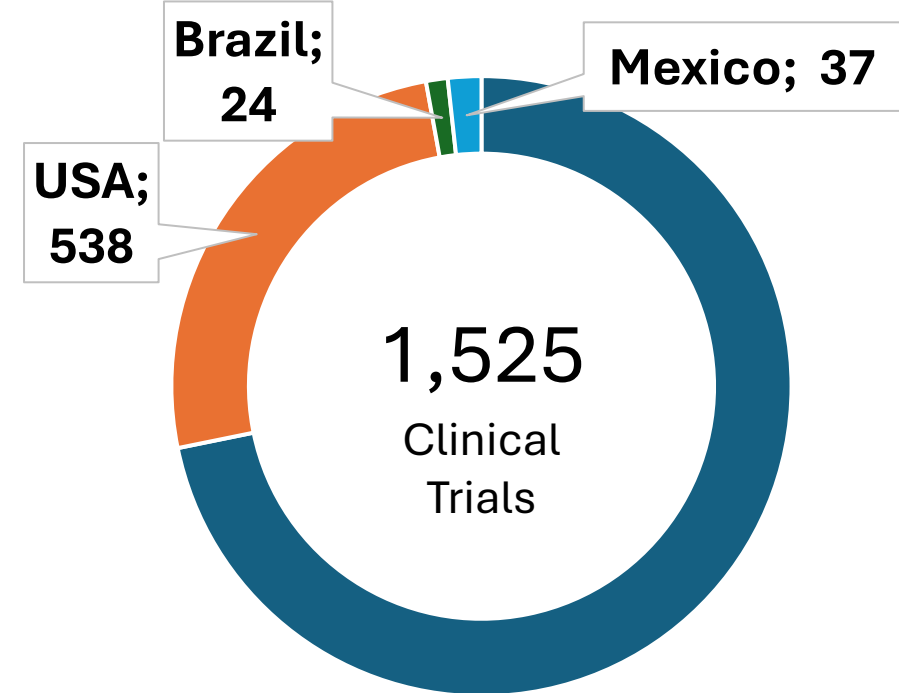
	%
Diabetes mellitus	8.7
Cardiopatía Isquémica	6.7
Enf. Renal Crónica	5.9
CIRRHOSIS	4.1
Anomalías Congénitas	3.5
Homicidios	3.1
Acc. de vehículo de motor	3.1
Enf. Cerebrovascular	2.7
Hipoacusia rel. con la edad	2.4
Depresión	2.2



Mexico Participation in Clinical Trials

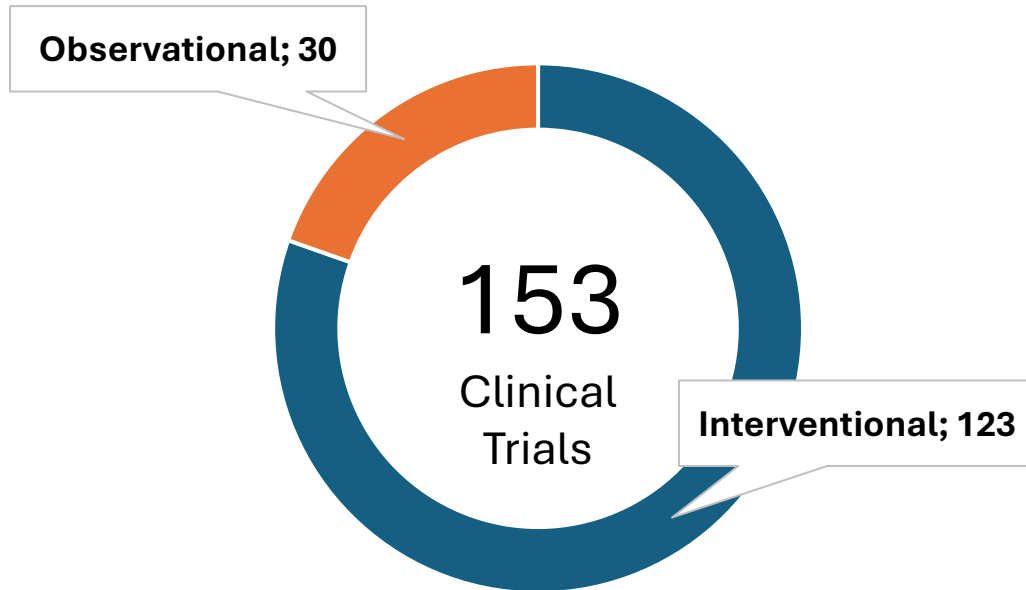


**Clinical trials globally in
Liver Diseases**

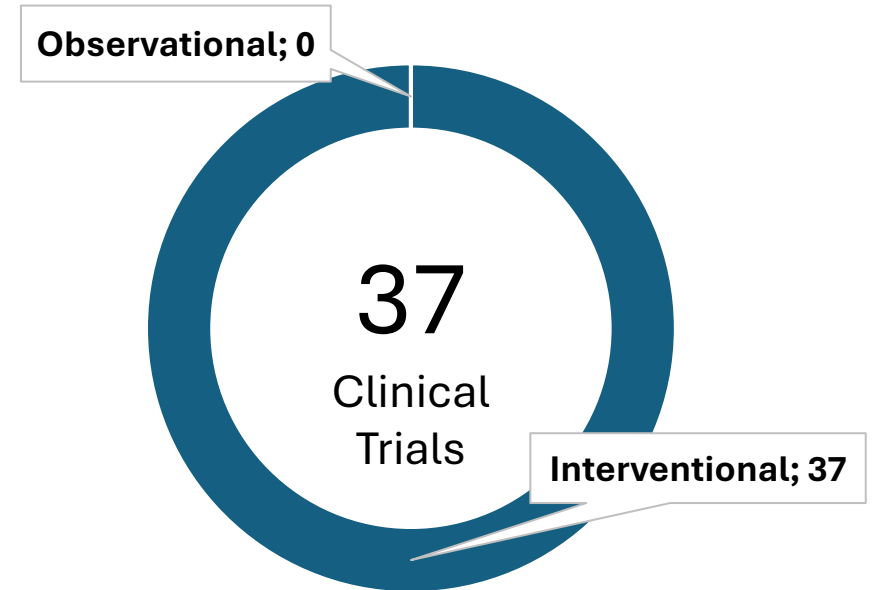


**Clinical trials globally in
MASH**

Type of clinical trials in Mexico

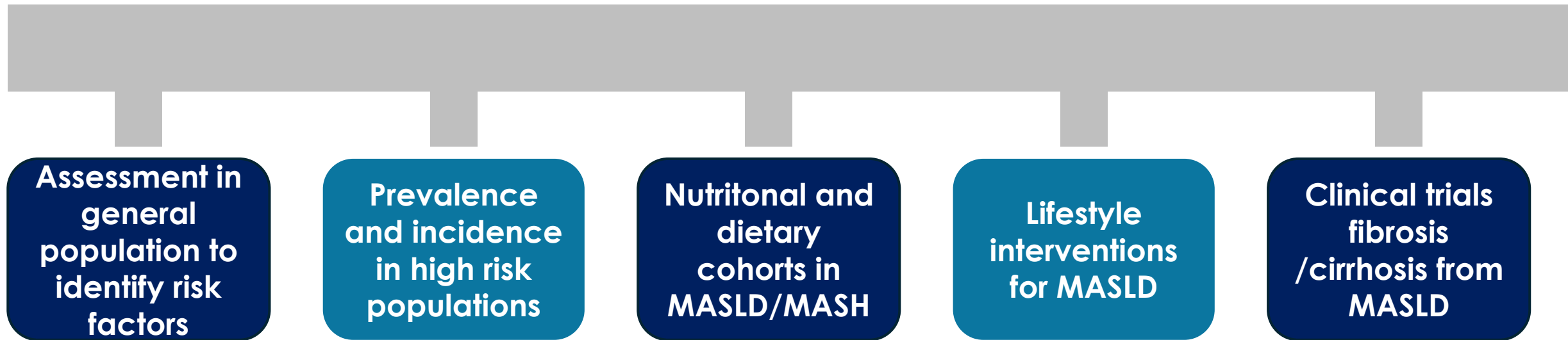


**Clinical trials in Mexico
For Liver Diseases**



**Clinical trials in Mexico
For MASH**

What's being done in Mexico?



Epidemiological data

Assessment of liver parameters in
general population
National Survey of Health and
Nutrition -Mexico

- **ENSANUT 2023
– 2024-2025**

- Steatosis
- Fibrosis

High risk population
(Scores) (2025- will
add imaging)

Will be derived to
INCMNSZ for full liver
disease assessment

- Results will be
analyzed



MASLD screening in high risk populations

			
Diabetes  CENTRO DE ATENCIÓN INTEGRAL DEL PACIENTE CON DIABETES.  UIEM	Obesity  INCMNSZ Obesity and Bariatric surgery Clinics	PCOS  INCMNSZ Reproductive Biology Clinic	Dyslipidemia  UIEM

Results from Diabetes Clinic

Prevalence and risk factors associated with presence of liver steatosis and fibrosis in patients with recently diagnosed type 2 diabetes mellitus (< 5 years)

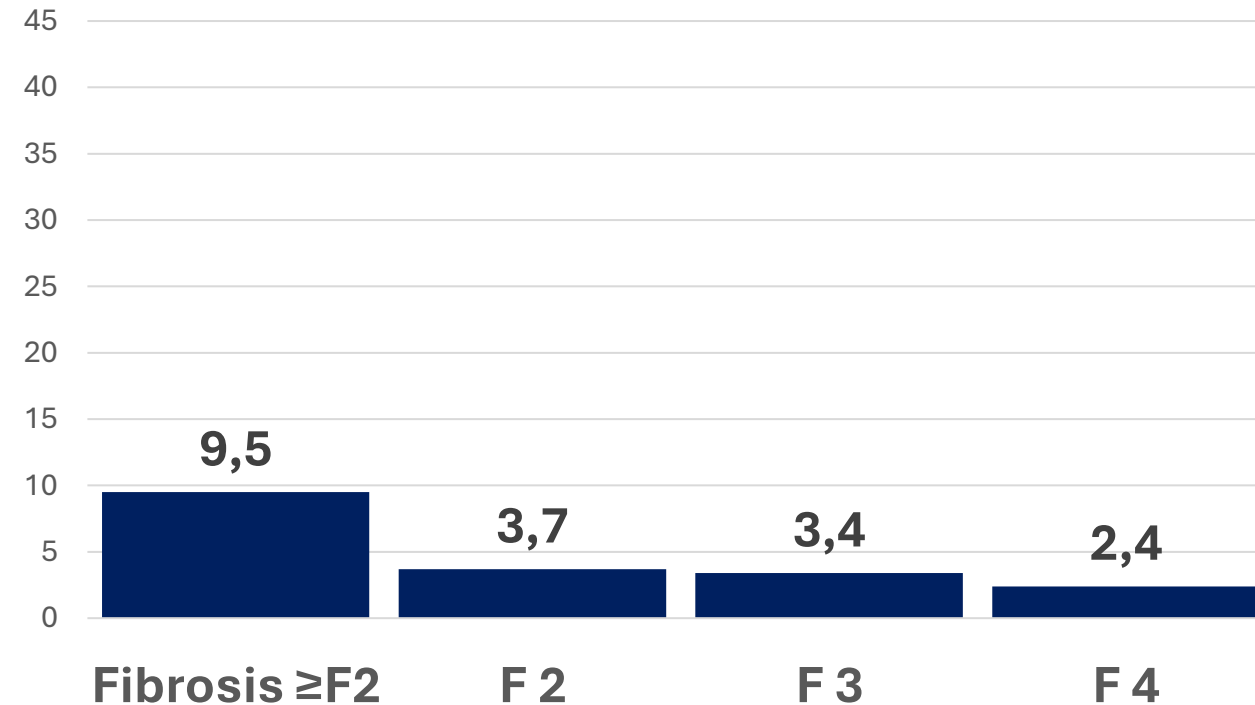
N= 1,377 | 60.9% women | BMI ≥ 25 78.2% | 4.8% of the patients were at-risk of MASH

Steatosis (%)



Macías-Rodríguez RU et al, Unpublished data

Liver fibrosis (%)



Prevalence and risk factors associated with presence of liver steatosis and fibrosis in patients with recently diagnosed type 2 diabetes mellitus (< 5 years)

Logistic regression to evaluate the risk factors associated with presence of liver steatosis				
	OR	CI 95%	β	p-value
Age and BMI				
Age	1.005	0.991-1.019	0.005	0.461
BMI (Kg/m ²)	1.121	1.086-1.156	0.114	<0.001
Liver fibrosis				
KPa	1.085	1.024-1.141	0.081	0.006
Biochemical parameters				
TGC (>150 mg/dL)	1.003	1.002-1.005	0.004	<0.001
TC (0-200 mg/dL)	1.003	1.000-1.007	0.003	0.084
ALT (>7-52 U/L)	1.040	1.025-1.056	0.040	<0.001
AST (>13-39 U/L)	0.959	0.939-0.980	-0.042	<0.001
GGT (9-64 U/L)	1.002	0.997-1.006	0.002	0.438
Creatinine (0.6-1.2 mg/dL)	0.825	0.431-1.579	-0.192	0.561
HbA1c (%)	0.974	0.905-1.048	-0.026	0.481



INCMNSZ

Lifestyle interventions

Randomized open clinical trial

Control



Intervention



**Diet: Carbs 50%, Protein 1.5g/Kg/d,
Lipids: (Saturated fats<10%)**

***Caloric Restriction-15%**

**Patients receive a personalized diet, with
standardized macronutrient proportions.
and nutritional counseling and follow-up**

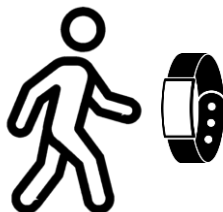
Lifestyle interventions

Randomized open clinical trial

Both groups: All patients receive a bracelet for step quantification and a heart rate monitor

Physical exercise program

Aerobic



5/7 week
20-60 min/session

- Baseline assessment of individual mean daily steps
- Week 1 - 2: + 1000 steps (Borg: 12-13)
- Week 3 - 4: + 2500 Steps Borg: 14-15)
- Week 4-16 : + 5000 Steps (Borg: 14-15)

Resistance



3/7 week
25-40 min/session

Exercises for different group muscles. (ACSM)

- S 1 - 2: BDW → 2 groups x 3 series 8
- S 3 - 4: BDW → 4 groups x 3 series 12
- S > 4: BDW → 4 groups x 3 series 15

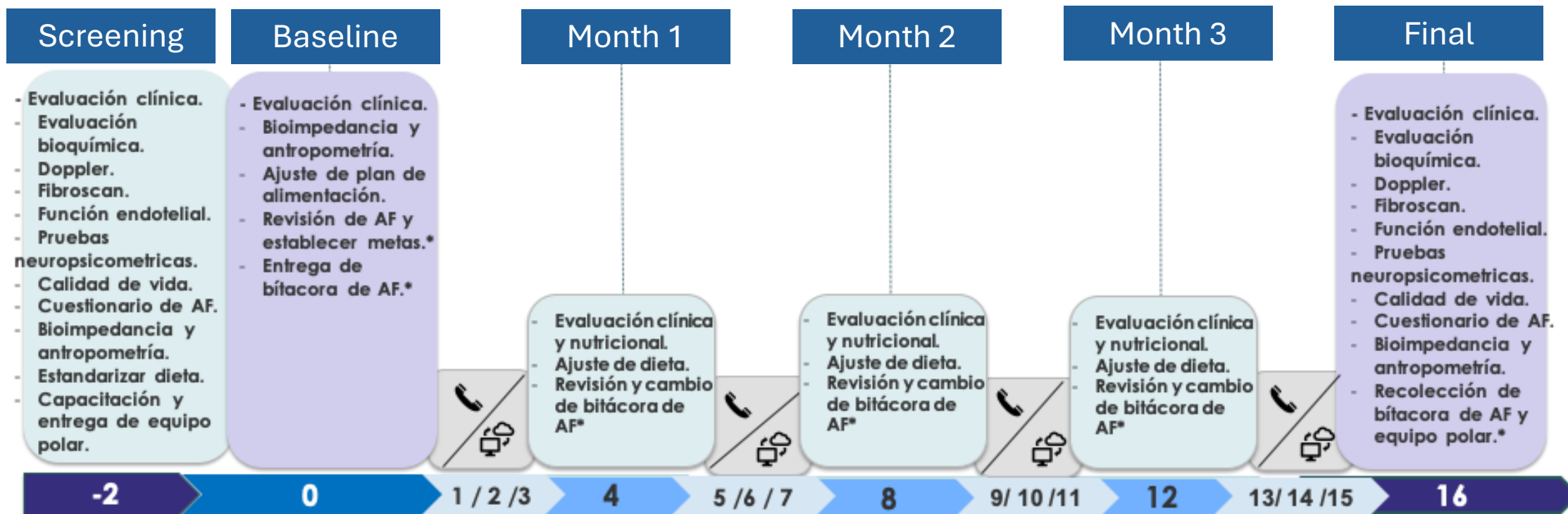


INCMNSZ

Lifestyle interventions

Randomized open clinical trial

Visits





INCMNSZ



EFFECT OF A PHYSICAL EXERCISE PROGRAM ON THE CEREBRAL HEMODYNAMICS OF PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

Berenice M. Román-Calleja¹, Carlos F. Martínez-Cabrera¹, Regina G. Romo-Arellano¹, Carlos Cantu-Brito², Carlos Aguilar-Salinas³, Ricardo U. Macías-Rodríguez¹, Astrid Ruiz-Margáin¹

¹Department of Gastroenterology, ²Department of Neurology and ³Direction of Research at Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico



INSTITUTO NACIONAL DE
CIENCIAS MÉDICAS
Y NUTRICIÓN
SALVADOR ZUBIRÁN

Introduction

Patients with Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) often exhibit significant microvascular alterations due to their underlying metabolic conditions. These vascular changes are crucial as they impair normal cerebral blood flow, potentially leading to cognitive deficits. Physical exercise (PE) is beneficial for patients with MASLD and can potentially help with cognitive function and cerebral hemodynamics, however this has not yet been explored.

Aim

To evaluate the effects of a physical exercise program on cerebral hemodynamics in patients with MASLD.

Method

16-week randomized open-label clinical trial (Clinical Trials: NCT05520697).

- Control group (n=20): Diet with a 20% caloric restriction based on energy needs determined by indirect calorimetry + cognitive exercise.
- Intervention group (n=20): Diet with the same 20% caloric restriction as the control group + cognitive exercise + physical exercise.
- Cognitive exercise consisted of reading a different book each month.

Aerobic exercise

- Gradual addition of 5,000 extra steps per day.
- Progress tracked using an activity monitor.

Resistance exercise

- Bodyweight exercises
- 2-6 muscle groups
- 3 sets of 8-15 reps
- Three times a week

Results

Table 1. Baseline Characteristics of the Population

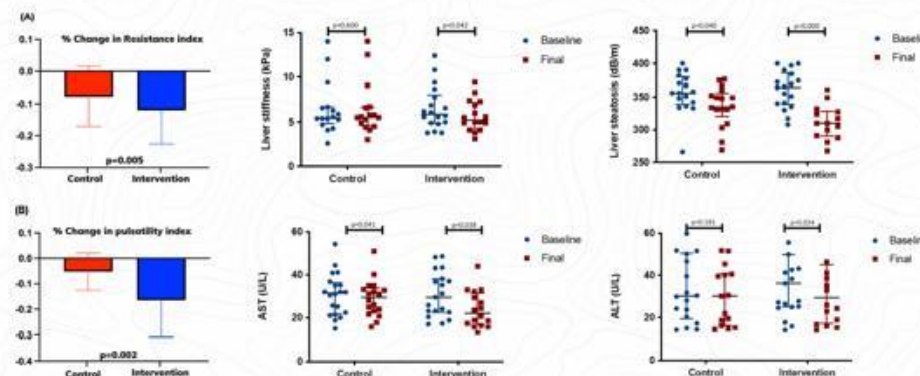
Variable	All (n=40)	Control (n=20)	Intervention (n=20)	p-value
Female (%)	23 (57.5)	13 (65)	11 (55)	0.519
Age (years)	46 ± 8	45 ± 8	47 ± 7	0.339
BMI (Kg/m ²)	36.5 ± 5.4	36.9 ± 5.1	34.8 ± 4.9	0.671
Fibrosis Grade n(%)				
0-1	28 (70.0)	14 (70.0)	14 (70.0)	0.842
2	7 (17.5)	4 (20.0)	3 (15.0)	
3	5 (12.5)	2 (10.0)	3 (15.0)	
Steatosis grade n(%)				
1	2 (5.0)	1 (5.0)	1 (5.0)	0.834
2	3 (7.5)	1 (5.0)	2 (10.0)	
3	35 (87.5)	18 (90.0)	17 (85.0)	
Comorbidities n(%)				
Prediabetes	3 (7.5)	2 (10.0)	1 (5.0)	0.548
Type 2 diabetes	24 (60.0)	11 (55.0)	13 (65.0)	0.648
Hypertension	13 (32.5)	7 (35.0)	6 (30.0)	0.736
Dyslipidemia	21 (52.5)	9 (45.0)	12 (65.0)	0.342
ALT (U/L)	30.3 (18.4-50.0)	30.2 (17.3-50.4)	30.1 (20.9-49.9)	0.245
AST (U/L)	26.9 (20.4-36.9)	25.5 (17.7-35.9)	27.4 (21.2-37.0)	0.098
Glucose (mg/dL)	117 (95-139)	118 (91-143)	119 (103-140)	0.245
Total Cholesterol (mg/dL)	174 ± 29	169 ± 31	175 ± 29	0.967
Triglycerides (mg/dL)	149 (118-187)	147 (114-186)	151 (121-187)	0.374
Platelets (x10 ³ /μL)	246 ± 63	242 ± 66	253 ± 60	0.300

Table 2. Changes in Endothelial Evaluation Parameters, Cerebral Hemodynamics, and Cognitive Function

	Control (n=20)				Intervention (n=20)				p-value between groups
	Baseline	Final	Δ %	P-value	Baseline	Final	Δ %	P-value	
>7% weight loss n(%)	6 (30)				11 (55)				0.037
PWV (cm/s)	6.8 (6.2 to 7.4)	6.7 (6.0 to 7.2)	-0.3 (-0.5 to 0.5)	0.127	6.9 (6.2 to 7.8)	6.3 (5.9 to 6.8)	-0.6 (-1.1 to 0.2)	0.045	0.117
Resistance Index	0.69 (0.48 to 0.85)	0.59 (0.47 to 0.68)	-0.09 (-0.20 to -0.04)	0.091	0.76 (0.51 to 0.98)	0.56 (0.43 to 0.73)	-0.22 (-0.19 to 0.08)	0.033	0.005
Pulsatility Index	0.99 (0.93 to 1.00)	0.88 (0.70 to 0.88)	-0.10 (-0.12 to 0.03)	0.132	0.99 (0.98 to 1.01)	0.74 (0.68 to 0.90)	-0.24 (-0.28 to 0.18)	0.012	0.002
Breath-Holding Index	0.67 (0.58 to 0.82)	0.71 (0.66 to 0.91)	0.09 (-0.16 to 0.18)	0.110	0.65 (0.54 to 0.72)	0.72 (0.63 to 0.89)	0.12 (-0.41 to 0.29)	0.096	0.107
MOCA test	26 (23 to 28)	27 (26 to 29)	1.1 (0.7 to 2.0)	0.156	27 (24 to 27)	29 (27 to 29)	1.3 (1.0 to 2.5)	0.079	0.174
Addenbrock's	88 (81 to 93)	93 (87 to 97)	4 (0 to 7)	0.083	86 (82 to 86)	96 (92 to 98)	8 (3 to 11)	0.002	<0.001

Table 3. Daily Step Count Changes Pre- and Post-Intervention.

	Control		p-value	Intervention		p-value
	Baseline	Final		Baseline	Final	
Number of steps	6339 (4982-8166)	7341 (6104-9111)	0.180	6177 (4881-9187)	10199 (9182-15767)	<0.001



Conclusions

Physical exercise program improved cerebral hemodynamics and cognitive function, and reduced hepatic steatosis and transaminase levels. Incorporating physical exercise into the treatment for patients with MASLD can benefit both brain and liver health.

Contact

- Berenice M Román Calleja / berermn@gmail.com
- Astrid Ruiz Margáin / astrid.ruizm@incmnsz.mx



INCMNSZ



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BMI (Kg/m ²)				
Fibrosis Grade n(%)				
0-1				
2				
3				
Steatosis grade n(%)				
1				
2				
3				
Comorbidities n(%)				
Prediabetes				
Type 2 diabetes				
Hypertension				
Dyslipidemia				
ALT (U/L)	30			
AST (U/L)	26			
Glucose (mg/dL)	1			
Total Cholesterol (mg/dL)				
Triglycerides (mg/dL)	1			
Platelets (x10 ³ /μL)				

Table 2. Changes in Endothelial Function

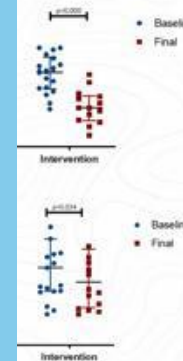
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PWV (cm/s)	6.8 (6.2 to 7.4)			
Resistance Index	0.69 (0.48 to 0.85)	0.59 (0.47 to 0.68)	-0.09 (-0.20 to -0.04)	0.091
Pulsatility Index	0.99 (0.93 to 1.00)	0.88 (0.70 to 0.88)	-0.10 (-0.12 to 0.03)	0.132
Breath-Holding Index	0.67 (0.58 to 0.82)	0.71 (0.66 to 0.91)	0.09 (-0.16 to 0.18)	0.110
AOCA test	26 (23 to 28)	27 (26 to 29)	1.1 (0.7 to 2.0)	0.156
Addenbrooke's	88 (81 to 93)	93 (87 to 97)	4 (0 to 7)	0.083

Table 3. Daily Step Count Changes Pre- and Post-Intervention.

	Control	p-value	Intervention	p-value
Baseline	6338 (4693-8155)		6137 (4693-8155)	
Final	7315 (5124-9111)	0.100	10109 (9182-15767)	<0.001

CONCLUSIONS

Physical exercise program improved cerebral hemodynamics and cognitive function and reduced hepatic steatosis and transaminase levels incorporating physical exercise into the treatment for patients with MASLD can benefit both brain and liver health.



Improved cerebral hemodynamics, and reduced transaminase levels. The treatment for both brain and liver health.

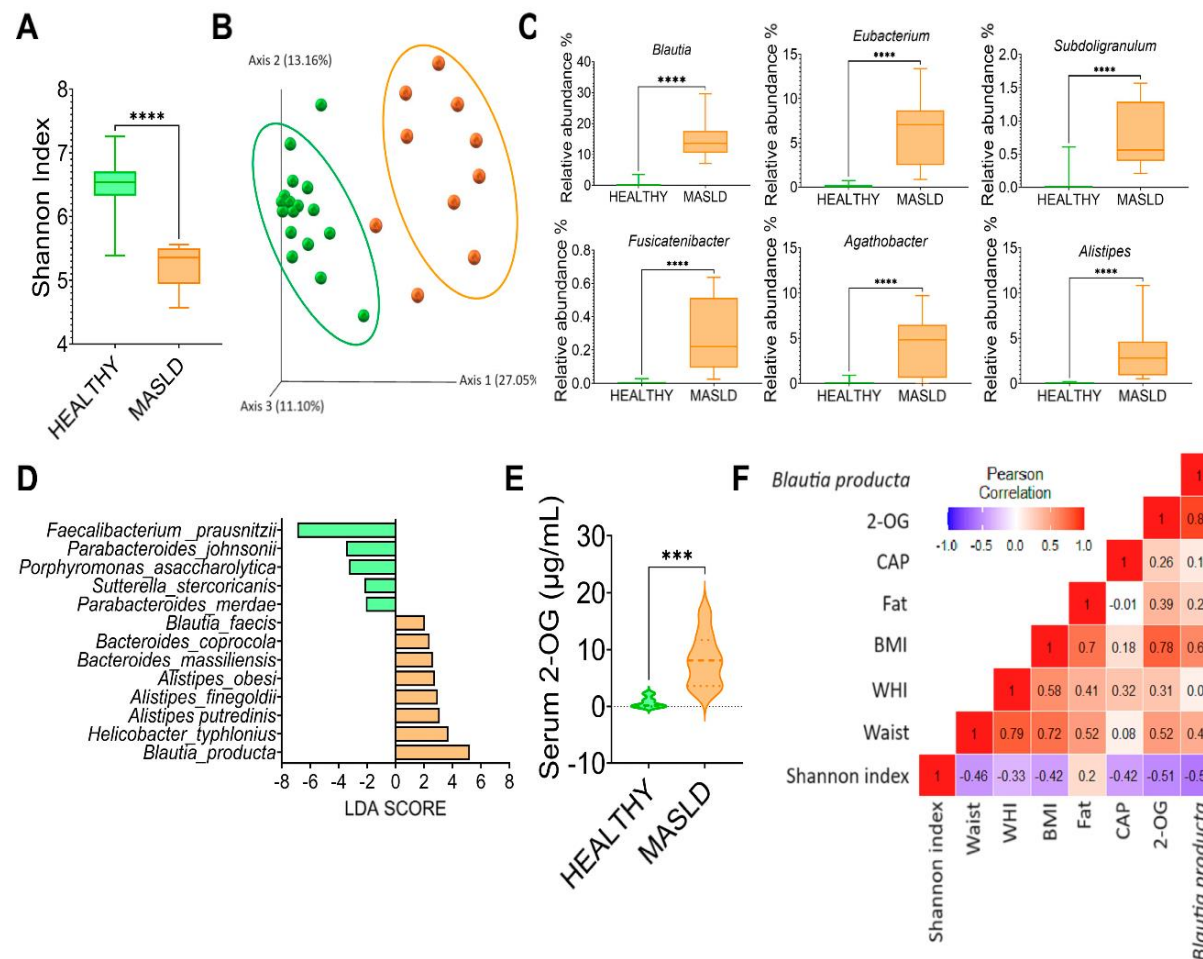
Contact

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Gut microbiota in MASLD

Subjects with MASLD increase *Blautia producta* and serum concentrations of 2-OG (2-oleoyl glycerol)

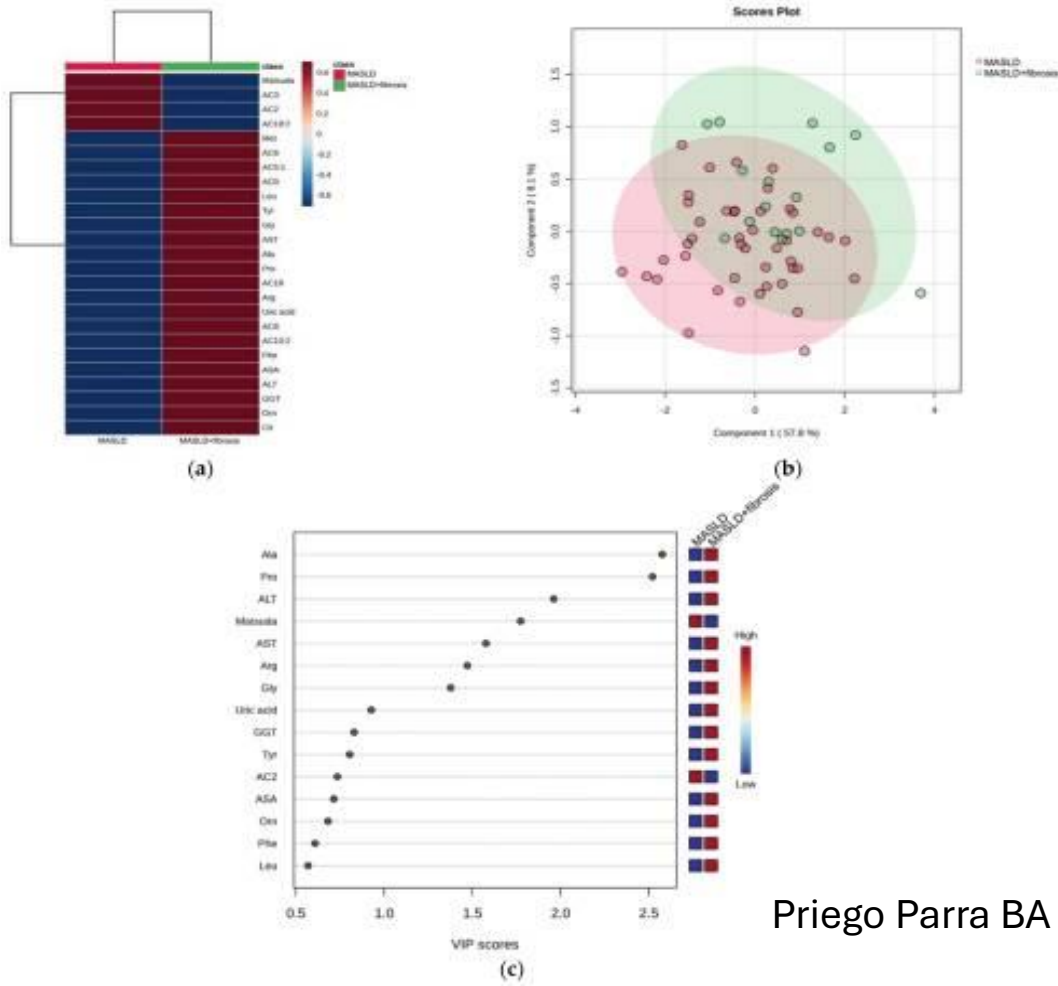
N= 10 (MASLD) and 10 (control without MASLD)
80% women, BMI 39.3 ± 1.9 and 21.9 ± 1.28 MASLD and control groups.



Development of atherothrombosis in MASLD patients

- atherogenic dyslipidemia
- low-grade vascular inflammation
- endothelial dysfunction
- foam cell formation
- proliferation of vascular smooth muscle cells
- insulin resistance
- gut microbiota dysbiosis
- activation of renin-angiotensin and sympathetic nervous systems
- hypercoagulability
- decreased fibrinolysis
- genetically driven liver fat and coronary heart disease mediated by the causal effect of apoB-containing lipoproteins.

Metabolomic phenotypes associated (MASLD (hepatic steatosis) and MASLD + fibrosis (hepatic steatosis + fibrosis) in Mexican children with obesity



MASLD was associated with a phenotype characterized by increased concentrations of ALT and decreased arginine, glycine, and AC5:1 (tiglylcarnitine).

MASLD + fibrosis was associated with a phenotype characterized by increased concentrations of ALT, proline, and alanine and a decreased Matsuda Index.

Cohorte de excelencia en investigación para la salud metabólica (CESAME)

Cohort of excellence in research for metabolic health (CESAME)

Detection of patients
with 3 or more metabolic
risk factors:

- arterial hypertension
- hyperlipidemia
- obesity/overweight
- diabetes mellitus
- chronic renal failure

AIM 500,000 participants

OBJECTIVES: Early detection, primary care, prevention, research

Federal Ministry of Health

- State Ministries of Health
- National Institutes of Health
- Hospitals (including IMSS, IMSS Bienestar and ISSSTE)

Federal Ministry of Sciences

Every institute and participating hospital will name a leader as principal investigator and coordinator of the CESAME project

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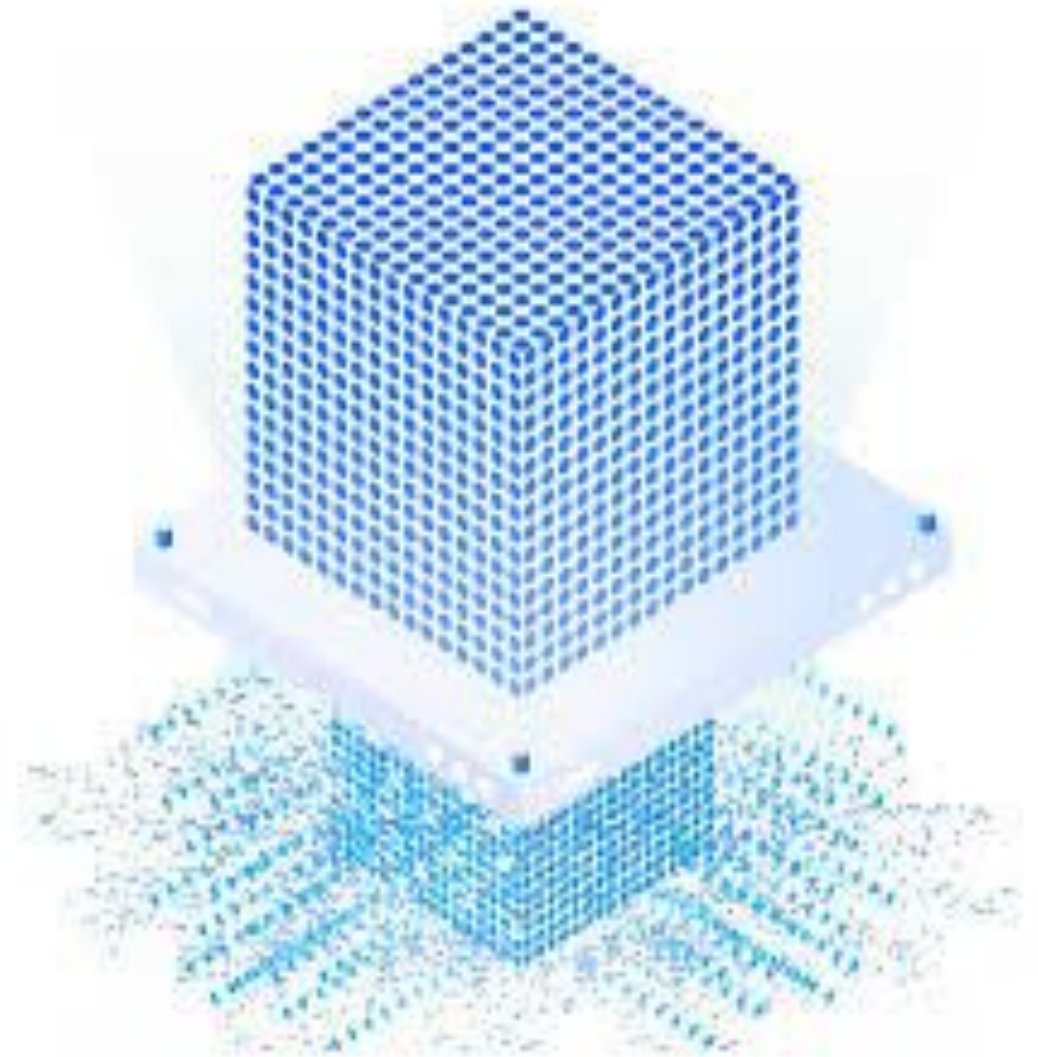
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SAMPLE CITES AND CENTRAL REFERENCE LABORATORIES





MEXICO HEALTH SYSTEMS
IN TRANSITION



Thank you!



supplementation with a mixture of Mexican foodstuffs (MexMix)—*Opuntia ficus indica* (nopal), *Theobroma cacao* (cocoa) and *Acheta domesticus* (crickets)—enriches several beneficial taxa in MASLD mice and overweight/obese humans. Thus, MexMix induces an important prebiotic effect. In mice, a restoration of intestinal health was observed due to the increased short-chain fatty acids (SCFAs) and intestinal crypt depth, *Ocln* and *Cldn1* expression, and decreased *Il6* and *Tnfa* expression. MexMix significantly reduced steatosis in the mice's liver and modified the expression of 1668 genes. By PCR, we corroborated a *Tnfa* and *Pparg* decrease, and a *Cat* and *Sod* increase. In addition, MexMix increased the hepatic NRF2 nuclear translocation and miRNA-34a, miRNA-103, and miRNA-33 decline. In overweight/obese humans, MexMix improved the body image satisfaction and reduced the fat intake. These findings indicate that this new food formulation has potential as a therapeutic approach to treat conditions associated with excessive consumption of fats and sugars.

Rebeca Rosas cCampos et al. A Novel Foodstuff Mixture Improves the Gut-Liver Axis in MASLD Mice and the Gut Microbiota in Overweight/Obese Patient Antioxidants (Basel) 2024 May 29;13 (6) 664

Prevalence and risk factors associated with presence of liver steatosis and fibrosis in patients with recently diagnosed type 2 diabetes mellitus (< 5 years)

Logistic regression to evaluate the risk factors associated with presence of liver fibrosis				
	OR	CI 95%	β	p-value
Age	1.035	1.007-1.064	0.034	0.015
BMI (Kg/m ²)	1.110	1.001-1.012	0.104	<0.001
CAP (dB/m)	1.007	1.001-1.012	0.007	0.013
Biochemical parameters				
TC (<200 mg/dL)	0.991	0.985-0.998	-0.009	0.009
ALT (7-52 U/L)	1.0	0.983-1.018	0.000	0.966
AST (13-39 U/L)	1.053	1.023-1.083	0.052	<0.001
GGT (9-64 U/L)	1.020	1.012-1.028	0.020	<0.001
Creatinine (0.6-1.2 mg/dL)	0.219	0.052-0.917	-1.520	0.038
HbA1c (%)	1.140	1.003-1.296	0.131	0.045

- metabolomic phenotypes associated with two stages of MASLD progression (MASLD (hepatic steatosis) and MASLD + fibrosis (hepatic steatosis + fibrosis)) in Mexican children with obesity compared to those with obesity but without MASLD.

MASLD was associated with a phenotype characterized by increased concentrations of ALT and decreased arginine, glycine, and AC5:1 (tiglylcarnitine).

On the other hand, MASLD + fibrosis, a progression stage of MASLD, was associated with a phenotype characterized by increased concentrations of ALT, proline, and alanine and a decreased Matsuda Index.



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Lifestyle interventions

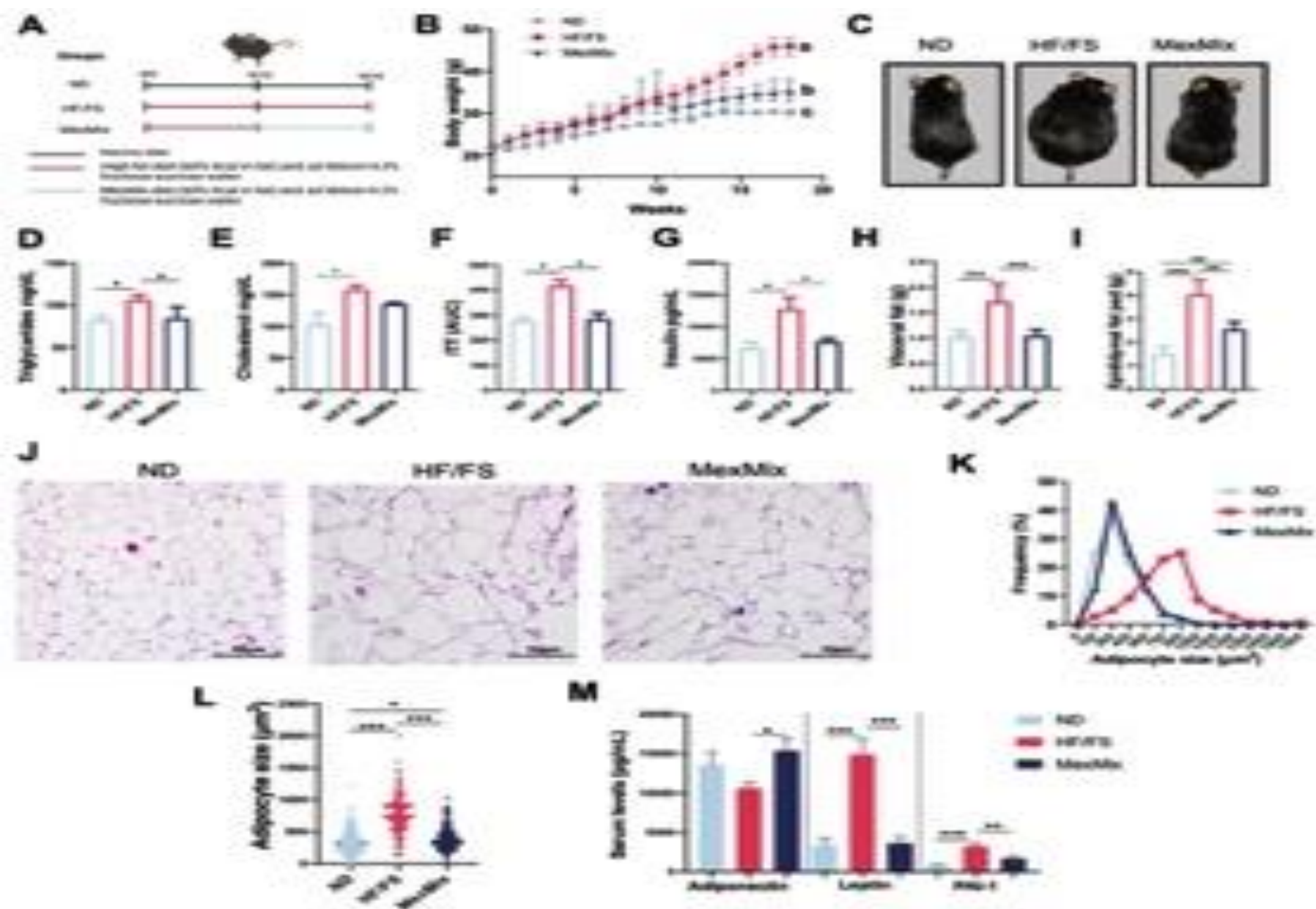
Coffe consumption and MASLD

n= 930

Tabla 3. Características del consumo de café de acuerdo con la presencia de esteatosis hepática.

	S0 N=421	S1 n=104	S2 n=66	S3 n=339	Valor p
Años de consumo	25(10-40)	229(10-40)	220(9-31)	30(10-40)	0.318
Número de tazas (%)					0.754
<i>No consumidores</i>	10.2	11.5	9.1	8.3	
<i>1 taza</i>	36.8	40.4	40.9	36.3	
<i>2 tazas</i>	34.2	33.7	39.4	38.3	
<i>3 o más tazas</i>	18.8	14.4	10.6	17.1	
Tamaño de taza (%)					
<i>Espresso (<60ml)</i>	2.6	1	3	2.9	0.724
<i>Estándar(240ml)</i>	44.9	51.9	33.3	41.3	0.058
<i>Chico (350ml)</i>	22.8	19.2	28.8	21.8	0.523
<i>Mediano(470ml)</i>	18.1	19.2	24.2	22.7	0.356
<i>Grande (590ml)</i>	3.8	1	7.6	5	0.150
Tipo de café (%)					
<i>Soluble</i>	53.7	45.2	59.1	61.4	0.018
<i>Grano</i>	36.8	49	42.4	36.3	0.089
<i>Capsulas</i>	3.8	3.8	3	4.1	0.979
<i>Descafeinado</i>	24.9	29.8	30.3	25.7	0.643
Añadidos (%)					
<i>Sin añadidos</i>	31.6	29.8	24.2	20.6	0.007
<i>Leche</i>	38.2	40.4	42.4	41.9	0.751
<i>Crema</i>	7.4	3.8	13.6	9.7	0.086
<i>Azúcar</i>	14.5	9.6	19.7	22.1	0.006
<i>Edulcorante</i>	18.3	21.2	24.2	23.9	0.052

Mediana (p25-p75), frecuencias absolutas (%)



Methods

steatosis was assessed using vibration-controlled transient elastography. MASLD was defined according to international standards. Assessed biomarkers included: Visceral Fat (VF), Waist Circumference (WC), Waist-Height Ratio (WHtr), Waist-Hip Ratio (WHr), Visceral Adiposity Index (VAI), Hepatic Steatosis Index (HSI), Body Mass Index (BMI), Homeostatic Model Assessment (HOMA), Weight-Adjusted-Waist Index (WWI), Lipid Accumulation Product (LAP), Uric Acid-Creatinine Ratio (UACR), Triglyceride-Glucose Index (TyG) and its variants TyG-WC, TyG-HDL, TyG-BMI, TyG-WHtr.

161 participants were included, of which 122 met MASLD criteria (56 % women, age 53.9 years [47.5–64]) and 39 were healthy controls (76 % women, age 52 [45–64]). After adjusting for sociodemographic variables, the TyG-WC index was the best predictor of MASLD.