

# Plan

1. Presentation of the MAUCO cohort.
2. Gene-environment Interaction in MAUCO





## MAUCO OBJECTIVES

1. Assess physical and mental health, a wide range of exposures of health and healthy aging.
2. Create a biobank
3. Follow-up changes in exposures and health outcomes.
4. Evaluate preventive interventions



# METHODS

**Location:** Molina.

## Participants:

- population-based, aged 38-74 years
- Target 10,000 participants.

**Baseline:** 2015-2019.

## Follow-up: 2017-2023

- Surveillance of events
- Re-examination years 2 and 5.

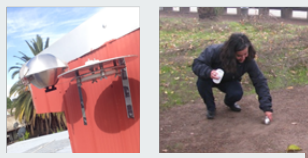


Empadronamiento

Enrollment  
(households+ elegibles)



MAUCO clinic



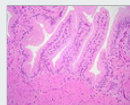
Soil+air samples

+



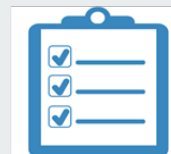
Aflatoxins in food

+



Tissue sample in  
cholecystectomy

+



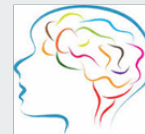
Health survey



Weight, height



Blood tests



Neuropsychological  
Test



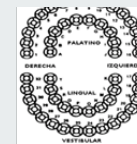
Waist, arm  
circumference



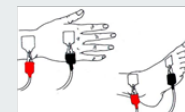
Hepato-biliary  
ultrasound



Up & go test  
Walk test



Tooth count



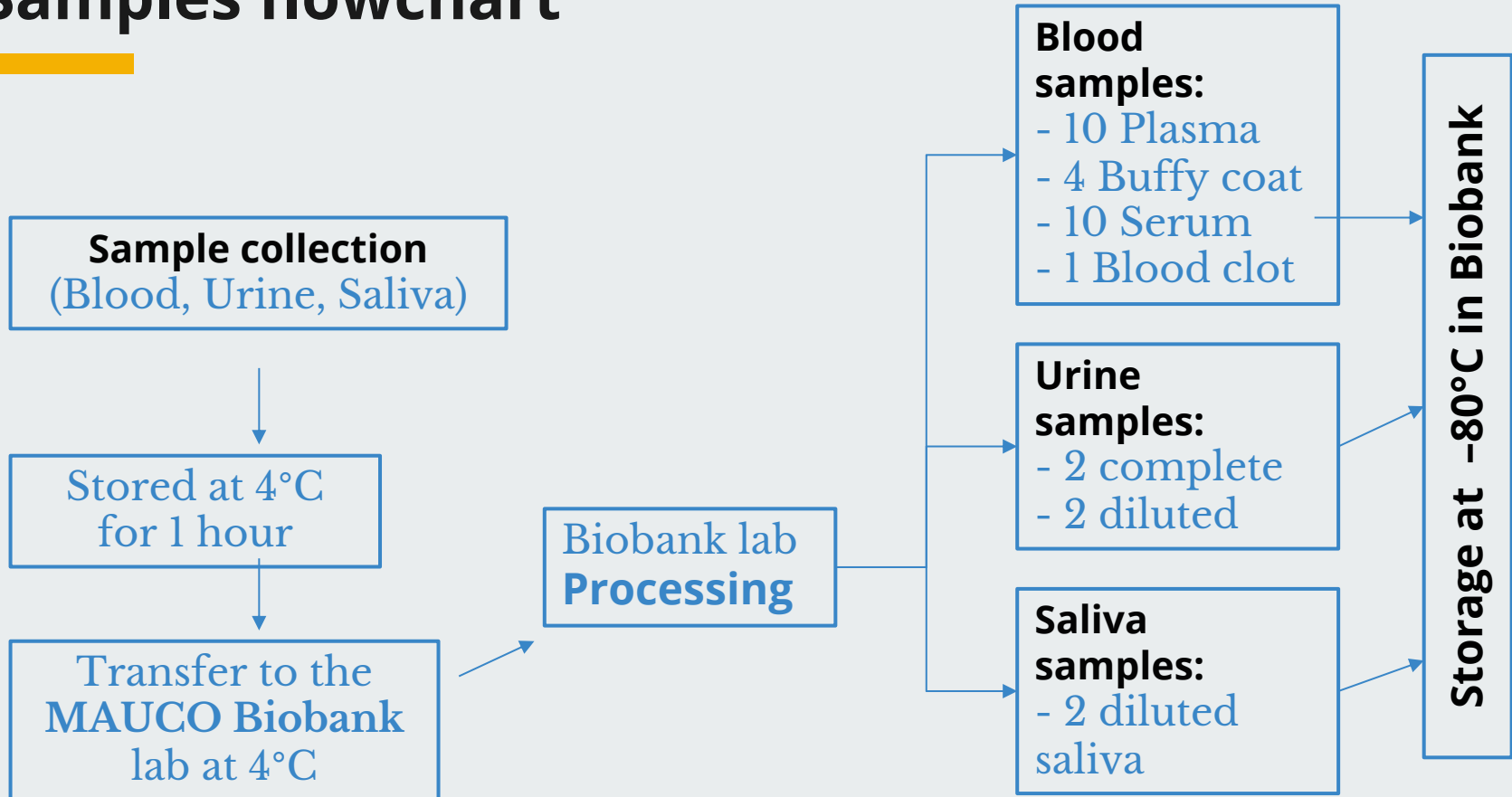
Bioimpedance



Peak Flow test



# Samples flowchart



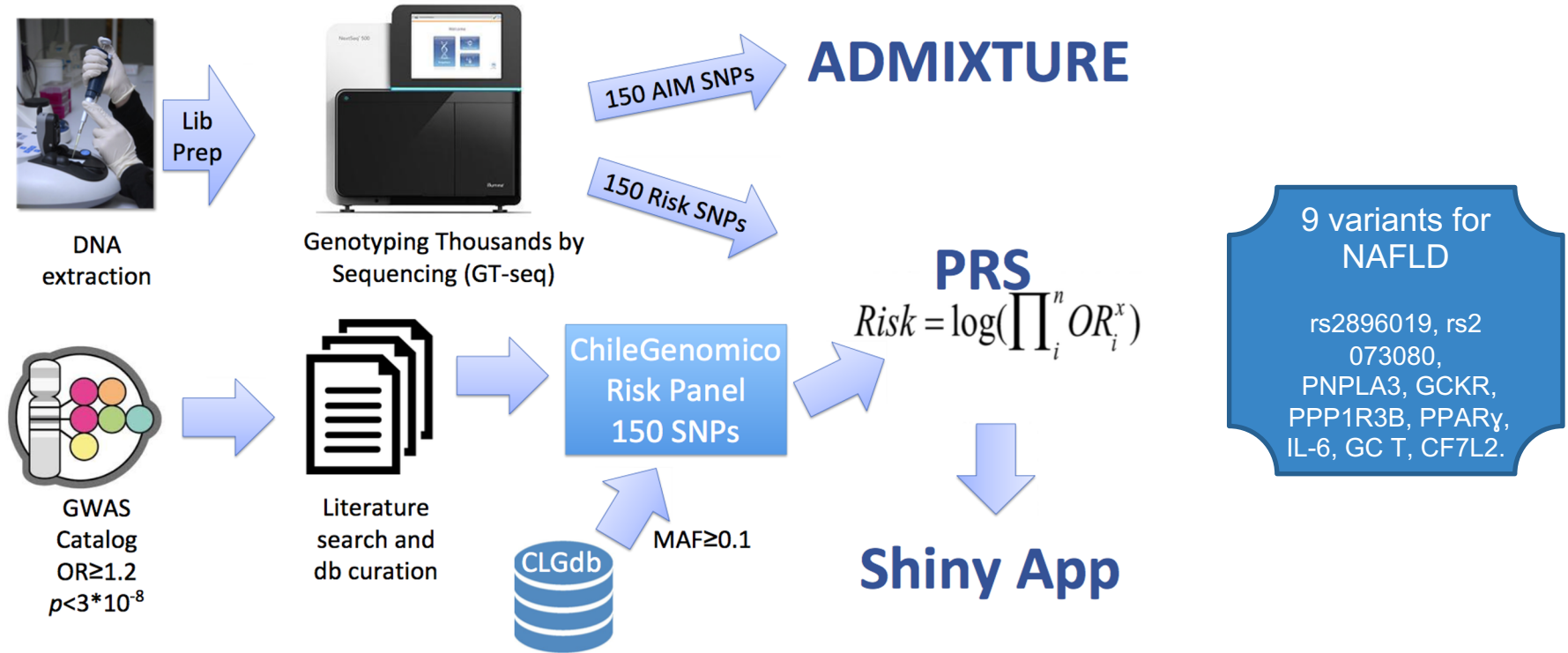
## 2. Gene-environment Interaction:

- Cholecystectomy (CCY) as a causal factor of Non-Alcoholic Fatty Liver Disease (NAFLD)
- Polygenic Risk Score associated with Fatty Liver Disease
- Interaction PRS-CCY and PRS-Obesity

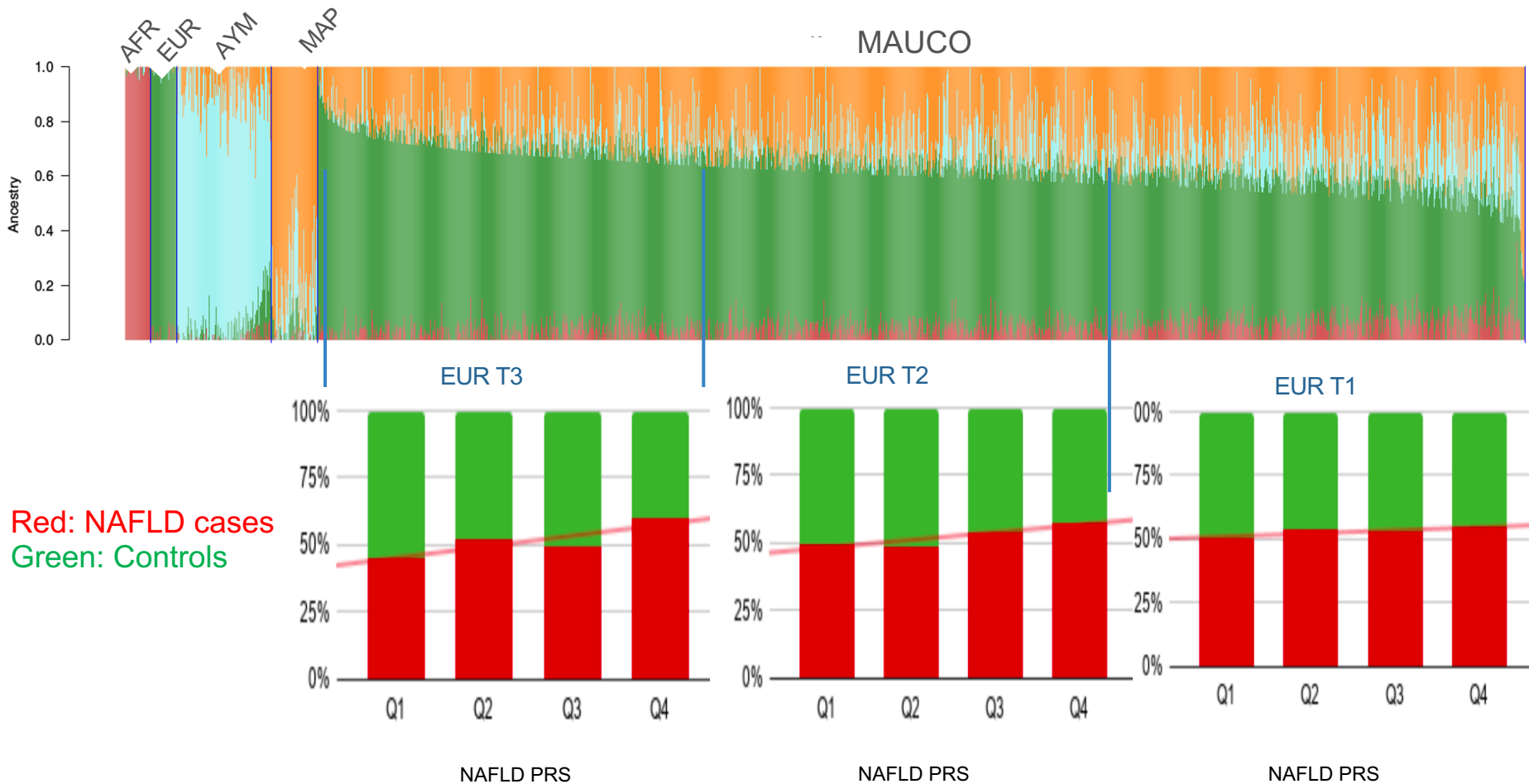
# Cholecystectomy affects metabolism causing NAFLD, Evidence

Author	YR/Place	N	EFFECTS OF CHOLECYSTECTOMY (CCY)
Houghton	1984 UK	103	CCY: 6 mo <b>Weight Gain</b> , men 4.6% and women 3.3%.
Juvonen	1995 Fin	35	CCY: 3 yrs <b>&gt;VLDL &amp; IDL-apoB</b> (P = 0.0019 and P = 0.0001)
Ioannou	2010 US	9072	CCY: <b>&gt; ALT or GGT</b> vs controls or vs gallstones
Amigo	2011 Mice	--	CCY mice: <b>&gt; serum and hepatic TG levels</b>
Ruhl	2013 US	12232	CCY: <b>NAFLD : OR = 2.4, 95% CI: 1.8-3.3</b>
Sonne	2013 Dan	20	CCY: Postprandial <b>glycemia</b> > control (1431 vs 1313, P = 0.023)
Shen	2014 Chin	5672	CCY: <b>Metabolic Syndrome</b> OR = 1.9, 95% CI: 1.2.-3.0;
Yun	2016 Kor	82	CCY: 3 mo <b>Hepatic Steatosis</b>
Zhang	2018 Mice		CCY: alter bil acids, their genes, <b>hepatic VLDL-TG, apoB</b>
Ferreccio	2020 Chile	8948	CCY increased risk of <b>NAFLD for men</b>

# Polygenic Risk Score (PRS) and Ancestry



# NAFLD risk from PRS increases with European ancestry





# PRS \*CHOLECISTECTOMY INTERACTION AND NAFLD

NAFLD ( n=1,763) vs Normal (n=1,635)

## Polygenic Risk Score NAFLD

Cholecystectomy	Q1	Q2	Q3	Q4
No	1,00	1.06 (0.93-1.20)	1.06 (0.93-1.21)	1.12 (0.98-1.28)
Yes	1.14 (0.98-1.33)	<b>1.23</b> <b>(1.06-1.42)</b>	<b>1.42</b> <b>(1.24-1.63)</b>	<b>1.43</b> <b>(1.26-1.63)</b>

**Synergy Index = 1.65 positive interaction PRS and CCY**



## DISCUSSION

- The risk of NAFLD associated to Cholecystectomy increases with the PRS score
- PRS was better predictor of NFLD in participants with higher European ancestry
- We need to identify better genetic predictors for common diseases in our population.

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