AUSTRALASIAN METABOLIC HEALTH SOCIETY

POSITION STATEMENT

Assessment of Insulin Resistance/Hyperinsulinaemia in Clinical Practice

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Purpose and Scope

This position statement provides Australian and New Zealand healthcare practitioners (HCP) with evidence-based guidance on the detection and quantification of insulin resistance (IR) and hyperinsulinaemia (HI) across the clinical spectrum. It addresses the practical limitations of laboratory reference ranges and offers clinically actionable thresholds for use in primary care.

This statement does not replace clinical judgement. Patient acceptability, cost, accessibility, and reproducibility over time must be considered when selecting tests. Funding for tests differs between Australia and New Zealand; these differences are noted throughout where clinically relevant.

Conceptual Framework

Insulin resistance (IR) and hyperinsulinaemia (HI) are related but distinct phenomena and should **not** be used interchangeably. IR refers to reduced tissue sensitivity to insulin's metabolic effects; HI refers to elevated circulating insulin levels, typically as a compensatory response. Both exist on a spectrum from subclinical dysfunction to severe end organ disease, and both can be present simultaneously or independently. Many of the measures used to detect IR and HI are surrogate markers, results vary by assay methodology, and in longitudinal monitoring should use consistent platforms where possible. Finally, IR and HI vary through the lifespan with physiological insulin resistance occurring during puberty and pregnancy, and thresholds established in adult populations require careful interpretation in children and adolescents.

AMHS Positions at a Glance

The following statements represent the core positions of AMHS on IR/HI assessment in primary care. Supporting evidence and clinical detail for each position are provided in the numbered sections below.

1. IR should be actively sought in primary care. Insulin resistance is the upstream driver of type 2 diabetes, cardiovascular disease, MASLD, CKD, PMOS (formerly PCOS), and related conditions. Early identification, before irreversible organ damage, is where general practice has its greatest impact.
2. Hyperinsulinaemia precedes hyperglycaemia by years to decades. While compensatory HI initially maintains normoglycaemia, its persistence becomes pathological driving oxidative stress, inflammation, vascular dysfunction and fibrosis, and emerging as an independent contributor to kidney and cardiovascular injury beyond its role in glucose regulation. Glucose-based measures alone (HbA1c, fasting glucose) miss this earliest and most reversible stage. A complete metabolic assessment requires lipid-based and, where indicated, insulin-based markers alongside glucose.

3. Standard laboratory reference ranges are insufficient. Population-derived reference intervals reflect a progressively metabolically unwell population. AMHS recommends applying evidence-based clinical thresholds, detailed in this document, rather than deferring to laboratory normals.

4. Waist-to-height ratio (WHtR ≥ 0.5) is the recommended first-line anthropometric screen. It is ethnicity-neutral, requires no equipment beyond a tape measure, and outperforms BMI for identifying IR risk.

5. The TG/HDL ratio should be calculated from every fasting lipid panel. It requires no insulin assay, is funded in both Australia and New Zealand, and is AMHS's preferred first-line biochemical surrogate marker of IR.

6. HbA1c ≥ 5.7% (≥ 39 mmol/mol) should trigger proactive clinical action. This threshold, lower than the Australian and New Zealand prediabetes diagnostic threshold, marks the point at which cardiovascular and metabolic risk begins to rise. Waiting for 6.0% to intervene is waiting too long.

7. Fasting insulin and HOMA-IR have an important but selective role. AMHS does not recommend indiscriminate fasting insulin measurement. A clinical triage framework (Section 4) defines when insulin testing is not required, when it may assist with monitoring, and when it will directly change management.

8. ALT thresholds should replace laboratory upper limits of normal. Men: > 30 U/L; Women: > 19 U/L. Normal transaminases do not exclude significant hepatic IR or fibrosis. FIB-4 should be calculated every 1–2 years in patients with any metabolic risk factors.

9. Annual Urine ACR and eGFR are indicated in all patients with IR risk factors. Early albuminuria is the first detectable renal consequence of IR and an independent cardiovascular risk marker. It will be missed without active testing.

10. Therapeutic carbohydrate reduction and lifestyle modification are the foundation of IR management. Pharmacotherapy is an adjunct where lifestyle intervention alone is insufficient, not a substitute for it.

Why Insulin Resistance and Hyperinsulinaemia Matter in General Practice

Insulin resistance and hyperinsulinaemia are not single diseases. They are upstream metabolic disturbances that reveal themselves across multiple organ systems and underlie many of the most common conditions encountered in primary care. These conditions include but are not limited to:

- Type 2 diabetes
- Hypertension
- Chronic kidney disease[1]
- Obesity
- Metabolic dysfunction-associated steatotic liver disease (MASLD / fatty liver)
- Polyendocrine Metabolic Ovarian Syndrome (PMOS; formerly known as polycystic ovary syndrome, PCOS)[2]
- Sleep apnoea
- Cardiovascular disease
- Stroke
- Atherogenic dyslipidaemia (hypertriglyceridaemia and low HDL)
- Chronic low-grade inflammation[3]
- Cognitive decline and dementia[4]
- Serious mental illness (schizophrenia, bipolar disorder): IR is elevated independent of medication effects, and cardiovascular mortality in this population is driven largely by undertreated metabolic dysfunction[5,6]
- Malignancy: IR/HI is independently associated with increased cancer mortality and tumour progression, particularly colorectal, pancreatic, and endometrial cancers[7]

Recognising IR/HI as upstream drivers of these conditions reframes the HCP role from managing individual diagnoses in isolation to identifying and treating a common underlying pathophysiology. Early detection and intervention, before irreversible organ damage occurs, is where HCPs can have greatest impact.

Pre-analytical reminders:

- Fasting insulin, glucose and lipids: fast 10–14 hours
- No vigorous exercise 48 hours prior (affects ALT, AST, and UACR)
- First morning urine for UACR; confirm abnormal result on a second sample
- Stop creatine supplementation one week prior to serum creatinine / eGFR

Quick Reference: IR/HI Assessment in Primary Care

Assessment	Finding / threshold	Action
ROUTINE AT EVERY METABOLIC REVIEW		
Waist circumference	≥ 94 cm (M) / ≥ 80 cm (F) Caucasian; ≥ 90 cm (M) / ≥ 80 cm (F) Asian/Pacific/Māori	Measure and document
Waist-to-height ratio	≥ 0.5 = increased risk; ≥ 0.6 = high risk	Calculate and document
Blood pressure	130–139/85–89 mmHg with adiposity	Assess for IR/HI
OPPORTUNISTIC FINDINGS, NOTE IF PRESENT		
Acanthosis nigricans or skin tags	Neck, axillae, groin	Marker of hyperinsulinaemia, investigate
FIRST-LINE INVESTIGATIONS		
TG/HDL ratio	≥ 1.0	IR and CVD risk marker
Fasting glucose	≥ 5.6 mmol/L	Warrants further assessment
Fasting insulin / HOMA-IR	> 1.0 warrants attention; > 2.0 significant; > 3.0 severe	Before testing apply triage framework (Section 4). Not funded in NZ. Advise lifestyle, TCR, exercise.
Fasting insulin	> 10 µU/mL	Hyperinsulinaemia confirmed, intervene. A normal result does not exclude IR.
HbA1c	≥ 5.7 (≥ 39 mmol/mol)	Proactive lifestyle intervention including TCR.
ALT / AST	ALT > 30 U/L (M); > 19 U/L (F)	No exercise 48 hours prior; check CK if AST disproportionate
Serum urate	> 0.42 mmol/L (M); > 0.36 mmol/L (F)	Marker of hyperinsulinaemia in metabolic context
Urine ACR	≥ 3 mg/mmol	Annual minimum with IR risk factors
eGFR	< 60 mL/min/1.73m²	Interpret alongside Urine ACR
SECOND-LINE INVESTIGATIONS		
FIB-4	< 1.3 low; 1.3–2.67 indeterminate; > 2.67 refer	Every 1–2 years with any metabolic risk factors. Normal LFTs do not exclude fibrosis.
Cystatin C	if suspect eGFR is falsely low, for example, in the setting of high skeletal muscle mass	More accurate GFR estimate

A Practical Guide: Identifying Insulin Resistance and Hyperinsulinaemia in Clinical Practice

1. History in Insulin Resistance Assessment

A focused history can identify IR risk before any investigation is ordered.

Symptoms

- Inability to skip meals or marked symptoms when fasting beyond 4 hours, is suggestive of impaired metabolic flexibility, typically driven by hyperinsulinaemia.[8]
- Snoring, unrefreshing sleep, or daytime sleepiness. Where present, formal OSA screening is recommended. OSA is an independent driver of IR and frequently undiagnosed.
- Acne, hirsutism, or menstrual irregularity in women, consider PMOS.

Relevant past history

- GDM, PMOS, gout, prediabetes or T2DM, MASLD, CKD, CVD, sleep apnoea, family history of T2DM

Medications that drive or worsen IR

- Corticosteroids, antipsychotics, mirtazapine, statins, beta blockers, thiazide diuretics combined OCP (particularly levonorgestrel or norethisterone, most relevant in women with PMOS or existing IR risk), depot progesterone, tacrolimus.[9]

2. Physical Examination in Insulin Resistance

Waist-to-Height Ratio (WHtR)

WHtR = Waist circumference (cm) ÷ Height (cm)

The threshold ≥ 0.5 ('keep your waist to less than half your height') is a robust, ethnicity-neutral marker of central adiposity and cardiometabolic risk. It outperforms BMI for identifying IR and is valid across Asian, South Asian, Pacific Islander, Māori, and Caucasian populations without ethnicity-specific adjustment.

- WHtR 0.5–0.59: Increased risk, lifestyle and dietary intervention indicated
- WHtR ≥ 0.6: High risk, intensive metabolic intervention warranted[10]

Blood Pressure

Even before formal hypertension is diagnosed, blood pressure patterns can signal IR:

- High-normal BP (130–139/85–89 mmHg) with central adiposity indicates hyperinsulinaemia-driven sympathetic activation. Assess for IR; do not simply monitor.
- Loss of nocturnal dipping on 24-hour ABPM is strongly associated with IR and MetS.
- BP target in patients with established CKM risk factors is < 130/80 mmHg.[11]

Opportunistic Findings

- Acanthosis nigricans: Velvety hyperpigmentation in body folds (neck, axillae, groin, under breasts). A dermatological marker of hyperinsulinaemia. More common in darker skin tones. Further IR/HI investigation warranted when present with central adiposity.
- Skin tags: Multiple acrochordons at neck and axillae correlate with IR, a useful opportunistic finding.

- Hepatomegaly: Palpable or enlarged liver with metabolic risk factors suggests MASLD. Order ALT and FIB-4.
- Neck size enlarged, > 40 cm, apply STOP-Bang screening.

3. Lipid-Based Surrogate Markers of IR: TG/HDL Ratio

TG/HDL Ratio

The fasting TG/HDL ratio is a valuable marker of IR. It correlates strongly with small dense LDL particle predominance and is an independent predictor of cardiovascular risk.[12]

- Suggested threshold (Australian and NZ units): TG/HDL ≥ 1.0 mmol/L, warrants further assessment for IR.[13]
- Reduced sensitivity in East Asian populations.

For routine primary care: calculate TG/HDL from every fasting lipid panel. Reserve HOMA-IR for cases where quantifying hyperinsulinaemia directly is clinically necessary.[14]

Further detail on atherogenic dyslipidaemia is addressed in the AMHS Position Statement on Lipids and Cardiovascular Risk (refer to separate document).

4. Fasting Insulin and HOMA-IR (Homeostasis Model Assessment of Insulin Resistance)

Background and Guideline Context

Current international guidelines do not recommend routine clinical measurement of insulin resistance using fasting insulin or HOMA-IR. The 2023 International Evidence-based PCOS Guideline[15] states explicitly that routinely available measures of insulin resistance are inaccurate and clinical measurement is not currently recommended. The American Association for Diagnostic Laboratory Medicine similarly recommends HOMA-IR be reserved for research purposes only.[16]

AMHS acknowledges this position but regards it as an evidence-practice gap. The metabolic consequences of undetected IR are sufficiently serious, and the available surrogate tools sufficiently practical, to justify a more proactive clinical approach than current guidelines endorse, particularly in the primary care setting where early identification and intervention are most impactful. AMHS therefore recommends the following framework, while fully acknowledging the limitations of each measure and recognising that clinicians must exercise judgement about when quantification will genuinely change management.

Calculation

HOMA-IR = (fasting glucose [mmol/L] × fasting insulin [µU/mL]) ÷ 22.5[17]

The normalising constant 22.5 is derived from the product of standardised physiological fasting values: a glucose value of 4.5 mmol/L × an insulin value of 5 µU/mL.

Unit note: Laboratories in Australia and New Zealand typically report insulin in pmol/L and convert to µU/mL for clinical reporting, using a conversion factor of either 6.0 or 6.75 depending on the platform. This introduces a potential discrepancy of up to 12.5% between results from different laboratories. If changing laboratories, check whether the new lab uses a different conversion factor as this can affect results.

HOMA-IR Reference Thresholds

- HOMA-IR > 1.0: Warrants clinical attention, cardiovascular and metabolic risk begins to increase from this threshold
- HOMA-IR > 1.4: Early IR, consider lifestyle intervention and monitoring
- HOMA-IR > 1.8: Moderate IR, associated with emerging metabolic syndrome
- HOMA-IR > 2.0: Significant IR, active intervention indicated in most patients
- HOMA-IR > 3.0: Severe IR, intensive intervention warranted; consider pharmacotherapy alongside lifestyle where lifestyle alone is insufficient

These thresholds are population-derived and should be interpreted alongside clinical findings, ethnicity, age, and trajectory over time.

- A low fasting insulin cannot be taken as confirmation of insulin sensitivity;[18] however, an elevated fasting insulin is a reliable indicator of insulin resistance.[14] There are no evidence based cutoffs due to the limitations discussed below. AMHS take the position that levels > 10 µU/mL indicate early IR warranting lifestyle intervention and monitoring.

Limitations of Fasting Insulin Measurement

AMHS acknowledges the following limitations, which are substantive and should inform clinical decision-making:

- Biological variability: Basal insulin secretion is pulsatile, with oscillations occurring approximately every 5–15 minutes. Three samples taken at 5-minute intervals from the same individual can yield markedly different results. This is compounded by insulin's short half-life of approximately 5 minutes and the physiological stress response to venepuncture itself.[19]
- First-pass hepatic extraction: The proportion of insulin removed by the liver before reaching peripheral venous blood varies between individuals. Peripheral venous insulin levels may therefore not accurately reflect portal insulin concentrations relevant to hepatic insulin resistance.
- Assay variability: Insulin immunoassays are not standardised across platforms. Results from different laboratories are not directly comparable, and assay precision is typically ±10%.
- Pre-analytical sensitivity: Insulin degrades rapidly in collected samples, particularly in the presence of even minor haemolysis. Delay in sample processing can significantly reduce measured levels.
- What HOMA-IR does and does not measure: HOMA-IR is validated against the hyperinsulinemic euglycemic clamp, which primarily measures glucose disposal rate in skeletal muscle and adipose tissue. In patients with established T2DM and beta-cell dysfunction, HOMA-IR may underestimate true IR because inappropriately low insulin levels reduce the calculated value regardless of tissue sensitivity. Furthermore, emerging evidence suggests that therapeutic carbohydrate reduction can resolve fasting hyperinsulinaemia without fully resolving underlying tissue IR, meaning HOMA-IR may normalise before IR itself is resolved.[14,20]

When to Measure Fasting Insulin, A Clinical Triage Framework

Given these limitations and the current guideline position, AMHS does not recommend indiscriminate fasting insulin measurement. In many patients, IR can be confirmed or strongly presumed on clinical and biochemical grounds without insulin testing. The framework below, adapted from Crofts,[21] provides a practical triage approach:

IR confirmed clinically; insulin testing not required:

- HbA1c > 40 mmol/mol (6.0%)
- PMOS (IR is a common defining feature)
- Type 1 diabetes requiring ≥ 1 unit/kg/day and/or using metformin
- Long-term oral corticosteroid use
- Long-term clozapine or olanzapine use
- Diabetic retinopathy in the presence of normoglycaemia (includes patients in glycaemic remission whose current HbA1c does not reflect prior metabolic disease)

IR should be presumed; testing may assist with monitoring and treatment decisions:

- Primary hypertension
- History of ≥ 2 GDM pregnancies
- Hypertriglyceridaemia
- Hyperuricaemia and/or gout
- WHtR > 0.5
- BMI > 35 kg/m² (or > 30 kg/m² if Indo-Asian and not an athlete)
- Obstructive sleep apnoea requiring CPAP
- First-degree relative with T2DM diagnosed before age 40
- Post renal transplant
- Chronic hepatitis C
- Long-term antipsychotic use (other than clozapine or olanzapine)

Fasting insulin testing recommended, result will guide management:

- Acanthosis nigricans or multiple skin tags
- Statin use, high-dose niacin, or combined oral contraceptive use
- BMI 25–35 kg/m² (or 23–30 kg/m² if Indo-Asian and not an athlete)
- Rapid or unexplained weight gain
- Unable to skip meals or becomes markedly symptomatic when fasting > 4 hours
- 10 years before recommended age for diabetes screening in high-risk individuals
- Post organ transplant (other than renal)
- Borderline metabolic markers where a baseline measurement would demonstrate response to dietary intervention
- Diagnostic uncertainty where a quantified IR index would resolve the management question
- PMOS where quantification would guide a specific treatment decision (e.g. whether to initiate metformin in a lean patient)

In the first two categories, TG/HDL ratio provides adequate monitoring of IR trajectory without an insulin assay. In New Zealand where fasting insulin is not publicly funded, TG/HDL is the preferred surrogate across all categories unless a specific management decision requires insulin quantification.

Paediatric assessment: In children and adolescents, HOMA-IR is preferred as the primary IR surrogate because normative paediatric data are more extensively available for HOMA-IR. Physiological IR occurs during puberty and should be factored into interpretation.[22]

Practical Considerations

- Always use the same laboratory and assay platform for longitudinal monitoring. If changing laboratories, check whether the new lab uses a different conversion factor (6.0 or 6.75) as this can affect results.
- Ensure the patient has fasted for 10–14 hours prior to blood draw (water permitted). Fasting insulin requires a minimum of 10 hours, longer than standard fasting bloods, as it is more sensitive to recent food intake. Do not exceed 14 hours.
- Avoid vigorous exercise for 48 hours prior to sampling.
- A single HOMA-IR result should be interpreted cautiously given biological variability; a trend across two or three measurements over time is more clinically meaningful than any single value.
- Ethnic limitations: HOMA-IR has reduced predictive accuracy in people of African, Afro-Caribbean, and South Asian descent. In these populations, TG/HDL ratio is the preferred surrogate, as it does not rely on insulin measurement and performs more consistently across ethnicities.
- Funding note: Fasting insulin is Medicare-rebatable in Australia. In New Zealand, fasting insulin is not publicly funded and attracts an out-of-pocket cost of approximately NZ$50. In NZ patients where cost is a barrier, TG/HDL ratio provides a funded surrogate marker without requiring an insulin assay.

5. HbA1c

HbA1c reflects average blood glucose over approximately 3 months and is widely used for diabetes screening. However, international thresholds for prediabetes differ, and the Australian and New Zealand threshold of 6.0% is among the highest:

- Australia / New Zealand / UK: Prediabetes defined as HbA1c 6.0–6.4% (42–46 mmol/mol)[23]
- USA / South Africa / Singapore: Prediabetes defined from HbA1c 5.7% (39 mmol/mol)

The ARIC cohort demonstrated that risk of myocardial infarction, stroke, all-cause death, and incident diabetes increases exponentially from an HbA1c of 5.6% (38 mmol/mol) in individuals without diagnosed diabetes.[24] AMHS therefore recommends that a HbA1c ≥ 5.7% should trigger proactive lifestyle and dietary review, irrespective of whether it meets formal Australian or New Zealand diagnostic criteria for prediabetes.

PBS Access for HbA1c Screening (Australia)

HbA1c may be requested for screening on the PBS every 12 months in patients at high risk of T2DM, including:

- Age ≥ 40 years with BMI > 25 kg/m²
- First-degree relative with diabetes
- Prior cardiovascular event
- South Asian, Pacific Islander, or Aboriginal and Torres Strait Islander ethnicity
- Prior gestational diabetes mellitus
- Polyendocrine Metabolic Ovarian Syndrome (PMOS)
- Current antipsychotic medication use

PBS eligibility criteria are subject to periodic review. Verify current criteria at racgp.org.au. Reference: RACGP. Management of type 2 diabetes: A handbook for general practice. Melbourne: RACGP; 2024.[23]

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6. Hepatic Insulin Resistance (MASLD / Fatty Liver)

Hepatic steatosis is the hepatic expression of IR. The preferred current nomenclature, as per international multisociety consensus (2023), is:

- MASLD (Metabolic dysfunction-Associated Steatotic Liver Disease), replaces NAFLD)[25]
- MASH (Metabolic dysfunction-Associated SteatoHepatitis), replaces NASH

MASLD requires hepatic steatosis plus at least one cardiometabolic risk factor (overweight/obesity, T2DM, hypertension, hypertriglyceridaemia, or low HDL).

ALT Thresholds

Laboratory upper limits of normal for ALT overestimate the threshold for hepatic steatosis. Evidence-based sex-specific thresholds associated with MASH are:

- Men: ALT > 30 U/L[26,27]
- Women: ALT > 19 U/L

AMHS recommends applying these thresholds in clinical practice. Where transaminase elevation is unexplained or not improving with metabolic intervention, the differential diagnosis should be reconsidered, including recent vigorous exercise, autoimmune hepatitis, haemochromatosis, thyroid disease, coeliac disease, alcohol use, and medications.

Radiological evidence of hepatic or pancreatic steatosis on incidental imaging is a clinically significant finding and should be documented and acted upon as a marker of visceral adiposity and IR.[26]

FIB-4 Score

FIB-4 index should be calculated every 1–2 years in patients with any metabolic risk factors, regardless of transaminase levels. MASLD can progress to significant fibrosis and cirrhosis with persistently normal ALT and AST, transaminases reflect hepatic inflammation, not fibrosis stage. Normal LFTs do not exclude advanced fibrotic disease.[27]

FIB-4 = (age [years] × AST [U/L]) ÷ (platelet count [10^9/L] × √ALT [U/L])

FIB-4 is available as a direct-access test through any pathology laboratory and attracts a Medicare rebate.[23]

- FIB-4 < 1.3: Low fibrosis risk (use < 2.0 if age > 65)
- FIB-4 1.3–2.67: Indeterminate, refer for FibroScan
- FIB-4 > 2.67: High fibrosis risk, refer to hepatology

Pre-analytical caution, exercise and transaminases: ALT and AST are present in skeletal muscle. Vigorous exercise can elevate both within 24–72 hours of activity. Patients should be instructed to avoid strenuous exercise for at least 48 hours prior to liver function testing. An unexplained isolated AST elevation with normal ALT and GGT should raise suspicion of muscle rather than hepatic origin, measuring CK will help differentiate.

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7. Kidney Assessment in IR: MA-CKD and UACR

Chronic kidney disease in primary care is predominantly metabolic in origin. AMHS uses the term metabolic dysfunction-associated CKD (MA-CKD) to encourage clinicians to look upstream to the metabolic driver rather than managing CKD in isolation.

The relationship between IR and CKD is bidirectional. IR damages the kidney, and CKD amplifies IR through chronic inflammation and impaired insulin signalling, measurable from early stages. A patient with an eGFR of 40 ml/min/1.73 m^2 has significant IR driven in part by their kidney disease, regardless of glucose levels. As kidney function declines, insulin clearance is also impaired, removing approximately 40% less circulating insulin and further worsening hyperinsulinaemia.[28]

Early albuminuria reflects systemic endothelial dysfunction and is an independent cardiovascular risk marker, its presence signals vascular injury well beyond the kidney. Persistent albuminuria also predicts faster CKD progression. Reducing albuminuria through metabolic intervention is a treatment target in its own right. Without measuring UACR, this is entirely invisible.[28]

Clinical implication: A patient with eGFR 78, waist 108 cm, UACR 20 mg/mmol, TG/HDL 1.5, and HbA1c 5.8%, no diabetes, no hypertension, has MA-CKD. Without UACR it would be missed.

AMHS recommends annual UACR and eGFR in all patients with any metabolic risk factors. Therapeutic carbohydrate reduction should be considered primary treatment alongside evidence-based pharmacotherapy where indicated.

Urine ACR: First morning void preferred. Confirm abnormal results on a second sample — transient albuminuria occurs with fever, exercise, UTI, and menstruation.[29]

UACR (mg/mmol)	Clinical significance	Action
< 3	Normal	
3–29	Moderately increased	Metabolic intervention and monitoring
≥ 30 (confirmed on second sample)	Severely increased	Nephrology referral

eGFR: Below 60 mL/min/1.73m² is CKD with or without albuminuria. eGFR 60-89 without albuminuria is not CKD - it warrants monitoring with UACR. It is the albuminuria, not the eGFR alone, that unmasks early metabolic kidney disease.[29]

Don't be misled by a low eGFR in muscular or active patients: High muscle mass and creatine supplementation both elevate creatinine, producing a falsely low eGFR. If suspected, request cystatin C — not Medicare-rebatable in Australia (approx. $60); funded by Health New Zealand with documented clinical indication. Stop creatine at least one week before testing.

Suggested Clinical Approach

Step 1. Physical examination

- Measure waist circumference and calculate WHtR
- Record blood pressure
- Note acanthosis nigricans, skin tags, neck size > 40 cm

Step 2. Investigations

- Fasting lipids (calculate TG/HDL ratio), fasting glucose, HbA1c, serum urate, ALT, UACR + eGFR. Calculate FIB-4 in patients with any metabolic risk factors.
- Where central adiposity, hypertension, or other IR risk factors are present, consider adding fasting insulin and calculate HOMA-IR. Apply the triage framework (Section 4) to guide interpretation.

Step 3. Interpret results

- Using AMHS thresholds, not standard laboratory reference intervals

Step 4. Document trajectory

- Repeat testing at 3-6 monthly intervals during active intervention: 12-monthly for monitoring

Step 5. Check for Metabolic Syndrome if multiple findings are positive

Metabolic Syndrome

Metabolic Syndrome represents established, multi-system IR. Its presence confirms the diagnosis and escalates the urgency of intervention. Diagnosis requires any three of the following five criteria: central adiposity, elevated triglycerides, low HDL, elevated blood pressure, or elevated fasting glucose.[30]

Importantly, any single criterion is sufficient to prompt further metabolic assessment. By the time full Metabolic Syndrome criteria are met, the early intervention window has already passed. The goal of this framework is to identify IR before that point.

Criterion	Threshold	Notes
Central adiposity	Waist ≥ 94 cm (M) or ≥ 80 cm (F) — Caucasian; Waist ≥ 90 cm (M) or ≥ 80 cm (F) — Asian/South Asian	Use ethnicity-specific cutoffs.
Triglycerides	≥ 1.7 mmol/L (or lipid-lowering Rx)	fast 12-14 hours prior
HDL cholesterol	< 1.03 mmol/L (M) or < 1.29 mmol/L (F) (or Rx)	
Blood pressure	≥ 130/85 mmHg (or antihypertensive Rx)	
Fasting glucose	> 5.5 mmol/L (or previously diagnosed T2DM)	

Step 6. Intervene

- Therapeutic carbohydrate reduction and lifestyle modification, including resistance training, sleep optimisation and circadian alignment, are first-line. Pharmacotherapy is an adjunct where lifestyle alone is insufficient.

Conclusion

Insulin resistance and hyperinsulinaemia are not rare or complex conditions. They are present in most patients presenting to general practice with cardiometabolic disease, and they are detectable with tools already available in primary care. A tape measure, a blood pressure cuff, and a standard fasting blood panel are all that is needed. No specialist referral, no new technology, no additional cost.

The evidence is clear that early identification and intervention changes outcomes, before irreversible organ damage, before the diagnostic labels accumulate, before the window for reversal closes. Effective treatment options include therapeutic carbohydrate reduction, lifestyle modification, and where necessary, pharmacotherapy is effective. That window is open longest in general practice.

We are living through a metabolic health crisis. HCP, and in particular general practitioners who see these patients most often, are uniquely placed to reframe this for their patients. Central obesity, a raised ALT, and a TG/HDL above 1.0 are evidence of metabolic dysfunction that deserves a conversation, not a filed result. Patients deserve to know what is happening in their body.

AMHS encourages clinicians to apply this framework routinely and treat a rising TG/HDL, a waist above threshold, or a fasting insulin above 10 as the early warning it is. These are not normal findings in an unwell population.

References

1. Spoto B, Pisano A, Zoccali C. Insulin resistance in chronic kidney disease: a systematic review. *Am J Physiol Renal Physiol*. Dec 1 2016;311(6):1087–1108. doi:10.1152/ajprenal.00340.2016
2. Teede HJ, Khomami MB, Morman R, et al. Polyendocrine metabolic ovarian syndrome, the new name for polycystic ovary syndrome: a multistep global consensus process. *The Lancet*. 2026;doi:10.1016/S0140-6736(26)00717-8
3. Tsalamandris S, Antonopoulos AS, Oikonomou E, et al. The role of inflammation in diabetes: current concepts and future perspectives. *European cardiology review*. 2019;14(1):50.
4. de la Monte SM, Wands JR. Alzheimer's Disease Is Type 3 Diabetes–Evidence Reviewed. *Journal of diabetes science and technology (Online)*. 2008;2(6):1101–1113.
5. Greenhalgh AM, Gonzalez-Blanco L, Garcia-Rizo C, et al. Meta-analysis of glucose tolerance, insulin, and insulin resistance in antipsychotic-naïve patients with nonaffective psychosis. *Schizophrenia Research*. 2017;179:57–63. doi:10.1016/j.schres.2016.09.026
6. Takayanagi Y, Ishizuka K, Laursen TM, et al. From population to neuron: exploring common mediators for metabolic problems and mental illnesses. *Molecular Psychiatry*. 2021;26(8):3931–3942. doi:10.1038/s41380-020-00939-5
7. Gallagher EJ, LeRoith D. Hyperinsulinaemia in cancer. *Nat Rev Cancer*. Nov 2020;20(11):629–644. doi:10.1038/s41568-020-0295-5
8. Cooper I, Brookler K, Kyriakidou Y, Elliott BT, Crofts C. Metabolic phenotypes and step by step evolution of type 2 diabetes: A new paradigm. *Biomedicines*. 2021;9(7):800. doi:10.3390/biomedicines9070800
9. Jain AB, Lai V. Medication-induced hyperglycemia and diabetes mellitus: a review of current literature and practical management strategies. *Diabetes Therapy*. 2024;15(9):2001–2025.
10. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: Systematic review and meta-analysis. *Obes Rev*. 2012;13(3):275–286.
11. Ndumele CE, Neeland IJ, Tuttle KR, et al. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation*. 2023;148(20):1636–1664.
12. Aneni EC, Osondu CU, De La Cruz J, et al. Lipoprotein Sub-Fractions by Ion-Mobility Analysis and Its Association with Subclinical Coronary Atherosclerosis in High-Risk Individuals. *J Atheroscler Thromb*. Jan 1 2019;26(1):50–63. doi:10.5551/jat.40741
13. Singh B, Saxena A. Surrogate markers of insulin resistance: A review. *World Journal of Diabetes*. 2010;1(2):36–47. doi:10.4239/wjd.v1.i2.36
14. Muniyappa R, Madan R, Varghese RT. Assessing insulin sensitivity and resistance in humans. *Endotext* MDText.com, Inc.; 2024.
15. Teede HJ, Tay CT, Laven JJE, et al. Recommendations From the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *J Clin Endocrinol Metab*. Sep 18 2023;108(10):2447–2469. doi:10.1210/clinem/dgad463
16. Association for Diagnostics & Laboratory Medicine. Optimal Testing: Guide to Lab Test Utilization: Insulin. The Association for Diagnostics & Laboratory Medicine (ADLM). Updated April 23, 2024. Accessed May 27, 2026. https://myadlm.org/advocacy-and-outreach/optimal-testing-guide-to-lab-test-utilization/g-s/insulin
17. Matthews DR, Hosker JP, Rudenski AS. Homeostasis model assessment: Insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28(7):412–419.
18. Crofts C, Schofield G, Zinn C, Wheldon M, Kraft J. Identifying hyperinsulinaemia in the absence of impaired glucose tolerance: An examination of the Kraft database. *Diabetes Res Clin Pract*. 2016;118:50–57. doi:10.1016/j.diabres.2016.06.007
19. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. *Diabetes Care*. 2004;27(6):1487–1495.
20. Pisprasert V, Ingram KH, Lopez-Davila MF, Munoz AJ, Garvey WT. Limitations in the Use of Indices Using Glucose and Insulin Levels to Predict Insulin Sensitivity: impact of race and gender and superiority of the indices derived from oral glucose tolerance test in African Americans. *Diabetes Care*. 2013;36(4):845–853. doi:10.2337/dc12-0840
21. Crofts CA. Prodromal Diabetes: A Proposed Framework for Identifying Hyperinsulinaemia in the Normoglycaemic Phase. in preparation;

22. Hammel MC, Stein R, Kratzsch J, et al. Fasting indices of glucose-insulin-metabolism across life span and prediction of glycemic deterioration in children with obesity from new diagnostic cut-offs. *The Lancet Regional Health–Europe*. 2023;30(100652)doi:10.1016/j.lanepe.2023.100652
23. Royal Australian College of General Practitioners. *Management of type 2 diabetes: A handbook for general practice*. RACGP; 2024. https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/management-of-type-2-diabetes
24. Selvin E, Steffes MW, Zhu H, et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. *New England Journal of Medicine*. 2010;362(9):800–811. doi:10.1056/NEJMoa0908359
25. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *J Hepatol*. Dec 2023;79(6):1542–1556. doi:10.1016/j.jhep.2023.06.003
26. Huang TD, Behary J, Zekry A. Non-alcoholic fatty liver disease: a review of epidemiology, risk factors, diagnosis and management. *Intern Med J*. Sep 2020;50(9):1038–1047. doi:10.1111/imj.14709
27. Vilar-Gomez E, Chalasani N. Non-invasive assessment of non-alcoholic fatty liver disease: Clinical prediction rules and blood-based biomarkers. *Journal of hepatology*. 2018;68(2):305–315.
28. Zaitoon H, Abdul-Ghani M, DeFronzo RA. Insulin resistance and hyperinsulinaemia in kidney disease: mechanisms and metabolic effects. *Nat Rev Nephrol*. Mar 25 2026;doi:10.1038/s41581-026-01066-0
29. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. Apr 2024;105(4S):117–314. doi:10.1016/j.kint.2023.10.018
30. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005;112(17):2735–2752. doi:10.1161/circulationaha.105.169404