

Metabolic Phenotyping for Early Diabetes Prevention: A Web-Based Clinical Tool

Running Title: Metabolic Risk Calculator

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Abstract

Background: The countries of the Gulf Cooperation Council (GCC) face a significant diabetes burden. Preventing, or at least delaying onset of Type 2 diabetes mellitus (T2DM) requires accurate and timely identification of at-risk individuals with prediabetes. Traditional screening focuses on glucose and HbA1c alone and does not include other readily available data that can better identify risk and guide intervention.

Methods: We developed a comprehensive web-based cardiometabolic risk calculator combining the classic homeostasis model assessment (HOMA1), triglyceride-glucose (TyG) index, metabolic syndrome evaluation (ATP III and IDF criteria), diabetes risk prediction adapted from validated models including QDiabetes-2018 and UK Biobank cohort studies, and cardiovascular risk trajectory with Lipoprotein(a) integration. The calculator uses ethnicity-specific thresholds for Middle Eastern, South Asian, and other populations, and provides AI-generated clinical summaries with multi-language patient education materials.

Case: An 18-year-old Emirati male with obesity, prediabetes, severe insulin resistance, and compensatory beta-cell hypersecretion had a calculated 10-year diabetes risk exceeding 55%. This quantitative risk estimate motivated intensive lifestyle modification combined with tirzepatide and metformin. After six months, he achieved 17% weight loss, normalization of insulin resistance and beta-cell function, prediabetes resolution and diabetes risk reduction to under 10%.

Conclusion: Comprehensive metabolic phenotyping with quantitative risk communication can identify high-risk individuals, characterize their metabolic dysfunction, and motivate behavioral change. This freely available tool addresses the need to identify individuals at high 10-year risk of progression to T2DM and elevated lifetime cardiovascular risk, thereby allowing more timely intervention.

Introduction

The GCC has a very high diabetes prevalence. In the UAE, rates range from 15% to 19% among adults [1] [2]. Similarly, in Oman, the 2017 STEPS survey reported a prevalence of

14.5% among Omani nationals, with projections suggesting a 174% increase in total cases by 2050 [3] [4]. Moreover, the age of onset is declining across the region, with type 2 diabetes increasingly diagnosed in young adults and adolescents [5]. Recent large-scale population studies found that 63.4% of UAE adults and 25.8% of children/adolescents are living with overweight or obesity [6] [7]. This is the principal risk factor for T2DM and earlier-onset T2DM inevitably means diabetes complications occurring at younger ages, with particularly poor outcomes seen in childhood-onset T2DM [5].

Diabetes risk prediction models derived from large cohort studies can estimate 10-year diabetes probability based on demographic, anthropometric, and metabolic parameters. The QDiabetes-2018 algorithm, developed and validated in over 11 million UK primary care patients, provides robust 10-year risk estimates incorporating clinical and laboratory variables [8]. The UK Biobank, with over 500,000 participants, has enabled identification of key predictors including HbA1c, BMI, waist circumference, and family history [9] [10]. However, most existing risk calculators use European-derived thresholds that may not accurately reflect diabetes susceptibility in Middle Eastern, South Asian, and Pacific Islander populations, who develop metabolic complications at lower BMI and waist circumference values than White Europeans [11].

Insulin resistance and beta cell dysfunction are the key factors driving development of T2DM, typically emerging years or even decades before overt hyperglycemia [12]. The homeostasis model assessment (HOMA), introduced by Matthews and colleagues in 1985, provides a practical method for estimating insulin resistance (HOMA-IR), beta-cell function (HOMA-%B), and insulin sensitivity (HOMA-%S) from fasting glucose and insulin measurements [12]. The original HOMA equations (HOMA1) remain the most widely used method in clinical practice and epidemiological studies due to their simplicity and extensive validation against the euglycemic clamp technique.

While newer computer models (HOMA2) exist to account for non-linear physiological dynamics [13] [14], HOMA1 remains the standard for direct comparison with the vast majority of published literature.

The triglyceride-glucose (TyG) index offers an alternative insulin resistance marker that requires only glucose and triglycerides, useful in resource-limited settings where insulin measurements are not available or affordable [15] [16]. Multiple studies have validated TyG as a reliable surrogate for HOMA-IR, with strong correlations to gold-standard hyperinsulinemic-euglycemic clamp measurements [17] [18]. Despite their clinical utility, HOMA and TyG remain underutilized in routine practice due to lack of practical tools to aid the clinician.

The web-based calculator integrates these assessments with metabolic syndrome evaluation (ATP III and IDF criteria), diabetes risk prediction, and lifetime cardiovascular risk trajectory with Lipoprotein(a) (Lp(a)) integration. The tool uses ethnicity-specific thresholds and emphasizes beta-cell preservation, a therapeutic approach that prioritizes interventions reducing beta-cell workload [19]. AI-powered clinical summary generation and multi-language patient education materials enhance clinical workflow and patient engagement. This paper describes the calculator methodology and presents a case demonstrating its clinical utility in motivating intensive intervention for a high-risk young adult.

Methods

We developed the HOMA & Metabolic Risk Calculator as a clinical decision-support tool to facilitate the use of advanced analytic methods in clinical practice. Together with other complementary tools, we created a comprehensive cardiometabolic risk assessment calculator.

Calculator Components

HOMA1 Model (Primary): The calculator uses the classic HOMA1 model as its primary assessment tool to ensure compatibility with standard reference ranges and historical data [12]:

- **HOMA1-IR** = (fasting glucose [mmol/L] × fasting insulin [mIU/L]) / 22.5
- **HOMA1-%B** = (20 × fasting insulin [mIU/L]) / (fasting glucose [mmol/L] – 3.5)
- **HOMA1-%S** = 100 / HOMA1-IR

HOMA Thresholds: Based on updated clinical guidelines, we apply the following interpretation thresholds for HOMA-IR:

- **Optimal:** < 1.5
- **Early Insulin Resistance:** 1.5 – 2.4
- **Insulin Resistance:** 2.5 – 3.4
- **Severe Insulin Resistance:** ≥ 3.5

TyG Index Calculation: $\ln[(\text{Triglycerides [mg/dL]} \times \text{Glucose [mg/dL]}) / 2]$. Interpretation thresholds: <8.5 (normal insulin sensitivity), 8.5–9.0 (borderline insulin resistance), 9.0–10.0 (moderate insulin resistance), ≥10.0 (severe insulin resistance) [15] [16]. When both HOMA-IR and TyG are available, automated concordance analysis either strengthens clinical confidence when both indicate similar severity or flags discordance requiring further investigation.

Metabolic Syndrome Evaluation: The calculator evaluates metabolic syndrome using both ATP III (Adult Treatment Panel III) from the NCEP (National Cholesterol Education Program) and IDF criteria [20]. ATP III requires ≥3 of 5 criteria: waist circumference (≥102 cm males/≥88 cm females for Europid populations), triglycerides (≥150 mg/dL or 1.7 mmol/L), HDL cholesterol (<40 mg/dL males/<50 mg/dL females), blood pressure (≥130/85 mmHg or on medication), and fasting glucose (≥100 mg/dL or 5.6 mmol/L). IDF criteria require central obesity (ethnicity-specific waist thresholds) plus ≥2 additional criteria. The calculator applies ethnicity-specific waist circumference thresholds: ≥90 cm males/≥80 cm females for South Asian, Chinese, Japanese, and Middle Eastern populations, reflecting their higher metabolic risk at lower waist circumferences.

10-Year Diabetes Risk Model: The calculator implements a risk prediction model adapted from validated algorithms including QDiabetes-2018 [8] and informed by UK Biobank cohort studies [9] [10]. The model assigns weighted points across demographic (age, sex, ethnicity, family history), anthropometric (BMI, waist circumference), and metabolic (fasting glucose, HbA1c, lipid profile, blood pressure) domains. Ethnicity-specific thresholds for Middle Eastern, South Asian, and Pacific Islander populations reflect WHO recommendations [11]: BMI overweight ≥23 kg/m² (versus ≥25 for European populations), obesity ≥27.5 kg/m² (versus ≥30), waist circumference ≥90 cm males/≥80 cm females (versus ≥102/≥88 cm). Risk is categorized as low (<10%), moderate (10–20%), high (20–30%), or very high (>30%).

Lipid Panel and Cardiovascular Risk Assessment: The calculator includes a lipid panel module that accepts total cholesterol, LDL, HDL, and triglycerides with automatic unit conversion between mg/dL and mmol/L. Advanced lipid markers include Apolipoprotein B and Lipoprotein(a) [Lp(a)] with unit selection (nmol/L or mg/dL) (if available). The calculator estimates ApoB from standard lipid values using the Sampson equation when measured ApoB is unavailable [21]. Non-HDL cholesterol is automatically calculated. Lp(a)

values are incorporated into lifetime cardiovascular risk calculations using published risk multipliers [22].

Lifetime Cardiovascular Risk and Trajectory: The calculator uses fasting lipid levels to generate 10-year and lifetime ASCVD risk estimates and displays a visual trajectory chart showing projected risk accumulation from current age to age 80. The chart displays three lines: baseline trajectory, Lp(a)-adjusted trajectory (when Lp(a) is elevated), and projected trajectory with optimal intervention (50% LDL reduction plus blood pressure control). A risk factor contribution breakdown shows the percentage contribution of each modifiable factor (LDL, HDL, blood pressure, smoking, diabetes, Lp(a)) to help clinicians prioritize interventions [23].

Medical Record Integration: The calculator provides a PDF summary which may be printed or copied for medical record purposes.

Clinical Summary Generation: The calculator provides AI-powered clinical summary generation that synthesizes all assessment data into a structured clinical note suitable for electronic medical records. The summary includes patient demographics, metabolic phenotype interpretation, risk stratification, and evidence-based clinical considerations. A separate patient-friendly summary feature generates explanations in non-technical language with support for English, Arabic, and French, using warm analogies (e.g., "your body is like a car, insulin is the key") to improve patient understanding and engagement [24] [25].

Calculator Availability: The web-based calculator is freely available at <https://homa.alsaffar.uk> for clinical and educational use.

Case Presentation

An 18-year-old Emirati male presented for evaluation of obesity and abnormal screening laboratories. Weight had been a lifelong challenge, with progressive gain through adolescence. Diet consisted primarily of refined carbohydrates and fast food, with minimal physical activity. Family history was notable for multiple affected family members. His father was diagnosed with T2DM at age 42; his paternal grandfather has visual impairment from long-standing T2DM with proliferative diabetic retinopathy; two paternal uncles have T2DM requiring insulin, and his mother had gestational diabetes in all three of her pregnancies.

Physical examination showed central adiposity (height 174 cm, weight 104 kg, BMI 34.4 kg/m²), waist circumference 112 cm (confirming central adiposity) [11], and blood pressure 138/86 mmHg. Acanthosis nigricans was present in neck and axillary skin folds.

Laboratory results showed fasting glucose 123 mg/dL (6.8 mmol/L), HbA1c 6.2%, fasting insulin 28.5 mIU/L, total cholesterol 5.8 mmol/L, LDL 3.9 mmol/L, HDL 0.88 mmol/L, triglycerides 3.2 mmol/L (283 mg/dL), and ALT 52 U/L.

Calculator Assessment The initial calculator results are shown in Figure 1. **HOMA1-IR** of 8.6 indicated severe insulin resistance. TyG index of 10.1 (severe insulin resistance) corroborated this finding. **HOMA1-%B** of 172% showed his beta-cells were functioning at nearly double normal capacity, yet dysglycemia was present. This compensatory hypersecretion typically precedes beta-cell exhaustion [26] [27], and his 10-year diabetes risk exceeded 55%.

The visual display of these results proved invaluable to the patient (see Figure 1). Seeing the data presented this way, with a >50% 10-year diabetes risk, transformed the abstract "prediabetes" label into something concrete. The patient later described this as a turning point

in understanding that diabetes was not a distant possibility but an imminent threat to his health and long-term prospects.

Six-Month Outcomes Table 1 and Figure 2 show changes over six months from baseline.

Table 1. Changes in anthropometric and metabolic parameters over six months.

Parameter	Baseline	3 Months	6 Months	Change (%)
Anthropometry				
Weight (kg)	104.0	94.5	86.3	-17.0%
BMI (kg/m ²)	34.4	31.2	28.5	-17.2%
Waist Circumference (cm)	112	102	94	-16.1%
Glycemic Control				
Fasting Glucose (mmol/L)	6.8	5.4	4.9	-27.9%
HbA1c (%)	6.2	5.6	5.2	-16.1%
Fasting Insulin (mIU/L)	28.5	14.2	8.4	-70.5%
Insulin Resistance				
HOMA1-IR	8.6	3.4	1.8	-79.1%
HOMA1-%B	172%	124%	98%	-43.0%
TyG Index	10.1	9.2	8.4	-16.8%
Lipid Profile				
Triglycerides (mmol/L)	3.2	2.1	1.5	-53.1%
LDL Cholesterol (mmol/L)	3.9	2.8	2.1	-46.2%
HDL Cholesterol (mmol/L)	0.88	1.02	1.15	+30.7%
Risk Prediction				
10-Year Diabetes Risk	>55%	22%	8%	-85.5%

Figure Legends

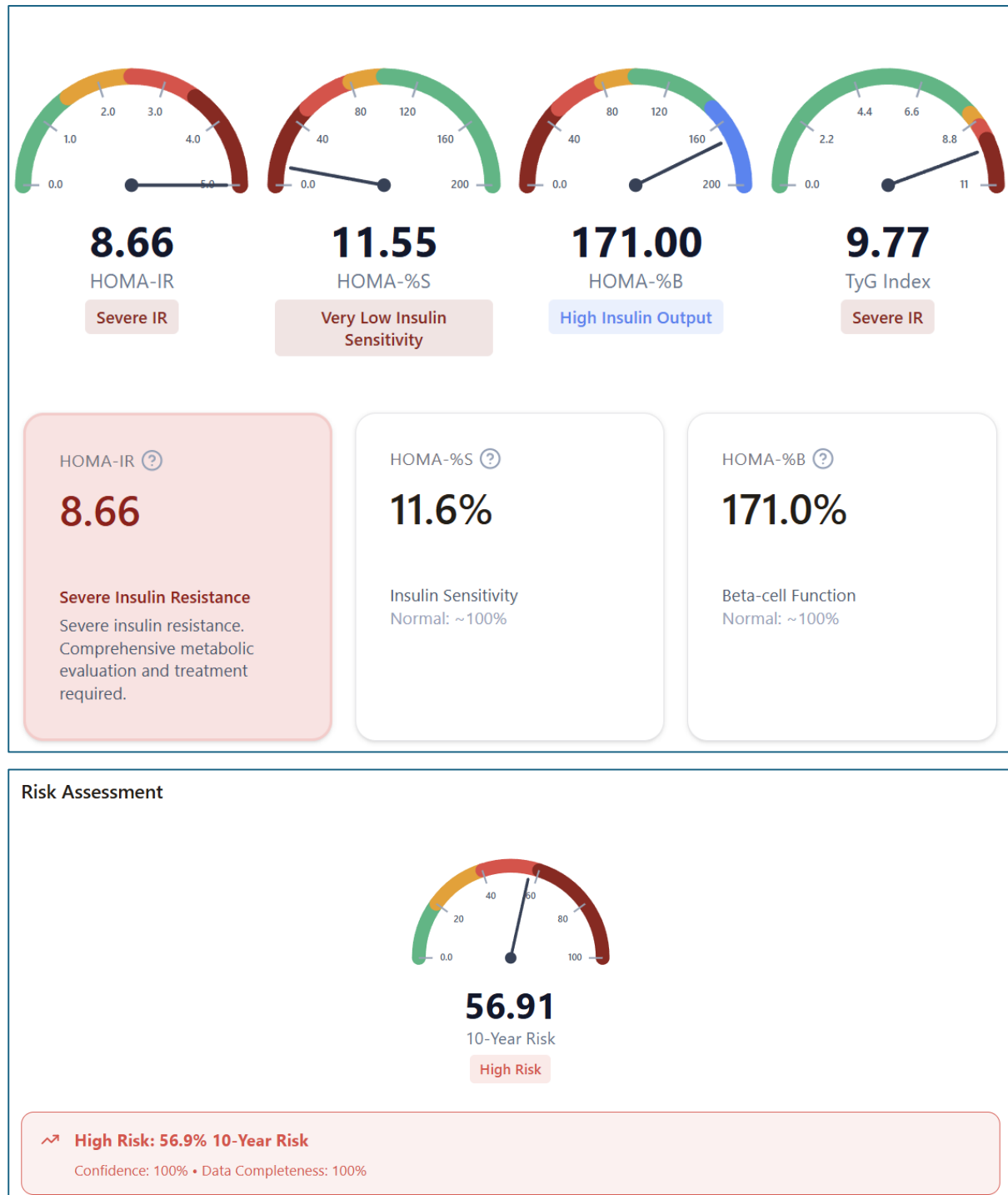


Figure 1. Integrated metabolic phenotyping and diabetes risk assessment at baseline. The dashboard displays severe insulin resistance (HOMA1-IR 8.66, TyG 9.77), compensatory beta-cell hypersecretion (HOMA1-%B 171%), and severely impaired insulin sensitivity (HOMA1-%S 11.6%) and a very high 10-year diabetes risk (>55%).

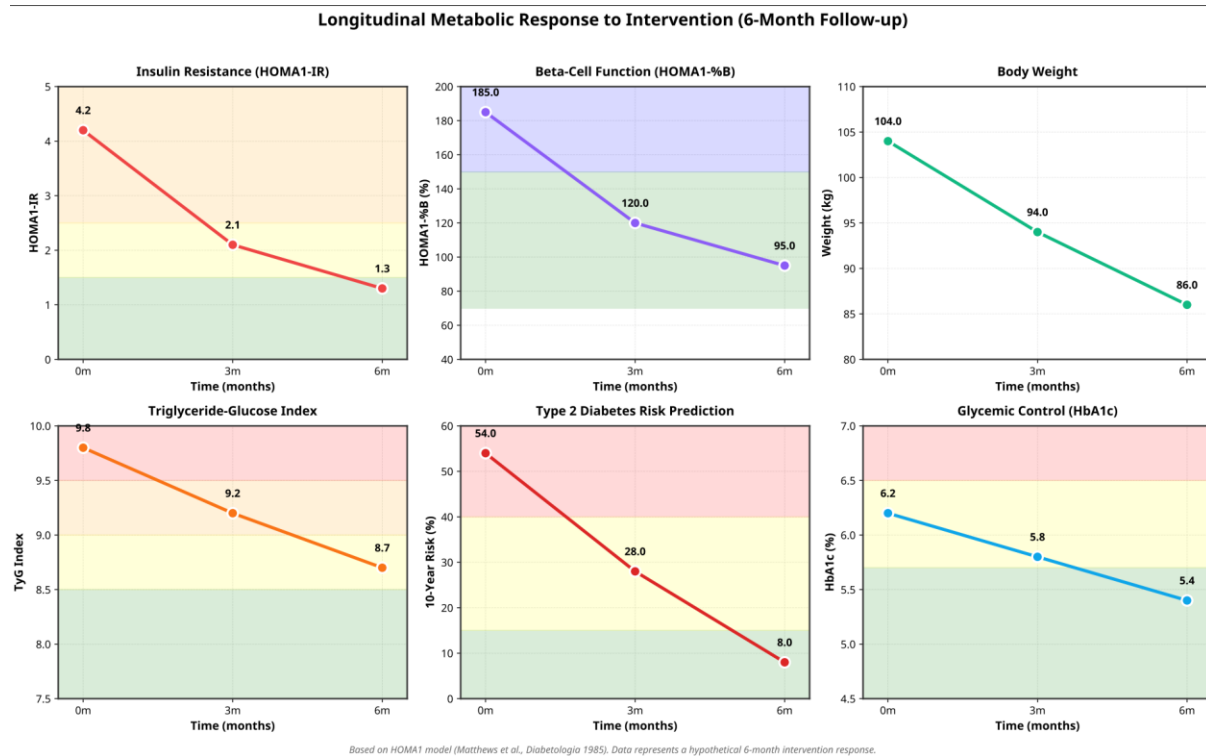


Figure 2. Trajectory of metabolic improvement over six months. The graphs illustrate the rapid normalization of insulin resistance (HOMA-IR) and beta-cell function (HOMA-%B) alongside weight loss, correlating with a dramatic reduction in predicted 10-year diabetes risk.

Discussion

This case demonstrates how integrated metabolic assessment can improve clinical practice. Rather than simply labeling a patient "prediabetes," the calculator provided a metabolic phenotype that clarified the need and urgency for intervention and enabled objective monitoring of treatment response in specific domains.

The Value of Metabolic Phenotyping

Standard screening showing fasting glucose 123 mg/dL and HbA1c 6.2% typically generates generic "prediabetes" counseling about weight loss, exercise, and diet. While reasonable, this approach misses important details. The calculator revealed severe insulin resistance (HOMA1-IR 4.2, TyG 9.8) with compensatory beta-cell hypersecretion, indicating active disease progression, not just static risk. This phenotype supported aggressive pharmacotherapy in addition to intensive lifestyle modification.

The distinction between insulin resistance with beta-cell compensation versus beta-cell failure has therapeutic implications [26][27]. Our patient's HOMA1-%B of 171% indicated preserved function with compensatory hypersecretion, making him a candidate for insulin sensitizers addressing root pathophysiology. Had HOMA1-%B indicated beta-cell failure, the treatment approach may have differed, potentially requiring earlier consideration of insulin. The decline in HOMA1-%B from 185% to 95% at six months represents normalization rather than deterioration, reversing the hypersecretion that typically precedes exhaustion.

TyG Index as Practical Alternative

TyG index provided corroborating evidence of severe insulin resistance without requiring insulin measurement. For resource-limited settings or when insulin assays are unavailable or unaffordable, TyG offers a validated alternative using routine lipid panel measurements. The

concordance between HOMA1-IR and TyG in this case (both indicating severe resistance at baseline, both improving substantially by month 6) strengthens confidence in the assessment.

Risk Assessment

The 10-year diabetes risk estimate proved particularly impactful for patient motivation. Abstract concepts like "prediabetes" or "insulin resistance" may not convey urgency to young patients who feel healthy. A concrete statement that "you have greater than 50% chance of developing diabetes within 10 years" creates a different psychological impact. Studies of risk communication in cardiovascular disease have demonstrated that personalized, quantitative estimates improve patient engagement and adherence [24],[28].

Beta-Cell Preservation

The calculator's metabolic phenotyping supports a beta-cell preservation approach to diabetes prevention. By quantifying both insulin resistance (HOMA1-IR) and beta-cell function (HOMA1-%B), clinicians can identify patients with compensatory hypersecretion who may benefit from interventions that reduce beta-cell workload [19]. Focusing on lifestyle modification, metformin, GLP-1 receptor agonists, and SGLT2 inhibitors reduce glucose through mechanisms that spare or protect beta-cells. The subsequent normalization of HOMA1-%B from 185% to 95% suggests successful beta-cell "rest". The calculator does not make specific medication recommendations, but the metabolic phenotype it provides can inform clinical decision-making.

HOMA1 as Primary Model

Our calculator uses the HOMA1 model as its primary assessment tool. The HOMA1 model, developed by Matthews and colleagues [12], remains the most widely published and clinically validated index of insulin resistance. The HOMA1 formula ($\text{Glucose} \times \text{Insulin} / 405$) is simple, reproducible, and requires no external software or iterative algorithms. This simplicity has made HOMA1 the standard reference in epidemiological studies, clinical trials, and longitudinal research spanning four decades.

The calculator implements the standard HOMA1 algorithm, providing clinically equivalent results to the original Oxford methodology. HOMA1 values are displayed as the primary assessment because the vast majority of published literature uses HOMA1, enabling direct comparison with reference ranges established across diverse populations. HOMA1 shows strong correlation ($r > 0.9$) with more complex non-linear models such as HOMA2 in most clinical ranges [14], and the percentage change over time is similar for both models, as demonstrated in our case where HOMA1-IR improved 69% over six months.

Limitations

This case report demonstrates the utility of integrated metabolic assessment in a single patient. Several limitations should be acknowledged. First, the 10-year diabetes risk model, while adapted from validated algorithms including QDiabetes-2018 and informed by UK Biobank data with ethnicity-specific adjustments, has not been independently validated in Middle Eastern populations specifically. Validity in pediatric and adolescent populations is not yet established, although the calculator will allow data entry for pediatric cases. Second, HOMA calculations assume steady-state fasting conditions and may be less accurate in patients with very high glucose levels ($>180\text{mg/dL}$ (10 mmol/L)) or very low insulin levels seen in advanced beta cell failure. Third, the HOMA-IR thresholds vary in the literature, and the thresholds used in the calculator represent a reasonable interpretation among several published options [14]. Finally, long-term follow-up will be needed to confirm durability of these metabolic improvements.

Conclusion

Integrated metabolic assessment combining HOMA1 indices, TyG index, metabolic syndrome assessment and quantitative diabetes risk prediction, and cardiovascular risk provides clinicians with a comprehensive cardiometabolic assessment, far more informative than fasting glucose and HbA1c testing alone. This freely available web-based calculator addresses the need for practical tools that can identify high-risk individuals, characterize their metabolic phenotype, and motivate behavioral change through personalized risk communication. The addition of lipid panel analysis with Lp(a) integration and lifetime cardiovascular risk visualization extends the tool's utility beyond diabetes prevention to comprehensive cardiometabolic risk assessment. Interpretive AI summary generation presents the findings as actionable outcomes but should be discussed with a physician. The case presented demonstrates that even young adults with severe metabolic dysfunction can achieve remarkable improvements with intensive, targeted intervention guided by comprehensive metabolic phenotyping.

Patient Consent

Verbal informed consent was obtained from the patient for anonymous publication of this case report, including clinical data, laboratory results, and metabolic trajectory visualization. All identifying information has been removed to protect patient confidentiality.

Conflicts of Interest

The authors declare no conflicts of interest related to this work. The web-based calculator described in this report is freely available for clinical and educational use with no commercial interests.

References

1. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021.
2. Al-Rifai RH, Abdo NM, Paulo MS, et al. Prevalence of type 2 diabetes mellitus among citizens of the United Arab Emirates: results of the UAE National Diabetes and Lifestyle Study. *BMJ Open Diabetes Res Care*. 2020;8(2):e001260.
3. Al-Mawali A, Jayapal SK, Morsi M, et al. Prevalence and risk factors of diabetes in a large community-based study in the Sultanate of Oman: STEPS survey 2017. *BMC Endocr Disord*. 2021;21(1):179.
4. Al-Lawati JA, Al-Riyami AM, Mohammed AJ, Jousilahti P. Increasing prevalence of diabetes mellitus in Oman. *Diabet Med*. 2002;19(11):954-957.
5. Lascar N, Brown J, Pattison H, et al. Type 2 diabetes in adolescents and young adults. *Lancet Diabetes Endocrinol*. 2018;6(1):69-80.
6. Al-Haddad F, Al-Nuaimi Y, Little BB, Thabit M. Prevalence of obesity among school children in the United Arab Emirates. *Am J Hum Biol*. 2000;12(4):498-502.
7. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014;384(9945):766-781.
8. Hippisley-Cox J, Coupland C. Development and validation of QDiabetes-2018 risk prediction algorithm to estimate future risk of type 2 diabetes: cohort study. *BMJ*. 2017;359:j5019.

9. Kengne AP. The ADVANCE cardiovascular risk engine and the UKPDS risk engine in the ADVANCE study. *Eur Heart J*. 2011;32(2):223-224.
10. Abbasi A, Peelen LM, Corpeleijn E, et al. Prediction of risk of type 2 diabetes by metabolic mediators. *Diabetes Care*. 2012;35(9):1907-1909.
11. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet*. 2004;363(9403):157-163.
12. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28(7):412-419.
13. Levy JC, Matthews DR, Hermans MP. Correct Homeostasis Model Assessment (HOMA) evaluation uses the computer program. *Diabetes Care*. 1998;21(12):2191-2192.
14. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. *Diabetes Care*. 2004;27(6):1487-1495.
15. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord*. 2008;6(4):299-304.
16. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J Clin Endocrinol Metab*. 2010;95(7):3347-3351.
17. Du T, Yuan G, Zhang M, et al. Clinical usefulness of lipid ratios, visceral adiposity indicators, and the triglycerides and glucose index as risk markers of insulin resistance. *Cardiovasc Diabetol*. 2014;13:146.
18. Vasques AC, Novaes FS, de Oliveira MS, et al. TyG index performs better than HOMA-IR in the Brazilian population: a hyperglycemic clamp validated study. *Diabetes Res Clin Pract*. 2011;93(3):e98-e100.
19. Buchanan TA. Pancreatic beta-cell loss and preservation in type 2 diabetes. *Clin Ther*. 2003;25 Suppl B:B32-B46.
20. 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(16):1640-1645.
21. Sampson M, Ling C, Sun Q, et al. A new equation for calculation of low-density lipoprotein cholesterol in patients with normolipidemia and/or hyperlipidemia. *JAMA Cardiol*. 2020;5(5):540-548.
22. Burgess S, Ference BA, Staley JR, et al. Association of LPA variants with risk of coronary disease and the implications for lipoprotein(a)-lowering therapies: a Mendelian randomization analysis. *JAMA Cardiol*. 2018;3(7):619-627.
23. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121(4):586-613.
24. Houts PS, Doak CC, Doak LG, Loscalzo MJ. The role of pictures in improving health communication: a review of research on attention, comprehension, recall, and adherence. *Patient Educ Couns*. 2006;61(2):173-190.

25. Kripalani S, Weiss BD. Teaching about health literacy and clear communication. *J Gen Intern Med.* 2006;21(8):888-890.
26. DeFronzo RA. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes.* 2009;58(4):773-795.
27. Weyer C, Bogardus C, Mott DM, Pratley RE. The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. *J Clin Invest.* 1999;104(6):787-794.
28. Walker JG, Mackinnon AJ, Batterham M, et al. Impact of risk presentation on intentions to change health behaviours: a systematic review. *Patient Educ Couns.* 2015;98(11):1345-1357.