

# Review of the Quantitative Insulin Sensitivity Check Index (QUICKI) Calculator

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### Abstract

The Quantitative Insulin Sensitivity Check Index (QUICKI) is a validated surrogate marker for estimating insulin resistance in individuals at elevated metabolic risk. QUICKI demonstrates strong correlation with gold standard measurements, particularly in patients with obesity, type 2 diabetes, and metabolic syndrome, but performs sub-optimally in healthy or African American cohorts. While not recommended for individual diagnosis, QUICKI remains a valuable non-invasive tool for population-level research. This review outlines its clinical utility, strengths, and limitations.

### 1. HOW TO USE

#### When to Use

QUICKI's primary utility is in large-scale epidemiological research settings where it is well-suited for detecting group-level differences and tracking changes in insulin sensitivity over time in response to interventions. It may also serve as a supplementary tool to support patient counseling and risk communication, with the understanding that individual values should not be used as a standalone diagnostic threshold. High-risk groups in whom QUICKI estimation may be informative include obesity or increased waist circumference, dyslipidemia, impaired fasting glucose or impaired glucose tolerance, hypertension, physical stigmata of insulin resistance (e.g., acanthosis nigricans, central adiposity), polycystic ovarian syndrome (PCOS), elevated cardiovascular-kidney-metabolic (CKM) risk, metabolic dysfunction-associated steatotic liver disease (MASLD).<sup>1-5</sup>

#### Pearls / Pitfalls

The index has strong correlation with euglycemic clamp (gold standard) in adults with obesity, type 2 diabetes, prediabetes and metabolic syndrome.<sup>6</sup> It also has a low coefficient of variation (0.05) and high discriminant ratio (10), making it more sensitive to detect differences in groups and tracking therapeutic changes over time.<sup>7</sup> There are also a few challenges with the calculator. The test is unreliable in the African American population where there was no significant correlation with the eu-

glycemic clamp.<sup>8</sup> It also demonstrates reduced accuracy (lower correlation with the euglycemic clamp) and reduced reliability (increased measurement variability) in healthy, normal-weight subjects, which limits its applicability in these individuals.<sup>9</sup> Furthermore, considerable overlap in individual scores across quartiles reduces its effectiveness for identifying insulin resistance in individual patients.<sup>10</sup> Values are insulin assay dependent, so can fluctuate widely depending on the laboratory used. As a result, reference intervals need to be individualized.

#### Why Use

Direct methods (hyperinsulinemic-euglycemic clamp) for measuring insulin resistance are resource intensive, invasive, and time consuming. QUICKI offers a practical non-invasive surrogate for population-level research and large-scale epidemiological studies. While aggregate findings from cohort studies using QUICKI can inform general patient education about metabolic risk, the index should not be applied as the sole diagnostic or risk-stratification tool for any individual patient. With this in mind some practical applications include serial monitoring of insulin sensitivity in response to lifestyle or pharmacological interventions, where trend direction over time is more meaningful than any single value; and supplementary patient counseling, where objective longitudinal data can help motivate adherence to treatment.

Both QUICKI and HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) are derived from fasting glucose and insulin and show similar overall correlation with the euglycemic clamp ( $r = 0.61$  vs.  $0.60$ ).<sup>10</sup>

QUICKI's key advantage is its higher discriminant ratio (10 vs. 1.6 for HOMA-IR) and lower cross-validation prediction error (1.45 vs. 3.17), making it more sensitive for detecting group differences and tracking therapeutic change.<sup>11</sup> HOMA-IR, by contrast, benefits from wider clinical familiarity and more established population-level cut-off values. In practice, HOMA-IR is preferred in the clinic to help recognize the presence of insulin resistance as it's easy to demonstrate to patients that higher values mean more insulin resistance, while QUICKI is the better choice when sensitivity to therapeutic change is the primary objective; ideally used in research settings but also as an adjunct to objectively document therapeutic change.

## II. NEXT STEPS

### Advice

There is no single universally accepted QUICKI cutoff in the United States, as the original developers emphasized that each laboratory should establish its own reference range due to insulin assay variability. However, the **most commonly cited threshold for insulin resistance is <0.357**, derived from the original validation study's 95% confidence interval lower limit in healthy subjects.<sup>12</sup>

Higher QUICKI values indicate greater insulin sensitivity and lower insulin resistance.

In healthy adults, fasting QUICKI values were approximately 0.366 (SD  $\pm$  0.029), based on the original validation cohort.<sup>12</sup> Note that these reference values were derived from a specific study population and may not be directly transferable across all demographics.

### Management

There are no validated management algorithms or guidelines using the QUICKI score. When monitoring a patient longitudinally, trending direction over time is more meaningful clinically than any single QUICKI value. Lifestyle intervention forms the foundation of management. Evidence supports Mediterranean, DASH (Dietary Approaches to Stop Hypertension), and low-carbohydrate diets as effective approaches. Regular physical activity, combining aerobic exercise with muscle-strengthening activities  $\geq 3$  times weekly, independently increases insulin sensitivity and reduces fasting insulin levels.<sup>13-15</sup> Pharmacological agents may be employed when lifestyle modification is insufficient to achieve control. Patients with obesity or prediabetes benefit from glucagon-like peptide (GLP-1) agonists, or dual (GLP-1 + glucose-dependent insulintropic peptide) agonists with a goal of promoting weight loss.<sup>16</sup> Metformin and pioglitazone both improve QUICKI scores in patients with type 2 diabetes, with pioglitazone producing the larger effect (QUICKI increase 0.019 for pioglitazone vs. 0.011 for

metformin at 52 weeks).<sup>17</sup> However, these findings are limited to patients with type 2 diabetes or obesity, and should not be extrapolated to individuals with normal weight.

### Critical Actions

N/A

## III. EVIDENCE

### Evidence Appraisal

The main formula was derived and validated from 56 subjects (age between 40–50 years) who had hyperinsulinemic euglycemic glucose clamp and insulin-modified frequently sampled intravenous glucose tolerance tests performed. The study population was further divided into 3 groups – 28 (15 Men, 13 Women) non-obese subjects, 13 (5 Men, 8 Women) obese subjects, and 15 (7 Men and 8 Women) patients with type 2 diabetes.<sup>6</sup> A sensitivity analysis demonstrated that fasting insulin ( $I_0$ ) and fasting glucose ( $G_0$ ) contain critical information about insulin sensitivity. This led to the mathematical formulation  $1/[\log(I_0) + \log(G_0)]$ , where insulin is measured in  $\mu\text{U/mL}$  and glucose in  $\text{mg/dL}$ . QUICKI correlated with clamp-derived insulin sensitivity at  $r = 0.78$  ( $r$  = correlation coefficient). The index showed a normal distribution and strong reproducibility, with a very low coefficient of variation (0.05) and a high discriminant ratio (10). Its performance closely matched that of the hyperinsulinemic clamp and exceeded that of other basic fasting measures such as HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) or fasting insulin.

Chen et al evaluated predictive performance in a validation cohort of 116 participants and showed that QUICKI was markedly more accurate than other simple surrogate indices for estimating clamp-derived insulin sensitivity like HOMA-IR, with a much lower cross-validation prediction error (1.45 vs. 3.17 for HOMA;  $p < 0.001$ ).<sup>11</sup>

Regarding performance across a broad spectrum of fasting glucose values, Yokoyama et al. showed that QUICKI strongly correlated with clamp-derived insulin sensitivity ( $r = 0.615$ – $0.788$ , all  $p < 0.001$ ), with the strength of the correlation increasing with higher glucose values in Japanese patients with type 2 diabetes (74 men and 34 women with a mean age of 52 years).<sup>18</sup>

Otten et al.'s meta-analysis, which combined results from 35 studies, showed that QUICKI correlated with clamp-derived insulin sensitivity at  $r = 0.61$  (95% CI 0.55–0.65). Among fasting-based measures, only the revised QUICKI performed better, with a correlation of  $r = 0.68$  (95% CI 0.58–0.77).<sup>19</sup>

Pisprasert et al. specifically examined racial differences and reported that QUICKI failed to correlate signifi-

cantly with euglycemic clamp-derived insulin sensitivity in African American participants, in contrast to its performance in non-Hispanic White participants.<sup>20</sup> The underlying physiological explanation relates to unique metabolic characteristics in African Americans, driven by higher fasting insulin levels independent of obesity and body fat distribution due to lower hepatic insulin clearance.<sup>21</sup> More inclusive validation studies are needed before QUICKI can be confidently applied across diverse populations.

The revised QUICKI adds fasting free fatty acid (FFA) levels to the original QUICKI equation, defined as  $1 / [\log(\text{fasting insulin}) + \log(\text{fasting glucose}) + \log(\text{fasting FFA})]$ . Including FFAs significantly enhances its correlation with clamp-derived insulin sensitivity in non-obese individuals compared with the standard QUICKI.<sup>22</sup> Fasting free fatty acid measurements are

more difficult to obtain (i.e., requires specialized assays that are less commonly available in clinical laboratories) than fasting glucose and insulin measurements when calculating the revised QUICKI, which limits its practical application despite superior performance in certain populations.

### Formula

$$1 / [\log(I_0) + \log(G_0)]$$

$I_0$ - Fasting insulin  $\mu\text{U/mL}$   
 $G_0$ - Fasting glucose in  $\text{mg/dL}$

### Facts & Figures

N/A

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