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Clinical Decision Tool Reviews

Metabolic Score for Insulin Resistance (METS-IR)

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Abstract

The Metabolic Score for Insulin Resistance (METS-IR) is a non–insulin-based surrogate marker of insulin resistance derived from routine metabolic parameters (fasting glucose, triglycerides, BMI, and HDL-C) that has been studied across largely Latin American, Asian, and United States cohorts. Originally shown to correlate with clamp-measured insulin sensitivity, METS-IR has been associated with cardiometabolic outcomes including incident type 2 diabetes, hypertension, kidney disease, stroke, ischemic heart disease, heart failure outcomes, coronary artery calcification, major adverse cardiovascular events, and both cardiovascular-related and all-cause mortality. Collectively, the literature supports METS-IR as a practical and inexpensive adjunctive marker for approximating insulin resistance. However, a significant methodological limitation is that most studies rely on population-based percentile comparisons rather than a single validated threshold, which substantially hinders the interpretation of individual patient values in clinical practice.

HOW TO USE

When to Use: The Metabolic Score for Insulin Resistance (METS-IR) is a non-insulin-based surrogate index for insulin resistance used in epidemiologic research and exploratory cardiometabolic risk assessment when fasting glucose and lipid values are available.

Pearls/Pitfalls

Pearls

- METS-IR utilizes routine clinical measures: fasting glucose, triglycerides, BMI, and HDL-C. These are inexpensive and scalable for epidemiologic and clinical research.
- METS-IR does not require fasting insulin, which differentiates it from other insulin resistance indices like HOMA-IR and QUICKI.
- Comparative performance across HOMA-IR, TyG, TG/HDL-C, METS-IR, and other indices of insulin resistance remain context dependent. No index is universally superior.
- METS-IR is validated against the gold-standard euglycemic–hyperinsulinemic clamp (EHC), and has been associated with incident type 2 diabetes, hypertension, cardiovascular disease, and mortality in observational cohorts.

Pitfalls and Limitations

- The majority of data on METS-IR are observational and often retrospective. Also, most studies rely on a single baseline measurement; dynamic trajectories are rarely assessed.
- The validation cohorts are predominantly in Latin American, Asian, and U.S. populations; generalizability to other populations is less clear, particularly as the relationship between BMI and insulin resistance is affected differently by race. This suggests a single universal METS-IR cut-off may not be appropriate across all racial and ethnic groups.
- There is no universally accepted clinical cutoff for METS-IR. Risk is commonly reported by tertiles or quartiles rather than validated outcome-based thresholds, limiting individual-level interpretation. Further, reported "optimal" thresholds have ranged from approximately 40-55 and vary by population and outcome.
- Nonlinear or U-shaped associations are observed for some outcomes (e.g., hypertension, mortality), complicating interpretation. A simple dichromatic

cutoff approach does not capture these nonlinear patterns and should not be used to infer that lower METS-IR values are uniformly favorable.
- Component variables can be altered by therapy (antihyperglycemic, lipid-lowering, anti-obesity agents), potentially lowering METS-IR independent of true changes in insulin sensitivity. METS-IR validation was conducted in populations without diabetes, and its application in individuals with diabetes or on an interfering medication is less certain.
- METS-IR components are susceptible to transient variation and should not be calculated during acute illness, hospitalization, severe stress, dietary fluctuation, alcohol use, or improper fasting.
- METS-IR does not fully capture all relevant variables (e.g., smoking, physical activity, family history). Also, BMI does not capture body fat distribution, visceral adiposity, or muscle mass, which may reduce discrimination in certain populations.
- METS-IR is positioned as an adjunctive risk marker and not validated as a stand-alone clinical decision tool.

Why Use

METS-IR addresses the need for a practical, inexpensive index that can be calculated without fasting insulin when studying insulin resistance and related metabolic conditions. The euglycemic-hyperinsulinemic clamp (EHC) remains the gold standard for measuring insulin sensitivity, yet its invasiveness, cost, and complexity render it unsuitable for routine screening or large-scale epidemiologic studies. While HOMA-IR and related insulin-based indices are widely used in research, they require fasting insulin measurements that are not standardized across assays and are often unavailable in resource-limited settings.

METS-IR eliminates this barrier by utilizing four routinely collected parameters without specialized equipment or additional cost, and studies have shown its association with EHC and clinical outcomes such as incident cardiometabolic disease.

NEXT STEPS

Advice

METS-IR is a surrogate index to approximate insulin resistance, rather than a diagnostic test for insulin resistance or diabetes, and does not replace HbA1c, fasting glucose, or oral glucose tolerance testing in diagnosing prediabetes or diabetes.

In clinical practice, METS-IR may be regarded as an adjunctive risk marker rather than a stand-alone metric. It may help identify individuals with heightened metabolic syndrome risk, but should always be interpreted in the context of the overall clinical picture. This is especially true as there are no standardized, validated cutoff values for interpreting the METS-IR; a cutoff of 50.39 was only used in a single study population in relation to the risk of developing type 2 diabetes.

There are no interventional data demonstrating that METS-IR reduction leads to improved clinical outcomes, nor are there treatment targets for METS-IR. Thus, clinicians should focus on modifying the underlying components (i.e. weight, glycemia, and lipids) according to guideline-directed care.

Management

Management should be based on established guideline-directed evaluation and treatment of the individual patient's risk factors, not on a METS-IR value. When an elevated METS-IR is noted in a clinically stable, fasting individual without diabetes, it may prompt a review of the underlying glucose, triglyceride, HDL-C, and BMI values and confirmation that standard diabetes and cardiovascular risk assessment has been completed.

Recommended approach:

- Screen for diabetes using appropriate glycemic testing: HbA1c, fasting plasma glucose, or oral glucose tolerance testing according to established screening recommendations
- Assess and manage blood pressure, lipid abnormalities, weight-related complications, smoking, physical activity, diet, and family history according to guideline-directed care
- Offer lifestyle or pharmacologic interventions as indicated by established diagnoses, risk estimates, or guideline criteria

Avoid using METS-IR as a treatment target or serial marker of therapeutic response, particularly as glucose-lowering, lipid-lowering, or weight-lowering therapies may alter score components without proven parallel changes in insulin sensitivity

EVIDENCE

Evidence Appraisal

Evidence supporting METS-IR as a surrogate of insulin sensitivity

METS-IR was originally developed by Bello-Chavolla et al. (2018) as a non-insulin-based index to approximate clamp-measured insulin sensitivity using fasting glucose, triglycerides, BMI, and HDL-C. Derived from 125 Mexican adults, it demonstrated a strong inverse correlation with EHC-measured insulin sensitivity (r=-0.62) and good discrimination for impaired insulin sensitivity (AUC 0.84). Vazquez et al. (2026) externally validated METS-IR against EHC in 286 indigenous American par-

ticipants (r=0.597, with AUC=0.688 for incident type 2 diabetes); in that same comparative study, METS-IR most closely correlated with EHC among indices that did not require insulin measurement, including TyG and TG/HDL-C. However, some markers that required fasting insulin (HOMA-IR, QUICKI, and fasting insulin) or oral glucose tolerance test results (Matsuda and Belfiore indices) outperformed METS-IR in that study (Vazquez, 2026).

Evidence associating METS-IR with clinical outcomes

In a study by Zhang et al. (2025) of 1,498 Chinese adults, METS-IR as a composite score performed better than individual components, including BMI, at predicting incidence of metabolic syndrome (AUC=0.713).

The original Bello-Chavolla study (2018) also contained a longitudinal component: in a cohort of 6,144 Mexican participants followed for two years, higher baseline METS-IR was associated with incident type 2 diabetes. Those in the highest quartile (>50.39) had an adjusted hazard ratio (HR) of 3.91 for incident diabetes.

This association has been further validated across large Asian populations. In a Chinese cohort of 116,855 patients, those in the highest quartile (>43.7) had a 6.3-fold higher risk of developing diabetes within 2 years compared to the lowest quartile (≤33.6), with a nonlinear relationship and an inflection point at 44.4 (Chen et al., 2022). Additional large studies in Chinese and Japanese populations (including non-obese adults) showed higher quartiles consistently conferred increased risk (Cai et al., 2021; Cheng et al., 2024). These studies support an association between higher METS-IR and future diabetes in their respective populations, but do not provide a clinical cutoff. Even for gestational diabetes (GDM), a study of 1,845 pregnant Iranian women demonstrated an association between METS-IR and GDM (AUC=0.82), and those in the highest quartile had adjusted RR=18.9 for developing GDM compared to those in the lowest (Rouholamin et al., 2025).

Beyond dysglycemia, METS-IR is associated with incident hypertension. In Mexican and U.S. cohorts, higher METS-IR levels predicted both increased pulse wave velocity and greater risk of developing hypertension (Bello-Chavolla et al., 2019; Guo et al., 2025).

METS-IR has also demonstrated prognostic significance for cardiovascular and renal outcomes. In Korean adults without diabetes, those in the highest quartile of METS-IR had HR 2.11 for ischemic heart disease, with an optimal cutoff of 31.1 (Yoon et al., 2021). In a Chinese cohort of 6,489 followed for a median of 10.6 years, METS-IR in the highest quintile (>43.3) had HR=1.8 for cardiovascular disease (CVD) compared to the lowest (<32.6) (Wu et al., 2023). Among those with hypertension and sleep apnea, a study of 2,031 Chinese adults showed that each standard deviation increase in METS-IR was associated with a 30% increased risk of new-onset overall CVD events (32% for coronary artery disease and 27% for stroke), the highest tertile associated with HR=2.05 (Yang et al., 2023). In a study of 3,248 patients with heart failure with preserved ejection fraction (HFpEF), those in the highest tertile (≥44.0) had HR=2.48 for all-cause and CV mortality over a median of 4.2 years compared to the lowest tertile (<36.5) (Zhou et al., 2024). There is similar data for higher incidence of major adverse cardiovascular events with higher baseline METS-IR in patients after CABG, or in those with type 2 diabetes with known ischemic cardiomyopathy, or in those with cardiovascular-kidney-metabolic syndrome stages 0-3 (Zhang et al., 2023; Zhang et al., 2023; Wang et al., 2025). In a U.S. population of 14,653 patients, METS-IR showed a U-shaped relationship with CVD-related and all-cause mortality over a median of 116 months, with inflection at 41.33 as the lowest risk point (Duan et al., 2024). The METS-IR also predicted the incidence of coronary artery calcification in asymptomatic adults (Wang et al., 2022). METS-IR was also significantly associated with urinary albumin-to-creatinine ratio in a study of Chinese adults (Su et al., 2022).

Collectively, the literature supports METS-IR as a practical and inexpensive risk marker for insulin resistance and predicting cardiometabolic disease. However, no major guidelines currently endorse its routine use, largely because clinically actionable thresholds have not been standardized or externally validated. A key methodological limitation of the existing literature is that most studies report risk according to population-based percentile comparisons (e.g., tertiles or quartiles). Differences in population characteristics, baseline metabolic status, outcome definitions, and follow-up duration yield different clinical cutoffs and preclude the creation of a single universal METS-IR threshold value and lack prospective validation. This approach limits translation to bedside practice and makes interpretation of an individual patient's result challenging. Accordingly, further investigation is needed in this area, and should include prospective studies examining longitudinal and dynamic changes in METS-IR and their relationship to incident cardiometabolic outcomes across diverse populations.

Formula

$$\text{METS-IR} = (\ln((2 \times G_0) + TG_0) \times \text{BMI}) / (\ln(\text{HDL-c})),$$

where G_0 is fasting glucose (mg/dL), TG_0 is triglyceride concentration (mg/dL), BMI is body mass index (kg/m^2), and HDL-c is high-density lipoprotein cholesterol (mg/dL).

Facts & Figures

METS-IR should be interpreted as a continuous surrogate index. There is no established threshold value for high insulin resistance by METS-IR. A value of >50.39

was derived in a large cohort for incident type 2 diabetes but should not be used as a universal cutoff.

Literature

Original/Primary

https://pubmed.ncbi.nlm.nih.gov/29535168/
Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. Eur J Endocrinol. 2018;178(5):533-544.

Validation

https://academic.oup.com/jcem/article/111/8/2251/8512919
Laura Vazquez, Elsa Vazquez Arreola, Murugasu Nagul, Jonathan Krakoff, Robert L Hanson, Comparing surrogate indexes for insulin resistance as predictors of type 2 diabetes, The Journal of Clinical Endocrinology & Metabolism, Volume 111, Issue 8, August 2026, Pages 2251–2261, https://doi.org/10.1210/clinem/dgag101

https://pubmed.ncbi.nlm.nih.gov/40051521/
Zhang Q, Wei Y, Huang S, et al. Association of metabolic score for insulin resistance with incident metabolic syndrome: a cohort study in middle-aged and older adult Chinese population. *Front Public Health*. 2025;13:1453144. Published 2025 Feb 18. doi:10.3389/fpubh.2025.1453144

https://pubmed.ncbi.nlm.nih.gov/36992743/
Chen Z, Huang C, Zhou Z, Zhang Y, Xu M, Tang Y, Fan L, Feng K. A nonlinear associations of metabolic score for insulin resistance index with incident diabetes: A retrospective Chinese cohort study. Front Clin Diabetes Healthc. 2023 Jan 12;3:1101276.

https://pubmed.ncbi.nlm.nih.gov/38569189/
Cheng H, Jia Z, Li YT, Yu X, Wang JJ, Xie YJ, Hernandez J, Wang HHX. Metabolic Score for Insulin Resistance and New-Onset Type 2 Diabetes in a Middle-Aged and Older Adult Population: Nationwide Prospective Cohort Study and Implications for Primary Care. JMIR Public Health Surveill. 2024 Jun 3;10:e49617.

https://pubmed.ncbi.nlm.nih.gov/34785931/
Cai XT, Zhu Q, Liu SS, Wang MR, Wu T, Hong J, Hu JL, Li N. Associations Between the Metabolic Score for Insulin Resistance Index and the Risk of Type 2 Diabetes Mellitus Among Non-Obese Adults: Insights from a Population-Based Cohort Study. Int J Gen Med. 2021 Nov 6;14:7729-7740.

https://pubmed.ncbi.nlm.nih.gov/40716693/
Rouholamin S, Razavi M, Pirjani R, Rezaeinejad M. Metabolic score for insulin resistance (METS-IR) as a predictor of gestational diabetes: Findings from a prospective Iranian cohort study. Clin Biochem. 2025 Oct;139:110982.

https://pubmed.ncbi.nlm.nih.gov/31318156/
Bello-Chavolla OY, Antonio-Villa NE, Vargas-Vázquez A, et al. Prediction of incident hypertension and arterial stiffness using the non-insulin-based metabolic score for insulin resistance (METS-IR) index. J Clin Hypertens . 2019;21(8):1063-1070.

https://pubmed.ncbi.nlm.nih.gov/39985010/
Guo Z, Guo X, Xu H, Chu H, Tian Y, Wang S, Wang Y. Association between metabolic score for insulin resistance (METS-IR) and hypertension: a cross-sectional study based on NHANES 2007-2018. Lipids Health Dis. 2025 Feb 21;24(1):64.

https://pubmed.ncbi.nlm.nih.gov/34442386/
Yoon J, Jung D, Lee Y, Park B. The Metabolic Score for Insulin Resistance (METS-IR) as a Predictor of Incident Ischemic Heart Disease: A Longitudinal Study among Korean without Diabetes. J Pers Med. 2021 Jul 28;11(8):742.

https://pubmed.ncbi.nlm.nih.gov/36125732/
Wu Z, Cui H, Zhang Y, Liu L, Zhang W, Xiong W, Lu F, Peng J, Yang J. The impact of the metabolic score for insulin resistance on cardiovascular disease: a 10-year follow-up cohort study. J Endocrinol Invest. 2023 Mar;46(3):523-533.

https://pubmed.ncbi.nlm.nih.gov/36815173/
Yang W, Cai X, Hu J, Wen W, Mulalibieke H, Yao X, Yao L, Zhu Q, Hong J, Luo Q, Liu S, Li N. The Metabolic Score for Insulin Resistance (METS-IR) Predicts Cardiovascular Disease and Its Subtypes in Patients with Hypertension and Obstructive Sleep Apnea. Clin Epidemiol. 2023 Feb 15;15:177-189.

https://pubmed.ncbi.nlm.nih.gov/39261964/
Zhou Y, Xie Y, Du L, Dong J, He K. Metabolic score for insulin resistance as a predictor of mortality in heart failure with preserved ejection fraction: results from a multicenter cohort study. Diabetol Metab Syndr. 2024 Sep 11;16(1):220.

https://pubmed.ncbi.nlm.nih.gov/37461067/
Zhang S, Wu Z, Zhuang Y, Sun X, Wang J, Chen S, Guo D, Xu P, Zhang C, Yang J. The metabolic score for insulin resistance in the prediction of major adverse cardiovascular events in patients after coronary artery bypass surgery: a multicenter retrospective cohort study. Diabetol Metab Syndr. 2023 Jul 17;15(1):157.

https://pubmed.ncbi.nlm.nih.gov/37179787/
Zhang X, Liu F, Li W, Zhang J, Zhang T, Yu X, Luo J, Zhao Q, Zhang J, Fang B, Yang Y, Li X. Metabolic Score for Insulin Resistance (METS-IR) Predicts Adverse Cardiovascular Events in Patients with Type 2 Diabetes and Ischemic Cardiomyopathy. Diabetes Metab Syndr Obes. 2023 May 5;16:1283-1295.

https://pubmed.ncbi.nlm.nih.gov/41327275/
Wang Y, Yu Q. METS-IR predicts new-onset stroke in older adults with stages 0-3 cardiovascular-kidney-metabolic syndrome: a prospective, multicohort, clinical study with statistical and machine learning. Diabetol Metab Syndr. 2025 Dec 1;18(1):6.

https://pubmed.ncbi.nlm.nih.gov/38987779/
Duan M, Zhao X, Li S, Miao G, Bai L, Zhang Q, Yang W, Zhao X. Metabolic score for insulin resistance (METS-IR) predicts all-cause and cardiovascular mortality in the general population: evidence from NHANES 2001-2018. Cardiovasc Diabetol. 2024 Jul 10;23(1):243.

https://pubmed.ncbi.nlm.nih.gov/36357872/
Wang Z, Hui X, Huang X, Li J, Liu N. Relationship between a novel non-insulin-based metabolic score for insulin resistance (METS-IR) and coronary artery calcification. BMC Endocr Disord. 2022 Nov 10;22(1):274.

https://pubmed.ncbi.nlm.nih.gov/35220678/
Su W, Wang J, Yu S, Chen K, Gao Z, Tang X, Wan Q, Luo Z, Ning G, Mu Y. Metabolic Score for Insulin Resistance, a novel score to evaluate insulin sensitivity, is associated with the urinary albumin-to-creatinine ratio in Chinese adults: A cross-sectional REACTION study. J Diabetes Investig. 2022 Jul;13(7):1222-1234.