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Cohort Profile

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Cohort Profile: The Maule Cohort (MAUCO)

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Why was the cohort set up?

The Maule Cohort (MAUCO) is the first prospective population-based cohort of cardiovascular disease (CVD) and cancer in central Chile. The rationale for this cohort is based on the social, environmental and health characteristics of an under-studied rural population at high risk for chronic diseases.[1] Chile is regarded as a model for social and economic transition in Latin America. Nevertheless, Chile's progress and economic growth hide persistent inequalities.[2] Poverty rates have declined from 38.6% in 1990 to 20.7% in 2017, when a large proportion of the population was still living in poverty based on their education, health care, employment, social security and housing conditions.[3,4] In Chile, as in other Latin American countries, obesity, CVD and cancer have reached epidemic levels, disproportionately affecting people with lower socioeconomic status and overshadowing the national progress.[5,6] Chilean cross-sectional national health surveys

held in 2003, 2009 and 2016 revealed high and increasing prevalences of diabetes (6.3%, 9.4%, 12.3%), metabolic syndrome (22.6%, 35.3%, 40.1%) and overweight/obesity (61.0%, 64.4%, 71.0%).[7–10]

In Chile, environmental risk factors for chronic diseases coexist with remnants of under-development, and health disparities are particularly aggravated in rural areas.[5] The MAUCO Cohort is located in the agricultural Molina County in the Maule Region, 200 km south of the capital city of Santiago. In 2016, the Maule Region had among the highest Chilean all-cause mortality rates per 1000 (regional 6.3 vs 5.7 nationwide)[11] and cause-specific mortality rates per 100 000 for gastric (17.3 vs 12.6 nationwide), colon (8.6 vs 7.2) and oesophageal (4.6 vs 2.5) cancers.[12] Additionally, this population is vulnerable to several important environmental exposures, such as agrochemicals, wood combustion and chronic infections. Little is known about the natural history of CVD and of cancer in this particular socioenvironmental context.

Launched in 2014, MAUCO is the core project of the Advanced Center for Chronic Diseases (ACCDiS), of the universities Pontificia Universidad Católica de Chile (PUC) and Universidad de Chile.[1] The general objectives of MAUCO are: (i) to analyse the natural history of CVD and cancer, where outcomes of interest include CVD, cancer, mental health, ageing, quality of life and respiratory diseases among others, whereas risk factors of interest include socioeconomic, lifestyle, environmental, genetic and ethnic factors; and (ii) to build institutional capacity for advanced research on chronic diseases, including a biobank. Our initial hypothesis is that CVD and cancer share environmental exposures, as well as social and lifestyle risk factors, which lead to chronic inflammation and oxidative stress as the common underlying mechanisms for the development of chronic conditions.[13–15] Examples of initial planned analyses include the association of CVD with pesticides and mycotoxins, social and psychosocial factors and inflammatory conditions such as gallstones.

Who is in the cohort?

The cohort is drawn from Molina County's adult residents. In 2015, Molina had 42 273 inhabitants of whom 50.1% were men,[16] and 30.1% lived in rural areas;[17] in 2011, 13.5% were living in poverty.[18] This population has a low rate of migration and most residents are served by the national health insurance system and the local municipality.[19] These two factors will facilitate follow-up and health demonstration projects at the local level, in the absence of a system to link participants with national databases.

Beginning in July 2014, we conducted a household census of Molina County to identify potential participants and record household members, geographical coordinates (latitude-longitude format; World Geodetic System 1984) and basic housing conditions. Contact was established in 70% of visited households, and in 95% of those, a resident agreed to respond to the survey. All potential participants whom we were able to contact were invited to join the study. Inclusion criteria were: age 38 to 74 years, residency in Molina for at least 6 months in the past year and plans to remain there for the next 3 years. Exclusion criteria were: inability to provide informed consent autonomously and a diagnosis of a terminal illness. Age criteria were decided on the basis that the cohort was designed for a duration of 10 years. Thus, taking into account the natural history of chronic diseases, we required an age range that would be close enough to the event to allow us to observe it in this period. We expect to obtain new funds to extend the follow-up of the cohort for another 10 years and eventually enrol younger participants.

Throughout March 2019, we identified 14 646 residents aged 38 to 74 years; we were able to contact 12 882, of whom 480 were ineligible. Of those who were eligible, 8970 (72.3%) were enrolled, 1215 (9.8%) refused to participate and 2217 (17.9%) were not reachable during the baseline period (Figure 1).

Compared with people who refused or were not reachable, participants were more likely to be women. Participants were slightly older and to have a rural place of residence than people who refused, and slightly younger and to have an urban place of residence than those who were not reachable (Table 1).

How often have participants been followed up?

Follow-up visits are planned at 2, 4 and 8 years after enrolment. Currently, we are conducting the first follow-up visit with 5748 visits completed (77.3% of target to date), 1286 (17.3%) pending contact, 114 (1.5%) withdrawals and 288 (3.9%) lost to follow-up (90 deaths, 106 not reachable, 92 moved to another region) (Figure 1). Participants who attended the year 2 visit were younger than people who withdrew or were lost to follow-up; they were also more likely to be married, have more schooling, be insured by the public health system and be currently employed (Table 2).

To identify health events of interest, we established a surveillance system of admissions in all local hospitals by linking participants to the regional health system database. Also, we regularly obtain notification of participants' deaths through the national death certificate registry.

What has been measured?

A detailed description of the measurements collected at each visit has been published previously.[1] At baseline,

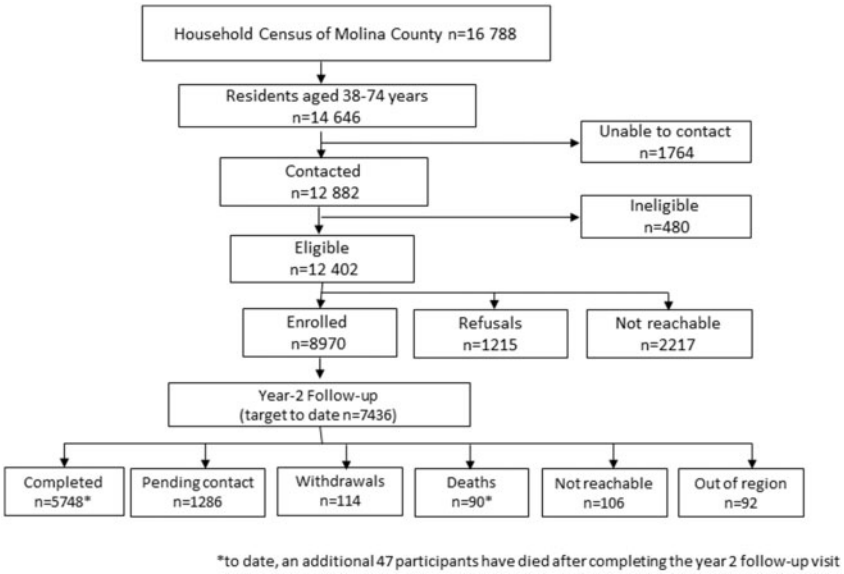

Figure 1. Flow diagram of the MAUCO cohort.

Table 1. Age, sex and residence of responders and non-responders in the MAUCO cohort

Sociodemographic characteristic	Participants $n = 8970$ (72.3%)	Refusals $n = 1215$ (9.8%)	Not reachable $n = 2217$ (17.9%)	*P*-value refusals vs participants	*P*-value not reachable vs participants
Age, mean ± SD	53.5 ± 9.8	52.3 ± 10.2	54.0 ± 10.2	0.0001	0.0329
Women, %	56.3	46.4	46.9	$3.8*10^{-11}$	$8.9*10^{-16}$
Rural residence, %	13.4	6.7	26.8	$2.1*10^{-11}$	$6.6*10^{-16}$

P-values obtained from t test (continuous variable) and chi square test (categorical variables).
SD, standard deviation.

Table 2. Sociodemographic characteristics of participants who have completed the first follow-up visit, refusals and lost to follow-up in the MAUCO cohort

Sociodemographic characteristic	Followed to date[a] $n = 5748$	Withdrawals $n = 114$	Lost to follow-up $n = 288$	*P*-value withdrawals vs followed	*P*-value lost to follow-up vs followed
Age, mean ± SD	53.7 ± 9.5	59.1 ± 9.6	56.9 ± 10.6	$1.5*10^{-9}$	$1.5*10^{-8}$
Women	63.3	54.4	59.4		
Self-identified ethnicity				0.093	0.319
Chilean/Hispanic	97.3	94.7	96.2		
Mapuche	2.2	4.4	2.4		
Marital status					
Married	65.9	64.1	52.1	0.688	$1.7*10^{-6}$
Separated/divorced	11.1	5.3	14.0		
Widowed	6.8	11.4	14.0		
Single	16.2	19.3	19.9		
Schooling, mean ± SD	8.8 ± 4.0	7.5 ± 4.8	7.8 ± 4.3	$8*10^{-4}$	$1*10^{-4}$
≤8 years	51.3	61.4	56.6		
9–12 years	37.5	28.1	36.1		
≥13 years	11.1	10.5	7.3		
Public health insurance	88.2	84.6	88.4	0.245	0.915
Currently employed	58.7	42.3	47.5	$5.3*10^{-4}$	0.0001
Agricultural worker (ever)	44.2	31.8	39.6	0.049	0.226
Rural residence	11.6	12.3	10.9	0.817	0.718

Values are presented as percentages unless otherwise indicated; *P*-values obtained from t test (continuous variables) and chi square test (categorical variables).
[a]Year-2 follow-up is ongoing.

Table 3. Data collected at baseline and first follow-up visit in the MAUCO cohort

Phase	Source	Collected data	*n* participants[a]
Baseline (2015–19)	Household census	Location, type, construction, main goods, water source, heating fuel, pets	16 788[b]
	Health and lifestyle questionnaire	Self-reported sociodemographics, health status, personal and family medical history,[c,d,e] mammogram and pap test history, cardiovascular and digestive symptoms,[d] medication use, tobacco and alcohol consumption, diet,[f,g] physical activity,[d] sedentary behaviour,[h] hearing and vision screening questions, employment history,[i] pesticide exposure,[j] depressive[k] and stress[l] symptoms, cognitive complaints, cognitive test,[m,n] instrumental activities of daily living,[o] social capital.[p]	8970
	Physical measurements	Height, weight, arm span, waist, hip, neck and calf circumferences, bioimpedance body fat, hepatobiliary ultrasound, blood pressure, electrocardiogram, peak expiratory flow, up and go test, hand-grip strength, tooth count	8475
	Laboratory tests	Glycaemia, triglycerides, cholesterol, bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase	8431
		Gamma-glutamyltransferase, insulin, C-reactive protein in a subgroup.[q]	4210
	Biospecimens	Blood components (serum, blood clot, plasma, buffy coat, erythrocytes), urine, saliva	8484
		Stools in a subgroup.	1000
Year 2 follow-up (2017–19)	Health and lifestyle questionnaire	Self-reported health status, personal medical history update, medication use, tobacco and alcohol consumption, sedentary behaviour, employment, cognitive complaints	5748
		Cardiovascular and digestive symptoms, 24-h recall of selected foods, physical activity, depressive symptoms, social capital in a subgroup.[q]	3716
	Physical measurements	Blood pressure, weight, waist circumference, peak expiratory flow	5748
		Full baseline examination excluding electrocardiogram in a subgroup.[q]	3716
	Laboratory tests	Same as baseline[q]	3716
	Biospecimens	Same as baseline excluding urine[q]	3716
Surveillance (ongoing)	Linkages	Regional Hospital Admission Registry	–
		Death Certificate Registry	–

[a]Participants for whom the instrument was applied (missing values exist).

[b]Households identified by census of Molina County.

[c]SF-12 Health Survey.

[d]Encuestas Nacionales de Salud (National Health Surveys) [http://epi.minsal.cl/bases-de-datos/].

[e]Minnesota Living with Heart Failure Questionnaire.

[f]Leighton F, Polic G, Strobel P *et al*. Health impact of Mediterranean diets in food at work. *Public Health Nutrition* 2009;**12**:1635–43. doi: 10.1017/S1368980009990486.

[g]PLCO Prostate Lung Colorectal and Ovarian Cancer Screening Trial.

[h]GPAQ- WHO Global Physical Activity Questionnaire.

[i]Encuesta Nacional de Empleo, Trabajo, Calidad de Vida y Salud de los Trabajadores y Trabajadoras de Chile 2009–2010 (National Survey of Employment, Labour, Quality of Life and Health of the Workers of Chile 2009–2010).

[j]PIPAH Prospective Investigation of Pesticide Applicators' Health Study.

[k]PHQ-9Patient Health Questionnaire.

[l]Lanas F, Avezum A, Bautista LE *et al*. Risk factors for acute myocardial infarction in Latin America: the INTERHEART Latin American study. *Circulation* 2007;**115**:1067–74.

[m]Addenbrooke's Cognitive Examination-Revised Spanish version.

[n]Reitan RM. *Trail Making Test: Manual for Administration and Scoring*. Tuscon, AZ: Reitan Neuropsychology Laboratory, 1992.

[o]Icaza *et al*.[22]

[p]Sapag JC, Aracena M, Villarroel L *et al*. Social capital and self-rated health in urban low income neighbourhoods in Chile. *J Epidemiol Community Health* 2008;**62**:790–2.

[q]All participants with gallstones, history of cholecystectomy, agricultural workers, abnormal electrocardiogram, a subset of participants with high cardiovascular risk, and age-sex group-matched controls.

participants answered health and risk factor surveys previously used in the Chilean population; these surveys included questions from the National Health Surveys as well as internationally validated instruments (detailed in Table 3) that had been adapted using vocabulary suitable for a low-schooling population. Participants underwent anthropometric and bioimpedance measurements, grip strength tests, electrocardiogram, hepatobiliary ultrasound and cognitive evaluation. They also provided urine, saliva and blood samples (for storage at −80°C, 30

aliquots from each participant); stool was obtained in a subgroup ($n = 1000$) (Table 3). In addition, we assessed environmental conditions in their households and neighbourhoods, and sampled air, water and soil from the Molina County area.[1]

At the year 2 follow-up, all participants completed a questionnaire to assess changes in exposures and health conditions and underwent blood pressure, weight and waist circumference and peak expiratory flow measurements. A subgroup of approximately 40% of the cohort underwent a complete examination similar to baseline (excluding electrocardiogram) and provided biological samples; this subgroup comprises all participants with gallstones, a history of cholecystectomy, abnormal electrocardiogram and a history of agricultural work, as well as a subset of participants at high risk for CVD and age-sex group-matched controls (Table 3).

Key initial findings and ongoing research

Baseline evaluation

Of the 8970 participants, 56.3% were women; compared with males enrolled, women were somewhat younger, had slightly less schooling and were less likely to have ever worked in agriculture. Public health insurance was predominant among participants, with a higher prevalence than the national average (78%)[19] (Table 4). Nearly all participants' households had solid floors, indoor drinking water supply, sewage disposal and a refrigerator, and most used natural gas or electricity for cooking and wood or coal for heating; fewer households had a computer, car, domestic animals or farm animals (Supplementary Table 1, available as Supplementary data at *IJE* online).

Women had a worse self-perception of health status than men, less hypertension, almost three times more history of cancer, a higher report of digestive symptoms (particularly biliary colic), more respiratory disease and three times more osteomuscular disease. Men reported consuming three times more alcohol per week than women, with a higher prevalence of risky alcohol intake (defined as ≥30 g for men or ≥20 g for women per week) and almost three times more binge drinking (≥4 drinks for men or ≥3 drinks for women per occasion).[8] Also, more men had a high consumption of sugary drinks (defined as >2 times per day) and processed meat (>4 times per week), and low vegetable and fruit consumption (>1 time per day for each) compared with women. In addition, men were more likely to be current or former smokers (Table 5).

Symptoms of depression were twice as high among women. Neurocognitive evaluation results were similar in men and women: mean scores of both the Mini-Mental State Examination[20] and the Addenbrooke's Cognitive Examination-revised[21] were below the cut-off point for normalcy (Table 5).

Table 4. Sociodemographic characteristics of MAUCO cohort participants

Sociodemographic characteristic	**All**[a] $n = 8970$	Women $n = 5052$ (56.3%)	Men $n = 3918$ (43.7%)	*P*-value sex difference
Age, mean ± SD	53.5 ± 9.8	53.1 ± 9.7	53.9 ± 9.8	0.001
35–44	22.1	22.7	21.6	0.005
45–54	33.0	34.3	31.7	
55–64	28.2	27.3	29.0	
65–74	16.7	15.7	17.6	
Self-identified ethnicity				0.084
Chilean/Hispanic	96.9	97.3	96.6	
Mapuche	2.5	2.1	2.8	
Marital status				$<2.2*10^{-16}$
Married	67.1	61.5	72.5	
Separated/divorced	10.6	12.6	8.7	
Widowed	5.9	9.4	2.6	
Single	16.4	16.5	16.3	
Schooling, mean ± SD	9.0 ± 4.1	8.8 ± 4.1	9.1 ± 4.1	0.005
≤8 years	49.2	49.4	49.0	0.365
9–12 years	38.7	39.1	38.4	
≥13 years	12.1	11.6	12.6	
Public health insurance	87.1	87.6	86.7	0.0003046
Currently employed	63.9	43.8	83.2	$<2.2*10^{-16}$
Agricultural worker (ever)	45.4	35.5	54.9	$<2.2*10^{-16}$

Values are presented as percentages unless otherwise indicated.

[a]Prevalence weighted to represent the sex distribution of Molina's population (49.9% women).

Table 5. Baseline health profile of MAUCO cohort participants

Health conditions		All[a] $n = 8970$ (100%)	Women $n = 5052$ (56.3%)	Men $n = 3918$ (43.7%)	*P*-value sex difference
Self-reported health status	Excellent, very good and good	44.7	37.9	51.2	$<2.2*10^{-16}$
	Fair	45.9	49.9	42.1	
	Bad	9.1	12.2	6.2	
Chronic conditions	Diabetes[b]	15.7	16.0	15.3	0.366
	Hypertension[c]	61.1	55.5	68.4	$<2.2*10^{-16}$
	Cardiovascular diseases[d]	7.3	7.0	7.5	0.324
	Myocardial infarction	2.5	2.2	2.8	0.096
	Heart failure	1.4	1.6	1.2	0.098
	Stroke	2.0	1.6	2.3	0.027
	Arrhythmia	1.1	1.2	1.1	0.586
	Cancer	3.5	5.2	1.8	$2.81*10^{-15}$
	Non-infectious digestive diseases	31.3	42.3	20.7	$<2.2*10^{-16}$
	Digestive symptoms[e]	39.7	50.1	29.8	$<2.2*10^{-16}$
	Respiratory diseases	5.3	6.5	4.2	$8.451*10^{-6}$
	Osteomuscular diseases[f]	5.2	8.1	2.5	$<2.2*10^{-16}$
Lifestyle factors	Alcohol intake (g) per week,[g] mean ± SD	57.5±174.6	27.2±113.7	86.6±211.8	$<2.2*10^{-16}$
	Risky alcohol intake[h]	20.5	9.9	30.7	$<2.2*10^{-16}$
	Binge drinking[i]	20.8	11.0	30.3	$<2.2*10^{-16}$
	Sugary drinks consumption >2 times/day	14.4	9.1	19.5	$<2.2*10^{-16}$
	Processed meat consumption >4 times/week	7.9	6.8	8.9	0.00047
	Vegetables consumption >1 time/day	66.4	73.6	59.5	$<2.2*10^{-16}$
	Fruits consumption >1 time/day	49.7	55.7	43.9	$<2.2*10^{-16}$
	Low physical activity[j]	92.7	92.6	92.7	0.932
	Smoking habit				$<2.2*10^{-16}$
	Never smoker	41.5	48.6	34.6	
	Current smoker	32.9	30.6	35.1	
	Former smoker	25.6	20.7	30.3	
Mental health and cognitive examinations	Depressive symptoms (PHQ-2)	17.0	23.2	11.1	$<2.2*10^{-16}$
	ACE-R[k], mean ± SD	73.2 ± 15.5	73.0 ± 15.5	73.3 ± 15.6	0.385
	MMSE[l], mean ± SD	25.8 ± 4.1	25.9 ± 4.0	25.8 ± 4.2	0.779
Physical examinations	High blood pressure[m]	56.6	49.4	65.9	$<2.2*10^{16}$
	Body mass index ≥30 kg/m^2	39.4	42.6	36.3	$5.071*10^{-9}$
	High body fat percentage[n]	76.1	87.4	65.2	$<2.2*10^{-16}$
	Remaining teeth, mean ± SD	18.7 ± 9.2	18.0 ± 9.5	19.4 ± 8.8	$8.207*10^{-7}$
	Peak expiratory flow <80%	45.2	40.0	50.1	$<2.2*10^{-16}$
	Handgrip strength test (kg),[o] mean ± SD	30.0 ± 10.5	21.9 ± 5.5	36.9 ± 9.5	$<2.2*10^{-16}$
	Abnormal electrocardiogram ($n = 6550$)	5.4	4.4	6.3	0.001
Hepatobiliary ultrasound	Fatty liver (any degree)	47.5	47.3	47.7	0.702
	Cholecystectomized	18.3	28.4	8.6	$<2.2*10^{-16}$
	Gallstones	11.2	13.3	9.2	$9.006*10^{-9}$
Laboratory examinations	Fasting blood glucose ≥100 mg/dL	30.0	26.1	33.7	$<2.2*10^{-16}$
	Fasting blood glucose ≥126 mg/dL	8.7	7.8	9.9	0.001
	LDL >160 mg/dL	9.9	10.8	9.1	0.012
	Triglycerides ≥200 mg/dL	25.6	21.1	29.9	$<2.2*10^{-16}$
	HDL ≤50 mg/dL women, ≤40 mg/dL men	49.6	59.2	40.3	$<2.2*10^{-16}$
	AST (GOT) ≥35 UI/L	16.4	12.7	20.0	$<2.2*10^{-16}$
	ALT (GPT) ≥35 UI/L	32.3	22.7	41.6	$<2.2*10^{-16}$
	Metabolic syndrome[p]	47.6	50.8	44.6	$2.552*10^{-7}$

(Continued)

Table 5. Continued

Health conditions		All[a] $n=8970$ (100%)	Women $n=5052$ (56.3%)	Men $n=3918$ (43.7%)	*P*-value sex difference
Framingham CV risk score[q]	High risk >10%	30.2	3.8	55.5	$<2.2*10^{-16}$
Chilean CV risk score[r]	High risk >10%	10.9	3.1	18.3	$<2.2*10^{-16}$

Values are presented as percentages unless otherwise indicated; all prevalence and mean values are age-adjusted.

SD, standard deviation; PHQ-2, Patient Health Questionnaire; ACE-R, Addenbrooke's Cognitive Examination Revised; MMSE, Mini Mental State Examination; AST (GOT), Aspartate aminotransferase (glutamic oxaloacetic transaminase). ALT (GPT), Alanine Aminotransferase (serum glutamic pyruvic transaminase); LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol.

[a]Prevalence weighted to represent the sex distribution of Molina's population (49.9% women)

[b]Self-report or glycaemia ≥126 mg/dL or use of hypoglycaemic drugs.

[c]Use of hypotensive drugs or measured systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg.

[d]Excluding hypertension.

[e]Includes biliary colic, gastroesophageal reflux and gastritis symptoms.

[f]Includes arthritis, arthrosis, disc disease, lumbar hernia.

[g]Among those who declared alcohol consumption at least once a month.

[h]≥20g for women or ≥30 g for men per week.

[i]≥Three drinks for women or ≥four drinks for men per occasion, *Encuesta Nacional de Salud (National Health Survey)* 2010. https://www.minsal.cl/portal/url/item/bcb03d7bc28b64dfe040010165012d23.pdf.

[j]<30 min of physical activity three times/week.

[k]Cut-off point for normality ≥76.

[l]Cut-off point for normality ≥27.

[m]Systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg.

[n]>25% for men or >35% for women, measured by bioimpedance analysis.

[o]Dominant hand.

[p]≥3 of the following: abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure and high fasting glucose.

[q]Considers age, sex, smoking, systolic blood pressure, HDL, triglycerides and cholesterol for risk of a cardiovascular event in the next 10 years.

[r]Considers age, sex, smoking, diabetes, systolic blood pressure, diastolic blood pressure, cholesterol and HDL for risk of a cardiovascular event in the next 10 years.[22]

Men had more clinically measured hypertension, altered electrocardiogram and abnormal peak expiratory flow. Women had more obesity, fewer remaining teeth and lower hand-grip strength. Based on hepatobiliary ultrasound examination, women and men had a similarly very high prevalence of fatty liver, but women had a much higher prevalence of cholecystectomy and gallstones, along with a higher ratio of cholecystectomies over gallstones (2.1 versus 0.9). Men had a higher prevalence of altered fasting glucose levels, high triglycerides and abnormal liver enzyme levels (Table 2). Whereas the prevalence of metabolic syndrome was higher in women, men were 14.6 times more likely to have a high CVD risk at 10 years based on the Framingham Cardiovascular Risk Score, but only 5.9 times with the Chilean adapted version[22] (Table 5).

A history of diabetes was reported by 32% of participants with glycaemia ≥100 mg/dl and 71% of those with glycaemia ≥126 mg/dl; 45% of participants with self-reported diabetes were taking oral hypoglycaemic medications. A history of hypertension was reported by 51% of participants with measured blood pressure ≥130/80 and 90% of those with measured blood pressure ≥140/90; 54% of participants with self-reported hypertension were taking antihypertensive medications.

The observed prevalences of obesity (39.4%) and hypertension (61.1%) are similar to those reported in the 2016–17 National Health Survey for the population of the same age (obesity 41.8%; hypertension 63.8%); however in MAUCO, the prevalence of diabetes (15.7%) is lower than the national prevalence (22.4%).[23]

Surveillance of health events

In the first 4 years of follow-up, we identified 1182 hospital admissions affecting 821 participants; cancer and CVD represented 8.5% and 10.2% of causes, respectively (main causes are available in Supplementary Table 2, available as Supplementary data at *IJE* online). To date, 137 participants have died; the main causes were CVD (27.7%) and cancer (26.3%) (other causes are available in Supplementary Table 3, available as Supplementary data at *IJE* online). A diagnosis of diabetes at baseline was associated with a higher risk of both hospitalization (cardiovascular and respiratory causes) and death (cancer and respiratory causes). The association of diabetes with increased cancer mortality has been previously described[24–26] and is thought to be in part related to a carcinogenetic effect of hyperinsulinemia, hyperglycaemic-induced oxidative stress and chronic inflammation.[27–29] The association of diabetes

Table 6. Hospitalizations and deaths during follow-up through March 2019 and selected baseline health conditions of MAUCO cohort participants

Baseline conditions	Selected causes of first hospitalization ($n = 821$); hazard ratio[a] (95% CI)			
	Cancer* n = 49	Cardiovascular[b] n = 77	Respiratory n = 43	Digestive n = 243
Diabetes[c]	1.78 (0.91–3.50)	2.01 (1.21–3.34)	2.54 (1.23–5.24)	0.87 (0.61–1.23)
Hypertension[d]	0.84 (0.47–1.53)	1.74 (1.01–2.97)	1.71 (0.85–3.44)	0.96 (0.73–1.25)
Metabolic syndrome[e]	1.36 (0.74–2.48)	1.26 (0.78–2.06)	1.37 (0.67–2.81)	1.17 (0.90–1.52)
Body mass index ≥30 kg/m^2	1.22 (0.68–2.18)	1.48 (0.92–2.38)	1.43 (0.73–2.81)	1.42 (1.10–1.83)
Body fat percentage >25% men, >35% women	1.04 (0.43–2.48)	2.70 (0.95–7.67)	2.34 (0.53–10.29)	1.50 (1.00–2.24)
Peak expiratory flow <80%	0.76 (0.47–1.22)	1.36 (0.84–2.21)	1.98 (0.97–4.02)	1.16 (0.89–1.50)
AST (GOT) ≥35 IU/L	1.12 (0.60–2.10)	1.07 (0.56–2.04)	1.63 (0.70–3.77)	0.93 (0.65–1.33)
	Selected causes of death ($n = 137$); hazard ratio[a] (95% CI)			
	Cancer $n = 36$	Cardiovascular[b] $n = 38$	Respiratory $n = 17$	Digestive $n = 11$
Diabetes[c]	2.68 (1.29–5.58)	2.02 (0.96–4.27)	4.40 (1.54–12.57)	2.43 (0.55–10.68)
Hypertension[d]	1.09 (0.53–2.25)	2.08 (0.90–4.81)	0.68 (0.25–1.83)	1.06 (0.29–3.86)
Metabolic syndrome[e]	1.09 (0.54–2.18)	1.69 (0.79–3.61)	1.47 (0.50–4.35)	0.83 (0.20–3.38)
Body mass index ≥30 kg/m^2	1.11 (0.55–2.22)	1.47 (0.72–2.98)	0.53 (0.17–1.68)	0.51 (0.10–2.54)
Body fat percentage >25% men, >35% women	0.95 (0.31–2.90)	4.01 (0.53–30.61)	—	1.06 (0.11–9.86)
Peak expiratory flow <80%	1.50 (0.74–3.04)	3.61 (1.47–8.88)	6.06 (1.36–27.05)	0.57 (0.13–2.42)
AST (GOT) ≥35 IU/L	1.62 (0.70–3.75)	2.21 (0.98–4.97)	0.47 (0.06–3.57)	6.29 (1.55–25.50)

Values are age- and sex-adjusted; *does not include cancer *in situ*; due to perfect separation.
AST (GOT), aspartate aminotransferase (glutamic oxaloacetic transaminase).
[a]Hazard ratio from Cox Proportional Hazard Model, counting the participant until their first hospitalization for each cause.
[b]Includes stroke, myocardial infarction, heart failure and arrhythmia.
[c]According to self-report or glycaemia ≥126 mg/dL or use of hypoglycaemic drugs, adjusted by age, sex and obesity.
[d]According to use of hypotensive drugs or systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg.
[e]Including ≥3 of the following: abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure or high fasting glucose.

with increased respiratory disease mortality has also been reported[24,25,30] and could be partly explained by the reduced pulmonary function observed in people with diabetes.[31–33] Additionally, hypertension and obesity were associated with an elevated risk of hospitalization, and altered liver enzyme levels and a low peak expiratory flow were associated with an increased risk of death (Table 6).

The observed death rate [5.3; 95% confidence interval (CI), 4.4–6.2] is lower than the 2016 regional rate for population aged 40–74 (6.7 per 1000; 95% CI, 6.5–6.8).[11] This relative lower risk in MAUCO can be explained by the exclusion from the cohort of people with terminal illness, who would have been more likely to die in this short period (Table 6).

Ancillary studies

An array of studies are nested in the MAUCO cohort: a study of the risk of non-alcoholic fatty liver disease associated with cholecystectomy and gallstones, including oral and enteric microbiome and *Helicobacter pylori* infection; a risk assessment of mycotoxins (especially aflatoxin) in food; a risk assessment of pesticide exposure in air, soil and urine; a risk assessment of processed meat and nitrites for gastric atrophy; and genetic markers for chronic diseases. In addition, many postgraduate theses have been completed on topics ranging from in-depth dental and dermatological examinations to walkability of Molina's streets for older participants.

What are the main strengths and weaknesses?

The strengths of MAUCO derive from the broad interdisciplinary collaboration among epidemiologists, laboratory scientists, and clinical specialists from ACCDiS, which represents major Chilean universities. This cohort is the first Latin American prospective study including measurements ranging from molecular and genetic testing to environmental, neuropsychological and social exposures.

MAUCO's leadership structure includes a scientific Directorate, an Executive Committee and an Advisory Board comprising representatives of the Ministry of Health, the Regional Health Service, FONDAP, non-profit health organizations, scientific societies and representatives

of the community, who define the use and sharing of data and samples. MAUCO's field team includes epidemiologists, nurses, medical technologists, health care assistants and administrative staff, who live in Molina County and are engaged with the community. MAUCO epidemiologists and data managers, led by the MAUCO Director, are responsible for the design, implementation, quality and accuracy of the data and analyses, as well as the quality of the biospecimens. This structure has enabled ACCDiS-MAUCO to engage with local and regional authorities that are committed to securing the sustainability of the cohort. Engagement with the Molina community as a partner in the study is a priority for MAUCO; as an example, we hold regular outreach activities to inform the community about study findings. Community involvement has been highly successful, resulting in a high participation rate and low loss to follow-up.

MAUCO is part of the World Health Organization consortium of agricultural cohort studies, AGRICOH, along with 29 other cohorts from around the world,[34] and is member of the International 100 K Cohort Consortium.[35] MAUCO offers an unprecedented opportunity to address the dearth of systematic research on the health needs of Chile's population in the context of accelerated development, which is also relevant to other Latin American countries and perhaps to Hispanic people in other countries.

The MAUCO Biobank, at the School of Medicine of PUC, follows the National Cancer Institute's Biobank Quality Control regulation.[36] Standard operating procedures are in place to ensure the quality of the MAUCO biological specimens from collection to storage. An inventory system of biological samples is used to identify the location and available quantity of each aliquot, using Biological Specimen Inventory (BSI) software [www.bsisystems.com].

The MAUCO information system ensures safe, complete and accurate data flow, including data collection, data entry and generation of databases. Data entry, supervised by the data manager, is done locally using REDCap™ (Research Electronic Data Capture).[37]

Funding for the MAUCO cohort currently depends on modest, highly competitive and short-term state funding, has only been secured for an initial period of 10 years from December 2013 to December 2023, and requires extra funding to ensure long-term follow-up. Compared with international population-based cohorts, we work in a relatively low-resource research environment while being subject to a high demand for productivity. These conditions create a major challenge for a prospective study such as MAUCO.

The external validity of MAUCO's findings might be limited, since this cohort represents an agricultural population from a small city and, therefore, some results may not be applicable to residents of large urban areas.

How can I access the data? Where can I find out more?

Access to data and biospecimens is regulated by the ACCDiS Directorate in accordance with the local institutional review board authorization [www.mauco.org]. The regulatory system was developed following the UK's Centre for Longitudinal Studies protocol[38] and aims to make the data and biospecimens available to researchers, while ensuring that ethical and scientific principles are upheld. All data and specimen requests must be approved by the Access Committee and a bilateral agreement must be signed before sharing data. Requests and research proposals can be submitted in English or Spanish and should be sent to: cferrec@med.puc.cl (application form available in Supplementary Appendix 1, available as Supplementary data at *IJE* online). Additional information can be requested at [contacto@mauco.org].

Profile in a nutshell

- MAUCO is the first prospective population-based cohort to study a unique Hispanic-Amerindian population with high rates of gastric cancer coupled with a high burden of cardiovascular disease, under an accelerated health transition and exposed to various environmental exposures (agrochemicals, wood combustion, chronic infections etc.).
- All residents aged 38 to 74 years from the agricultural county of Molina in Central Chile were invited beginning in 2015, and 8970 participants entered the cohort.
- Epidemiological and sociodemographic information is collected for all participants as well as full anthropometric examinations, physical condition tests, tooth count, electrocardiogram, hepatobiliary ultrasound, peak expiratory flow measurements, neurocognitive examinations and blood, urine and saliva samples collected for measurement at baseline. Surveillance is in place to identify hospitalizations and deaths since enrolment. Additionally, we measure environmental quality of air and soil and the occurrence of multi-resistant bacteria in Molina.
- To date, 5748 participants have completed the year 2 follow-up, which is ongoing. The attrition rate of 5.9% is due to death (1.8%), change of place of residence (1.2%), study withdrawal (1.5%) and not reachable (1.4%); 8521 participants are currently available for further follow-up.
- Data and sample sharing regulations are established. Interested investigators should contact MAUCO's Director, Catterina Ferreccio [cferrec@med.puc.cl].

Supplementary Data

Supplementary data are available at *IJE* online.

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