MASLD in Australia – Epidemiology Prevalence, patterns of disease and at-risk priority populations

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What do we mean by MASLD and MAFLD?

Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD)

- Presence of any of the cardiometabolic criteria
- Low to minimal alcohol
- No causes of 'secondary' steatosis'

Hepatic Steatosis

Hepatocytes containing ≥ 5% fat

Metabolic Dysfunction Associated Fatty Liver Disease (MAFLD)

- Defined by *positive* criteria
- Overweight (by BMI), T2DM, and/or two features of the metabolic syndrome
 - Allows concurrent liver disease & alcohol

Diagnosis of MASLD



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Diagnosing MASLD



Right renal cortex

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MASLD – Why Does it Matter?



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MASLD – How Big is the Problem?

- Very big in Australia and globally!
- Approx. >30% of all Australians¹
- Likely to become the largest cause of liver-related mortality and liver transplant by 2030 in the USA²
- Strongly associated with cardiovascular disease as well as extra-hepatic malignancy, chronic kidney disease, incident diabetes³



- 1. Adams LA et al., Nonalcoholic fatty liver disease burden: Australia, 2019-2030. JGH 2020
- 2. Charlton MR et al., Frequency and outcomes of liver transplantation for nonalcoholic steatohepatitis in the United States. Gastroenterology 2011
- 3. Byrne CD & Targher G. NAFLD: a multisystem disease. J Hepatol 2015.

High burden of MASLD in Australia



Younossi Z, LA et al. Nature Reviews Gastro Hepatol 2018; 15:11-20

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Prevalence of MASLD in Australia 2015-2030

Model estimates of MASLD burden – Australia, 2015-2030

	Year			
	2015	2020	2025	2030
Country population	23 816 000	25 710 000	27 794 000	29 747 000
Prevalent cases				
MASLD cases	4 915 000 (4 220 000-	5 710 000 (4 879 000-	6 424 000 (5 387 000-	7 026 000 (5 842 000-
	5 605 000)	6 483 000)	7 253 000)	7 890 000)
MASLD prevalence rate (all ages)	20.6% (17.7-23.5%)	22.2% (19.0–25.2%)	23.1% (19.4–26.1%)	23.6% (19.6–26.5%)
F0	4 211 000 (3 541 000-	4 818 000 (4 009 000-	5 337 000 (4 334 000-	5 741 000 (4 557 000-
	4 840 000)	5 515 000)	6 087 000)	6 581 000)
F1	360 000 (244 000-	438 000 (295 000-	513 000 (344 000-	582 000 (389 000-
	509 000)	619 000)	724 000)	812 000)
F2	186 000 (116 000-	238 000 (149 000-	293 000 (184 000-	347 000 (218 000-
	282 000)	361 000)	443 000)	524 000)
F3	105 000 (62 000-153 000	0)140 000 (83 600-204 000)180 000 (108 000-	223 000 (134 000-
			261 000)	322 000)
Compensated cirrhosis	47 900 (28 600-80 200)	67 000 (39 900–111 000)	89 400 (53 200-148 000)	115 000 (68 700–190 000)

Adapted from Adams LA et al., Nonalcoholic fatty liver disease burden: Australia, 2019-2030. JGH 2020

UASTRIE

Burden of MASLD in Australia now and in the future



Prevalent NAFLD Cases

Age Pyramid, NAFLD and Non-NAFLD Population – Australia, 2019 (Thousands)

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Adams LA et al., Nonalcoholic fatty liver disease burden: Australia, 2019-2030. JGH 2020

Rising burden of major adverse liver outcomes related to MASLD in Australia



Adams LA et al., Nonalcoholic fatty liver disease burden: Australia, 2019-2030. JGH 2020

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Prevalence of NAFLD in Regional Victoria: a population-based study



- Prospective, cross-sectional, observational study (CrossRoads II)
- Four towns in the Goulburn valley
- Randomly selected households
- 705 invited adult participants
- Fatty Liver Index (FLI) > 60 used to define NAFLD
- Crude NAFLD prevalence 38.9%
- Age- and sex-standardised prevalence was 35.7%

Numbers of people, by age and sex: 18–29 years (15 men, 22 women), 30–39 years (31 men, 46 women), 40–49 years (30 men, 39 women), 50–59 years (41 men, 81 women), 60–69 years (88 men, 98 women), 70–79 years (83 men, 82 women), and 80–89 years (25 men, 24 women); all ages: 313 men, 392 women.

High prevalence of MAFLD in regional Victoria



Proportion (%) of study participants with MAFLD stratified by age group and gender. MAFLD, metabolicassociated fatty liver disease. Total cohort; **1**, male; **.**, female.

A total of 722 participants were included. Mean age was 59.3 ± 16 years, and 55.3% were women with a median body mass index of 27.8 kg/m2. Most (75.2%) participants were overweight or obese

Prevalence of NAFLD in regional Victoria according to metabolic risk factors

	All participants					
Characteristic	< 60 years	Proportion (95% CI)	≥ 60 years	Proportion (95% CI)		
Participants	305		400			
Participants with NAFLD	102	33% (28–39%)	172	43% (38-48%)		
Body mass index						
< 25 kg/m ²	1/87	1% (0–6%)	3/90	3% (0.7–9%)		
25–29 kg/m ²	22/109	20% (13–29%)	60/167	36% (29–44%)		
≥ 30 kg/m ²	79/109	73% (63–81%)	109/143	76% (68–83%)		
Diabetes						
Yes	16/23	70% (47–87%)	37/64	58% (45–70%)		
No	86/282	30% (25–36%)	135/336	40% (35–46%)		
Hypertension						
Yes	59/128	46% (37–55%)	121/257	47% (41–53%)		
No	42/174	24% (18–31%)	51/142(36% (28–44%)		
Dyslipidaemia						
Yes	73/137	53% (45–62%)	99/174	57% (49–64%)		
No	29/168	17% (12–24%)	73/226	32% (26–39%)		
Metabolic syndrome						
Yes	50/68	74% (61–83%)	92/136	68% (59–75%)		
No	51/230	21% (16–27%)	77/254	30% (25–36%)		
CI = confidence interval. 🔶						

4 Age- and sex-adjusted non-alcoholic fatty liver disease prevalence ratios, by metabolic risk factor

Characteristic	Adjusted prevalence ratio (95% CI)
Body mass index	
< 25 kg/m ²	1
25–29 kg/m ²	12 (4.6–33)
≥ 30 kg/m ²	32 (12–86)
Diabetes	
Yes	1
No	1.6 (1.3–2.0)
Hypertension	
Yes	1
No	1.5 (1.2–1.8)
Dyslipidaemia	
Yes	1
No	2.1 (1.8–2.6)
Metabolic syndrome	
Yes	1
No	2.6 (2.2–3.1)
CI = confidence interval. 🔶	

Roberts SK, et al. Med J Aust 2021; 215:77-82

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Markers of liver disease severity were higher in NAFLD subjects

5 Non-invasive markers of liver disease severity in patients with and without non-alcoholic fatty liver disease (NAFLD)							
	Participants with NAFLD		Participants without NAFLD				
Characteristic	All	Men	Women	All	Men	Women	Р
All participants	274	136	138	431	177	254	
Alanine aminotransferase (U/L), mean (SD)	29 (17)	32 (14)	27 (20)	24 (14)	28 (13)	21 (14)	< 0.001
> 1.5 × upper limit of normal*	48 (18%)	19 (14%)	29 (21%)	44 (10%)	16 (9%)	28 (11%)	0.006
Aspartate aminotransferase (U/L), mean (SD)	26 (9)	28 (7)	25 (10)	26 (9)	28 (9)	24 (9)	0.68
Median liver stiffness measurement (kPa), mean (SD)	6.5 (5.6)	6.1 (4.8)	6.9 (6.3)	5.3 (2.0)	5.7 (2.3)	4.9 (1.7)	0.005
< 7 kPa	114/143 (80%)	60/74 (81%)	54/69 (78%)	197/232 (85%)	85/104 (82%)	112/1228 (88%)	0.21
≥ 8 kPa	18/143 (13%)	9/74 (12%)	9/69 (13%)	21/232 (9%)	12/104 (12%)	9/128 (7%)	0.30
Controlled attenuation parameter dB/m), mean (SD)	305 (63)	323 (52)	282 <mark>(</mark> 69)	256 (52)	263 (65)	250 (42)	0.001
Participants with valid measurements	22	13	9	47	25	22	

Roberts SK, et al. Med J Aust 2021; 215 (2): 77-82c

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Change in Prevalence of NAFLD in regional Victoria 2003-2018



, NAFLD male standardized; ___, NAFLD female s ___, NAFLD male crude; ___, NAFLD female crude.



Vaz K, et al. JGH 2023; 38(10):1823-1831

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Change in Prevalence of Metabolic Risk Factors and Lifestyle Factors 2003-2018



CrossRoads 1; CrossRoads 2



Vaz K, et al. JGH 2023; 38(10):1823-1831

Steatotic liver disease in regional Victoria according to the NAFLD and newer diagnostic criteria

2 Crude and age- and gender-standardised prevalence (with 95% confidence intervals) of steatotic liver disease among participants in the two CrossRoads studies, by diagnosis

Characteristic	Non-alcoholic fatty liver disease (NAFLD)	Metabolic dysfunction-associated fatty liver disease (MAFLD)	Metabolic dysfunction-associated steatotic liver disease (MASLD)
Participants meeting diagnosis			
CrossRoads I	340/1040	419/1040	360/1040
CrossRoads II	272/704	338/721	275/704
Crude prevalence			
CrossRoads I	32.7% (29.8-35.6%)	40.3% (37.3-43.3%)	34.6% (31.7–37.6%)
CrossRoads II	38.6% (35.0-42.3%)	46.9% (43.2-50.6%)	39.1% (35.4-42.8%)
Difference	5.9 percentage points (5.7–6.1 percentage points)	6.6 percentage points (4.4–8.8 percentage points)	4.5 percentage points (2.3–6.9 percentage points)
Standardised prevalence			
CrossRoads I	32.0% (28.9–35.2%)	38.5% (35.2-41.7%)	33.6% (30.4–36.7%)
CrossRoads II	34.7% (30.2-39.1%)	42.6% (38.1-47.2%)	35.0% (30.5–39.5%)
Difference	2.7 percentage points (–2.9% to 8.2 percentage points)	4.1 percentage points (-1.4 to 9.8 percentage points)	1.4 percentage points (–4.1% to 6.9 percentage points)

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Prevalence of MAFLD in the AusDiab cohort: population based study in 2012



Figure 1. Frequency of mafld, alt elevation, obesity and the metabolic syndrome by age groups.

- Large, prospective, observational cohort study (AusDiab)
- 4747 adults returning third survey in 2012
- MAFLD defined by FLI > 60 and standard metabolic criteria
 - Crude MAFLD prevalence 37.0%
- MAFLD associated with:
 - Sedentary lifestyle
 - Less likely tertiary education

Farrell AM, et al. Scientific Reports 2022; 12:1956

Prevalence of, and associations with MASLD among community dwelling older adults: the ASPREE study

- 9097 Australian participants aged ≥70 years in ASPREE study with sufficient data to identify MASL via FLI ٠
- 33.0% had prevalent MASLD with the prevalence decreasing with increasing age (adjusted RR [aRR] 0.96, 95% CI: 0.96–0.97) ۲
- MASLD associated with poorer metabolic health, frailty and social disadvantage



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Clayton-Chubb D, et al. Liver Int. 2024; 44(1):39-51.

High prevalence of diabetes among young First Nations Peoples hospitalised in QLD with MASLD: a population-based study



- Compared to non-Indigenous Australians
 First Nations patients were:
 - younger
 - lived in remote and socioeconomic disadvantaged areas, and had
 - higher comorbidity
 - diabetes was overrepresented (43.5% vs 30.8%, P<0.001, respectively)
- Rates of progression within 10 years to liver decompensation were similar
- On MVA, no association with indigenous status with progression to decompensation and survival

UASIRO

MAFLD but not MASLD increase the risk of All-Cause Mortality in Regional Victoria

Multivariable Cox proportional hazard regression analysis of overall mortality for MASLD and MAFLD

Model	MASLD HR	95% confidence interval	MAFLD HR	95% confidence interval
Univariate	1.25	0.98-1.61	1.40	1.12-1.76
Model 1	1.27	0.98-1.63	1.36	1.08-1.72
Model 2	1.26	0.98-1.63	1.37	1.08-1.73
Model 3	1.33	0.98-1.81	1.34	1.00-1.78
Model 4	1.17	0.84-1.63	1.18	0.87-1.60
Model 5			1.35	1.07-1.71
Model 6			1.35	1.07-1.71
Model 7			1.28	0.96-1.71
Model 8			1.14	0.84-1.54

Data presented as hazard ratio (HR) of main effect (fatty liver disease)

MASLD = metabolic-(dysfunction) associated steatotic liver disease; MAFLD = metabolic-(dysfunction) associated fatty liver disease

Model 1 = fatty liver disease + age, gender

Model 2 = Model 1 + rurality, ethnic background, education, insurance

Model 3 = Model 2 + smoking status, physical activity per week, takeaway food consumption, healthy diet

Model 4 = Model 3 + hypertension, type 2 diabetes mellitus, dyslipidaemia

Model 5 = Model 1 + excessive alcohol consumption, viral hepatitis

Model 6 = Model 5 + rurality, ethnic background, education, insurance

Model 7 = Model 6 + smoking status, physical activity per week, takeaway food consumption, healthy diet

Model 8 = Model 7 + hypertension, type 2 diabetes mellitus, dyslipidaemia

Overall survival according to cumulative metabolic risk factors in A. MASLD and B. MAFLD



10

No MAFLD

MAFLD with 2 criteria

analysis time

0.50

0.25

MetS RF = metabolic syndrome risk factors (1 point for each of hypertension, dyslipidaemia, type 2 diabetes mellitus and overweight/obesity). Criteria = number of metabolic diagnostic criteria met for MAFLD diagnosis (1 point each for overweight/obesity, type 2 diabetes mellitus and metabolic dysfunction)

Vaz K, et al. Hep Int. 2024 (under 2nd review)

p<0.001

20

15

MAFLD with 1 criteria MAFLD with 3 criteria

NAFLD/MASLD and MAFLD increase the risk of Major Cardiovascular Events

Hepatology International (2024) 18:1135–1143 https://doi.org/10.1007/s12072-024-10706-1

ORIGINAL ARTICLE

NAFLD and MAFLD independently increase the risk of major adverse cardiovascular events (MACE): a 20-year longitudinal follow-up study from regional Australia

Karl Vaz^{1,2} · William Kemp^{1,2} · Ammar Majeed^{1,2} · John Lubel^{1,2} · Dianna J. Magliano³ · Kristen M. Glenister⁴ · Lisa Bourke⁴ · David Simmons^{4,5} · Stuart K. Roberts^{1,2}

Table 2 Cox proportional hazards regression evaluating association between fatty liver disease and 3-point major adverse cardiovascular events (MACE)

	NAFLD	MAFLD
Univariate	1.70 (1.26-2.30)	1.76 (1.33-2.34
Model 1	1.59 (1.16-2.17)	1.57 (1.17-2.10
Model 2	1.67 (1.21-2.30)	1.64 (1.22-2.21
Model 3	1.56 (1.12-2.19)	1.51 (1.11-2.06

Data presented as sub-hazard ratios (sHR) with 95% confidence intervals

NAFLD non-alcoholic fatty liver disease, MAFLD metabolic-(dysfunction) associated fatty liver disease

Model 1 = fatty liver disease, age, gender and education

Model 2=Model 1+smoking status and diet adequacy

Model 3=Model 2+baseline MACE, type 2 diabetes mellitus, hypertension and dyslipidaemia
 Table 4
 Incident non-fatal cardiovascular events in fatty liver disease participants without prevalent major adverse cardiovascular events at baseline

	NAFLD $(n=413)$	MAFLD (n=519)
Myocardial infarction	4.87 (3.57-6.63)	5.11 (3.84-6.79)
Cerebrovascular accident	2.75 (1.83-4.14)	2.67 (1.81-3.96)
Congestive cardiac failure	6.87 (5.28-8.92)	5.21 (3.93-6.92)
Unstable angina	2.30 (1.37-3.60)	2.16 (1.40-3.35)

Data presented as incidence rate per 1000 person-years (95% confidence interval)

NAFLD non-alcoholic fatty liver disease, MAFLD metabolic-(dysfunction) associated fatty liver disease



- In Australia, there is a high prevalence of both MASLD and MAFLD at around 30-35% and 40% respectively
- There has been a significant increase in the prevalence of MASLD over the past 15 years, particularly among women, that is expected to continue over the next decade
- The trend increase in the prevalence of MASLD is in the setting of a significant increase in the prevalence of obesity over the same period
- There is a high prevalence of MASLD among those with metabolic risk factors including T2DM, hypertension, dyslipidaemia and the metabolic syndrome
- MASLD and MAFLD are associated with an increased risk of major CV events and in the case of MAFLD, reduced overall survival