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Supporting Information

Supplementary methods and results

This appendix was part of the submitted manuscript and has been peer reviewed.
It is posted as supplied by the authors.

Appendix to: Vaz K, Kemp WW, Majeed A, et al. Steatotic liver disease in rural and regional Victoria, according to the NAFLD and newer diagnostic criteria: retrospective cohort analyses of 2001–2003 and 2016–2018 data. *Med J Aust* 2024; doi: 10.5694/mja2.52189.

1. Supplementary methods information

Both CrossRoads studies were conducted in Shepparton, Mooroopna (regional centre), and Benalla, Cobram and Seymour (rural towns). Houses were randomly selected from local government lists for a health questionnaire. One adult (18 years or older) from each household was invited to participate in a clinic sub-study that collected detailed data on demographic characteristics, anthropometry, vital signs, and laboratory tests including full blood examination, liver function tests, fasting lipid profile and glycaemic parameters, and viral serology (CrossRoads II only), as well as to complete more extensive questionnaires on diet, lifestyle, social factors, and health. The main difference between the two studies in enrolment strategy was that CrossRoads I undertook 2:1 regional:rural recruitment, and CrossRoads II undertook 1:1 regional:rural recruitment.

Study definitions

Hypertension was defined as systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, or need for anti-hypertensive therapy. Dyslipidaemia was defined according to lipid parameters published by the Australian Institute of Health and Welfare.(1) Metabolic syndrome was diagnosed according to criteria published by the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity.(2)

Adequate physical activity was defined as at least 150 minutes of dedicated exercise per week; adequate diet was defined as the consumption of at least four serves of vegetables and at least two serves of fruit per day.

References

1. Australian Institute of Health and Welfare. Risk factors to health: Abnormal blood lipids (dyslipidaemia) 2017. Canberra. https://www.aihw.gov.au/reports/biomedical-risk-factors/risk-factors-to-health/contents/abnormal-blood-lipids-dyslipidaemia (viewed Dec 2022).

2. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120: 1640-1645.

Table 1. Baseline demographic characteristics of participants in the two CrossRoads studies

Characteristic	CrossRoads I	CrossRoads II	*P*
All participants	1040	721	
Gender (men)	462 (44.4%)	322 (44.7%)	0.92
Age (years), mean (SD)	52.8 (15.6)	59.9 (16.1)	<0.001
Born in Australia	915 (88.0%)	613 (85.1%)	0.08
Ethnic background			<0.001
White	1011/1038 (97.4%)	656/706 (92.9%)	
Asian	11/1038 (1.1%)	30/706 (4.2%)	
Aboriginal and Torres Strait Islander	7/1038 (0.7%)	6/706 (0.8%)	
Other	9/1038 (0.9%)	14/706 (2.0%)	
Residential location			<0.001
Regional centre	692 (66.5%)	336 (46.6%)	
Smaller rural town	348 (33.5%)	385 (53.4%)	
Private health insurance	498 (47.9%)	444 (61.6%)	<0.001
Education: Completed secondary school	488/1034 (47.2%)	446 (61.9%)	<0.001
Clinical characteristics			
Weight (kg), mean (SD)	78.8 (16.7)	82.0 (18.9)	<0.001
Body mass index (kg/m^2), mean (SD)	27.9 (5.4)	29.0 (6.1)	<0.001
Overweight/obese*	711 (68.4%)	526 (73.0%)	0.038
Waist circumference (cm), mean (SD)	94.7 (14.4)	98.4 (15.1)	<0.001
Elevated waist circumference†	749 (72.0%)	577 (80.0%)	<0.001
Hypertension	578 (55.6%)	392 (54.7%)	0.73
Dyslipidaemia	669 (64.3%)	420 (58.3%)	0.010
Type 2 diabetes mellitus	76 (7.3%)	68 (9.7%)	0.07
Metabolic syndrome‡	343 (33.0%)	258 (35.9%)	0.21
Lifestyle factors			
Excess alcohol intake§	166 (16.0%)	100/707 (14.1%)	0.30
Smoking status	1037	695	<0.001
Current smoker	179 (17.3%)	67 (9.6%)	
Ex-smoker	345 (33.3%)	238 (34.2%)	
Non-smoker	513 (49.5%)	390 (56.1%)	
Physical activity (min/week), mean (SD)	278 (293)	264 (228)	0.36
Adequate physical activity¶	480/718 (66.9%)	337/508 (66.3%)	0.85
Adequate diet**	228/1036 (22.0%)	136/695 (19.6%)	0.22
Take-away food at least once a week	271/1037 (26.1%)	213/695 (30.6%)	0.040
Laboratory factors			
γ-glutamyl transferase (U/L), mean (SD)	34 (41)	33 (44)	0.74
Alanine aminotransferase (U/L), mean (SD)	25 (19)	26 (17)	0.18
Alanine aminotransferase ≥ 1.5x upper limit of normal††	165 (15.9%)	112 (15.5%)	0.85
Aspartate aminotransferase (U/L), mean (SD)	26 (10)	26 (9)	0.47
Bilirubin (μmol/L), mean (SD)	7.4 (0.5)	8.8 (4.5)	<0.001
Fasting glucose (mmol/L), mean (SD)	5.4 (1.3)	5.3 (1.3)	0.59
Glycosylated haemoglobin (mmol/mol), mean (SD)	34.5 (6.2)	36.2 (8.1)	<0.001
Total cholesterol (mmol/L), mean (SD)	5.3 (1.0)	4.9 (1.0)	<0.001

Characteristic	CrossRoads I	CrossRoads II	*P*
Low density lipoprotein cholesterol	3.2 (0.9)	2.8 (0.9)	<0.001
High density lipoprotein cholesterol	1.4 (0.4)	1.4 (0.4)	0.74
Low high density lipoprotein cholesterol‡‡	288 (27.7%)	219 (30.4%)	0.22
Elevated triglycerides (≥ 1.70 mmol/L)	342 (32.9%)	226 (31.3%)	0.50
Fibrosis-4 index, mean (SD)	1.25 (0.78)	1.33 (0.70)	0.020
Fibrosis-4 index, categorical	1040	658	<0.001
< 1.30	678 (65.2%)	366 (55.6%)	
1.30–2.67	313 (30.1%)	267 (40.6%)	
> 2.67	49 (4.7%)	25 (3.8%)	
NAFLD fibrosis score, mean (SD)	–1.648 (1.404)	–1.417 (1.328)	0.011
NAFLD fibrosis score, categorical	1040	624	0.001
< –1.455	605 (58.2%)	308 (49.4%)	
–1.455 to 0.676	380 (36.5%)	283 (45.4%)	
> 0.676	55 (5.3%)	33 (5.3%)	

NAFLD = non-alcoholic fatty liver disease.

* Body mass index (BMI) of 23 kg/m^2 or more (Asians), 25 kg/m^2 or more (other ethnic groups).

† Asians: greater than 90 cm (men) or 80 cm (women); other ethnic groups: greater than 94 cm (men) or 80 cm (women).

‡ Metabolic syndrome considered if any three of the following five criteria met: elevated waist circumference, elevated triglycerides (or on lipid-lowering therapy), reduced high density lipoprotein cholesterol (or on lipid-lowering therapy), elevated blood pressure (or on anti-hypertensive therapy), and elevated fasting glucose (or on medication for elevated glucose).

§ Men, ≥ 30 g/day; women, ≥ 20 g/day.

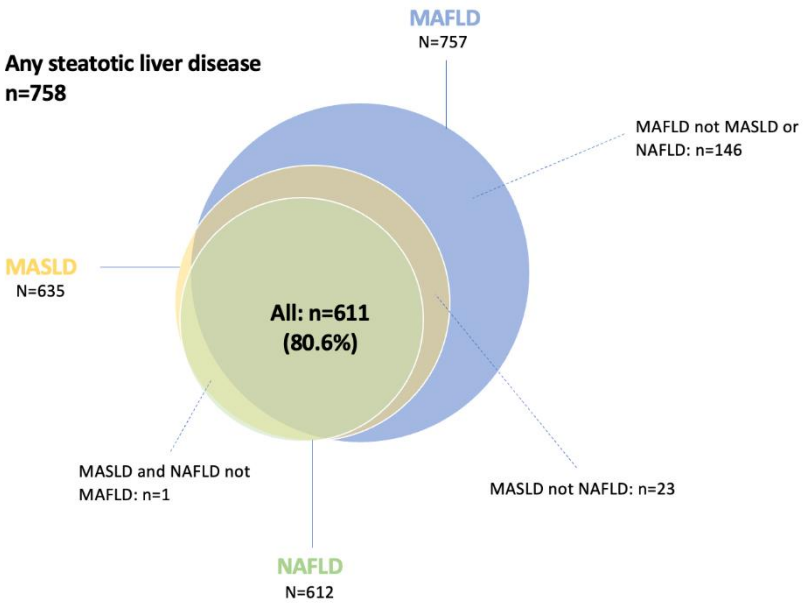
¶ At least 150 minutes of dedicated exercise per week.

** At least four serves of vegetables and at least two serves of fruit per day.

†† Upper limit normal men, 30 U/L; women, 20 U/L.

‡‡ Men, < 1.0 mmol/L; women and people using lipid-lowering therapy, < 1.3 mmol/L.

Figure 1. Diagnoses of steatotic liver disease among 758 of 1761 participants in the two CrossRoads studies, by specific diagnosis criteria*



MAFLD = metabolic dysfunction-associated fatty liver disease; MASLD = metabolic dysfunction-associated steatotic liver disease; NAFLD = non-alcoholic fatty liver disease.

* The viral hepatitis status of all 758 people defined as having steatotic liver disease in the two studies was known.

Table 2. Age- and gender-standardised prevalence (with 95% confidence intervals) of steatotic liver disease, by specific diagnosis criteria and remoteness

	NAFLD		MAFLD		MASLD	
Study	**Rural**	**Regional**	**Rural**	**Regional**	**Rural**	**Regional**
CrossRoads I	34.7 (29.1–40.3)	30.4 (26.7–34.1)	43.9 (38.1–49.8)	35.5 (31.8–39.2)	37.1 (31.4–42.7)	31.4 (27.7–35.1)
CrossRoads II	36.1 (29.2–43.0)	33.8 (27.9–39.7)	42.1 (35.2–49.0)	43.3 (37.4–49.2)	36.9 (30.0–43.8)	33.9 (28.0–39.8)

NAFLD = non-alcoholic fatty liver disease; MAFLD = metabolic dysfunction-associated fatty liver disease; MASLD = metabolic dysfunction-associated steatotic liver disease.