

## *InsuTAG and Early Salutogenic Screening of Cardiometabolic Risk in Obese Adolescents*

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### ABSTRACT

**Background:** Insulin resistance (IR) is considered the common underlying cause of metabolic syndrome (MetS). Predicting the incidence of MetS and IR at the individual level is essential, especially in obese adolescents who are at high risk of cardiovascular disease (CVD). InsuTAG has shown reliable results in predicting IR and MetS in healthy elderly populations. This study aimed to investigate the use of InsuTAG as an assessment tool to predict IR and MetS in obese adolescents, using the homeostasis model assessment (HOMA) to quantify insulin resistance. **Methods:** A cross-sectional analytic study was conducted from January to May 2020 in healthy obese adolescents aged 13-18 years-old. Blood analyses included lipid profile (LDL-c, HDL-c, total cholesterol, and triglycerides), fasting blood glucose, and fasting insulin. IR was defined as HOMA-IR > 5.22 for boys and > 3.82 for girls during the pubertal period. **Results:** The receiver operating characteristic (ROC) curve for InsuTAG demonstrated a greater area under the curve (AUC) for identifying IR than MetS (0.877 vs. 0.743,  $p = 0.000$ ; 95% CI). The optimal InsuTAG cut-off to determine IR was > 23.48, with 78.43% sensitivity and 87.38% specificity. The cut-off to identify MetS was > 23.36, yielding 67.97% sensitivity and 72.82% specificity. **Conclusion:** InsuTAG is a useful tool for identifying IR and MetS. The optimal cut-off values are > 23.48 for IR and > 23.36 for MetS in obese adolescents. These findings support early prevention and health promotion efforts, ultimately strengthening self-care practices among obese adolescents.

**Keywords:** HOMA-IR, InsuTag, IR, MetS, Obese Adolescents

### INTRODUCTION

Adolescent obesity in Indonesia presents an urgent public health challenge. National data indicates a persistent burden among adolescents aged 13-15 years, where the prevalence of overweight increased from 11.20% in 2018 to 12.10% in 2023, while obesity prevalence remains significant at 4.10% (Ministry of Health RI, 2018, 2023). This condition places adolescents at high risk of developing Metabolic Syndrome (MetS), a cluster of metabolic abnormalities including abdominal obesity, dyslipidemia, and hypertension that increase the risk of

cardiovascular disease (Canale *et al.*, 2013). Insulin resistance (IR) is considered the common underlying cause of MetS (Cho *et al.*, 2017). Therefore, early detection and intervention at this stage are crucial to prevent long-term comorbidities and improve quality of life in adulthood (Belhayara *et al.*, 2020); (Lee and Sanders, 2012).

Addressing this double burden requires a paradigm shift from merely treating disease (pathogenesis) towards creating health (salutogenesis). According to Antonovsky, the key to adolescents

successfully adopting a healthy lifestyle lies in the formation of a strong Sense of Coherence (SoC). This encompasses the capacity to comprehend health status (comprehensibility), manage available resources (manageability), and find emotional meaning in maintaining health (meaningfulness) (Mittelmark and Bauer, 2022). To build this SoC, adolescents require detection tools capable of providing objective risk feedback to serve as motivators for behavioral change.

Although biomarker feedback alone may not be sufficient, studies show that its effectiveness increases significantly when combined with appropriate support to enhance adolescent self-efficacy (Li *et al.*, 2025). Currently, several assessments have been established to predict IR and MetS, such as HOMA-IR, the TyG index, and lipid ratios (Chu *et al.*, 2019); (Irace *et al.*, 2013); (Kurtoğlu *et al.*, 2010). However, a more practical yet accurate method is needed to support mass screening and education. InsuTAG has shown reliable results in predicting IR and MetS in a healthy elderly population (Thota *et al.*, 2017), but its utility in obese adolescents has not been widely explored.

Therefore, this study aims to investigate the accuracy of InsuTAG in predicting IR and MetS in obese adolescents using HOMA-IR as the assessment standard. This validation is essential to position InsuTAG as a strategic instrument supporting promotive and preventive interventions within the salutogenic framework, helping adolescents detect risks early and build awareness for a healthier life.

## METHODS

A cross-sectional analytic study was conducted from January to May 2020 in junior and senior high schools in Sidoarjo and Surabaya.

### Population and samples

The study population consisted of obese adolescents aged 13-18 years from junior and senior high schools in Sidoarjo and Surabaya, East Java, Indonesia. The research sample was selected randomly based on BMI calculations to determine obesity. Eligible subjects were required to be healthy and meet the following criteria: not taking corticosteroids or dyslipidemia medications within the past 3 months, not

taking antibiotics, not smoking, not undergoing hormonal therapy, not consuming alcohol or drugs that affect body composition, and not having infections, immune disorders, or endocrine disorders.

Before enrollment, the researchers visited the selected schools to present the study plan to the parents and teachers. When parents agreed to allow their children to participate by signing informed consent forms, blood collection and anthropometric measurements were scheduled for the following week. One day prior to data collection, subjects were instructed to fast for 12 hours after their last meal. Blood samples were collected in the morning after the 12-hour fasting period.

A total of 5 senior high schools and 8 junior high schools agreed to participate, resulting in 473 students screened during the initial phase. However, 135 students were excluded because they had eaten breakfast before coming to school or because their parents did not provide consent, leaving 339 eligible subjects. After further screening based on BMI, only 268 subjects met the criteria for obesity and were included in the study. The remaining 71 students were classified as overweight or normal weight, as illustrated in Figure 1. The final sample size met the minimum requirement of 260 subjects based on the Lemeshow formula.

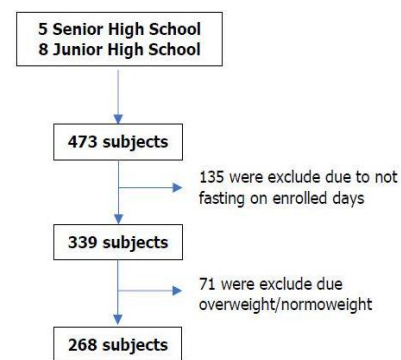


Figure 1. Subject's recruitment flowchart

### Anthropometry measurements

Body weight was measured using a digital stepping scale (Seca Robusta 813) with an accuracy of 0.1 kg. Measurements were taken with the subjects standing upright, without footwear or accessories. Height was measured using a Seca 206

microtoise with an accuracy of 0.1 cm, from the vertex of the head to the heel, with the subjects standing straight and not wearing footwear or headgear. Body mass index (BMI) was calculated using the formula: body weight (kg) / height (m<sup>2</sup>).

Waist circumference was measured using a flexible tape measure with 0.1 cm accuracy, at the midpoint between the lowest rib and the iliac crest, at the end of a normal expiration. Hip circumference was measured at the widest part of the hips, around the point of greatest gluteal protrusion.

### Blood analysis

Blood samples were drawn from the cubital vein in the morning after the subjects had fasted for 12 hours. A total of 5 mL of blood was collected by laboratory staff and placed into an EDTA-containing tube. Using a cooling box, the samples were transported to the laboratory for further analysis, including lipid profile (LDL-c, HDL-c, total cholesterol, and triglycerides), fasting blood glucose, and fasting insulin. Blood pressure was measured using an Omron automatic blood pressure monitor (HEM-8712).

### IR and Mets determination

HOMA-IR was calculated using formula:

$$HOMA-IR \equiv \left[ \text{Fasting blood glucose} \left( \frac{mg}{dL} \right) \times \text{insulin} \left( \frac{\mu U}{L} \right) \right] \div 405$$

The determination of IR if HOMA-IR > 5.22 for boys and > 3.82 for girls in pubertal periods (Kurtoğlu *et al.*, 2010).

MetS in this study must meet the IDF criteria (Al-Hamad and Raman, 2017); (Zimmet *et al.*, 2007) if we found out 3 of the 5 criteria for risk factors are obtained, namely abdominal obesity accompanied by two other criteria:

1. hypertension (systole pressure > 130 mmHg or diastole > 85mmHg),
2. hyperglycemia (if fasting blood glucose (FBG) > 100 mg/dL),
3. hypertriglyceridemia (if triglyceride > 150 mg/dL in subjects > 16 years old; and > 110 in subjects < 16 years old) and
4. low-level HDL-c (HLD-c < 40 mg/dL for adolescents < 16 years old; < 40 mg/dL for boys and < 50 mg/dL for girls with age >16 years old).

InsuTAG calculated using the formula [14]:

$$InsuTAG = \text{fasting insulin} \left( \frac{\mu U}{L} \right) \times \text{fasting TG} \left( \frac{mmol}{L} \right)$$

TG (mg/dl) converts to mmol/l using online converter available at [http://www.scymed.com/en/smnxpb/pbxhd419\_c.htm].

All the data must be completed. If the data was missing, the researchers visit the student to complete the data.

### Variables

Dependent: IR (IR vs. non-IR) and MetS (MetS vs. non-MetS) to investigate InsuTAG sensitivity.

Independent: age, body weight, body height, body mass index (BMI), waist circumference (WC), hip circumference (HC), WHR (waist-to-hip ratio) and WHtR (Weight-to-height ratio), fasting blood glucose (FBG), fasting insulin, total cholesterol, low-density lipoprotein-cholesterol (LDL-c), high-density lipoprotein (HDL-c), triglyceride (TG), systole blood pressure (systole-BP) and diastole blood pressure (diastole-BP), HOMA IR and InsuTAG.

### Statistical analysis

Tests of normality and homogeneity were performed. Data were considered normally distributed if  $p > 0.05$  based on the Kolmogorov-Smirnov test, and homogeneous if  $p > 0.05$  based on Levene's test of homogeneity. Further analyses included the paired-sample t-test or the Mann-Whitney U test, depending on data distribution. For correlation analyses, Pearson's correlation or Spearman's Rho correlation was used, with statistical significance set at  $p < 0.05$ .

Receiver operating characteristic (ROC) analysis was performed using SPSS version 21 (IBM). Cut-off points were determined based on the highest Youden Index, calculated using NCSS 12 (NCSS, LLC).

### Ethical Clearance

The study has been reviewed and approved by the Research and Ethics Scientific Committee number No. 65/EC/KEPK/FKUA/2020 released by Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, and declared to be appropriate.

## RESULTS AND DISCUSSION

### Result

The characteristics of the subjects are summarized in Table 1. A total of 256 subjects were enrolled in this study, consisting of 56.25% boys and 43.75% girls. The average age was  $179.91 \pm 17.45$  months, with a minimum age of 147 months and a maximum age of 226 months. The mean body weight was  $83.56 \pm 13.69$  kg (range: 53.50-130.00 kg), and the mean height was  $160.79 \pm 7.74$  cm (range: 140.80-186.00 cm). The average BMI was  $32.19 \pm 4.28$  kg/m<sup>2</sup> (range: 25.32-47.57). The mean waist circumference (WC) was  $97.71 \pm 10.45$  cm (range: 74.00-123.00 cm), and the mean hip circumference (HC) was  $107.78 \pm 9.50$  cm (range: 85.00-143.00 cm).

Body weight, BMI, WC, HC, waist-to-hip ratio (WHR), and waist-to-height ratio

(WHtR) were significantly higher among subjects with MetS compared with those without MetS ( $p < 0.05$ ). Among subjects with IR, body weight, BMI, WC, HC, and WHtR were significantly higher than in the non-IR group ( $p < 0.05$ ). However, no significant differences were observed in height or WHR between the IR and non-IR groups ( $p > 0.05$ ).

Fasting blood glucose (FBG) and total cholesterol levels were significantly higher in the IR group compared with the non-IR group ( $p < 0.05$ ), but no significant differences were found between the MetS and non-MetS groups ( $p > 0.05$ ). Triglyceride (TG) levels and diastolic blood pressure were significantly higher in the MetS group than in the non-MetS group ( $p < 0.05$ ), while no significant differences were observed between the IR and non-IR groups ( $p > 0.05$ ).

Table 1. Subject's characteristics

Variables	Mean $\pm$ SD	MetS (n=103)	Non-MetS (n=153)	p	IR (n=103)	Non-IR (n=153)	p
Age (months)	179.91 $\pm$ 17.45	180.40 $\pm$ 17.93	179.58 $\pm$ 17.18	0.714	178.74 $\pm$ 18.16	180.69 $\pm$ 16.983	0.277
Body weight (kg)	83.56 $\pm$ 13.69	88.17 $\pm$ 13.62	80.45 $\pm$ 12.88	0.000	85.92 $\pm$ 12.25	81.97 $\pm$ 12.25	0.023
Body height (cm)	160.79 $\pm$ 7.74	163.06 $\pm$ 8.05	159.26 $\pm$ 7.15	0.000	160.61 $\pm$ 7.40	160.91 $\pm$ 7.98	0.759
BMI (kg/m <sup>2</sup> )	32.19 $\pm$ 4.28	33.08 $\pm$ 4.22	31.60 $\pm$ 4.23	0.006	33.07 $\pm$ 0.50	31.61 $\pm$ 3.80	0.007*
WC (cm)	97.71 $\pm$ 10.45	100.54 $\pm$ 10.46	95.81 $\pm$ 10.03	0.000	99.48 $\pm$ 9.71	96.52 $\pm$ 9.71	0.026*
HC (cm)	107.78 $\pm$ 9.50	109.64 $\pm$ 9.16	106.53 $\pm$ 9.54	0.010	109.91 $\pm$ 10.40	106.35 $\pm$ 8.58	0.003
WHR	0.91 $\pm$ 0.07	0.91 $\pm$ 0.07	0.90 $\pm$ 0.07	0.044	0.91 $\pm$ 0.1	0.908 $\pm$ 0.07	0.730
WHtR	0.61 $\pm$ 0.06	0.62 $\pm$ 0.06	0.60 $\pm$ 0.06	0.050	0.62 $\pm$ 0.07	0.60 $\pm$ 0.056	0.012
FBG (mg/dl)	85.16 $\pm$ 7.33	85.98 $\pm$ 8.65	84.62 $\pm$ 6.26	0.146	87.17 $\pm$ 8.19	83.82 $\pm$ 6.36	0.000
Fasting insulin ( $\mu$ U/L)	22.53 $\pm$ 14.58	27.84 $\pm$ 18.71	18.95 $\pm$ 9.48	0.000	34.67 $\pm$ 15.89	14.35 $\pm$ 4.49	0.000*
Total cholesterol (mg/dl)	173.37 $\pm$ 32.28	177.02 $\pm$ 26.74	170.92 $\pm$ 35.39	0.139	181.33 $\pm$ 32.06	168.02 $\pm$ 31.41	0.001
LDL-c (mg/dl)	113.95 $\pm$ 27.92	118.51 $\pm$ 22.37	110.87 $\pm$ 30.79	0.031	120.64 $\pm$ 28.61	109.44 $\pm$ 26.59	0.002
HDL-c (mg/dl)	43.35 $\pm$ 7.75	39.00 $\pm$ 6.87	46.28 $\pm$ 6.92	0.000	41.83 $\pm$ 8.31	44.38 $\pm$ 7.21	0.010
TG (mg/dl)	115.78 $\pm$ 64.53	144.84 $\pm$ 64.01	96.22 $\pm$ 57.25	0.000	136.42 $\pm$ 66.69	136.42 $\pm$ 59.31	0.207
Systole-BP (mmHg)	123.97 $\pm$ 13.16	130.50 $\pm$ 10.99	119.57 $\pm$ 12.70	0.000	126.00 $\pm$ 12.15	122.60 $\pm$ 13.68	0.043

Variables	Mean $\pm$ SD	MetS (n=103)	Non-MetS (n=153)	p	IR (n=103)	Non-IR (n=153)	p
Diastole-BP (mmHg)	81.72 $\pm$ 10.22	86.77 $\pm$ 9.50	78.33 $\pm$ 9.27	0.000	82.32 $\pm$ 10.60	81.33 $\pm$ 9.98	0.447
HOMA-IR	4.78 $\pm$ 3.27	5.99 $\pm$ 4.25	3.97 $\pm$ 2.03	0.000	7.48 $\pm$ 3.61	2.96 $\pm$ 0.94	0.000
InsuTAG	32.92 $\pm$ 40.03	49.59 $\pm$ 54.50	21.70 $\pm$ 19.49	0.000 *	56.40 $\pm$ 53.28	17.12 $\pm$ 12.58	0.000*
Paired sample T-test * Mann Witney significant if p>0.05							

There were significant differences in fasting insulin, adiponectin, LDL-c, HDL-c, systolic blood pressure, HOMA-IR, and InsuTAG not only between the MetS and non-MetS groups but also between the IR and non-IR groups. All variables are presented in Table 1.

The frequency of MetS in the study population was 39.5%, while the prevalence of IR was 40.2%. Abdominal obesity was the most common component, present in 91.8% of subjects. Dyslipidemia was observed in 70.7% of subjects, including low HDL-c levels (43%) and hypertriglyceridemia (41%). Hypertension was found in 41.4% of subjects, whereas hyperglycemia had the lowest prevalence at 3.9%. The distribution of MetS components is summarized in Figure 2.

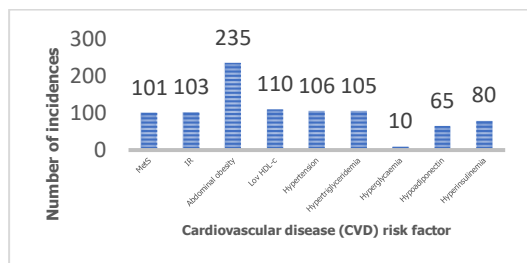


Figure 2. Frequencies of cardiovascular disease (CVD) risk factor in obese adolescents

The correlations between InsuTAG and anthropometric measurements and MetS parameters are summarized in Table 2. InsuTAG was significantly correlated with BMI ( $r = 0.256$ ,  $p = 0.035$ ), body weight ( $r = 0.182$ ,  $p = 0.003$ ), body height ( $r = 0.128$ ,  $p = 0.040$ ), and waist circumference (WC) ( $r = 0.016$ ,  $p = 0.011$ ). However, it did not correlate with hip circumference (HC), waist-to-hip ratio (WHR), or waist-to-height ratio (WHtR) ( $p > 0.05$ ). InsuTAG was not correlated with fasting blood glucose (FBG) or blood pressure ( $p > 0.05$ ), but showed significant correlations with

lipid profiles, adiponectin, and fasting insulin ( $p < 0.05$ ).

Table 2. Correlation between InsuTAG with anthropometric parameters, lipid profiles and blood pressures

Parameters	r	p
BMI	0.256	0.035
Body weight	0.182	0.003
Body Height	0.128	0.040
WC	0.160	0.011
HC	0.114	0.068
WHR	0.069	0.270
WHtR	0.111	0.077
FBG	0.049	0.432
TG	0.690	0.000
HDL-c	-0.278	0.000
LDL-c	0.133	0.034
Total cholesterol	0.218	0.000
Systole-BP	0.120	0.055
Diastole-BP	0.000	0.998
Adiponectin	-0.197	0.002
Fasting Insulin	0.770	0.000
HOMA-IR	0.770	0.000

The receiver operating characteristic (ROC) analysis for InsuTAG demonstrated a greater area under the curve (AUC) for identifying IR than MetS (0.877 vs. 0.743,  $p = 0.000$ ; 95% CI), as shown in Figures 3 and 4. The optimal InsuTAG cut-off point for determining IR was  $> 23.48$ , with a sensitivity of 78.43% and a specificity of 87.38%. The optimal cut-off point for identifying MetS was  $> 23.36$ , with 67.97% sensitivity and 72.82% specificity, based on the highest Youden Index.

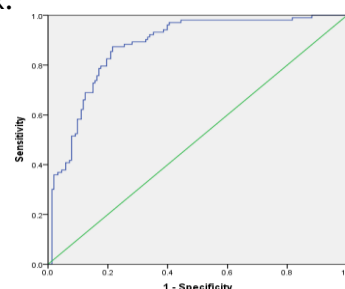


Figure 3. Receiving operation curve (ROC) of InsuTAG to determines IR

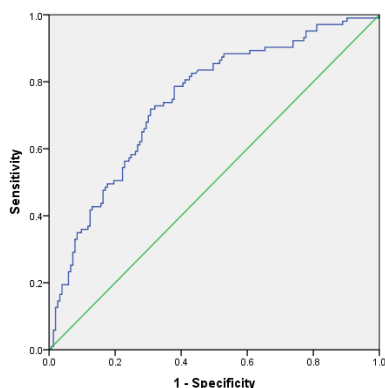


Figure 4. Receiving operation curve (ROC) of InsuTAG to determine MetS

## Discussion

Central obesity is a major risk factor for MetS, with IR playing a central role in the associated comorbidities and mortality. Metabolic abnormalities linked to IR are most commonly observed in individuals with abdominal obesity. Adolescents with IR have a significantly higher prevalence of MetS than those without IR (88.23% vs. 11.77%) (Adnan, Rahman and Faridin, 2019). IR accompanied by central obesity increases the risk of hypertension due to alterations in the renin-angiotensin-aldosterone system (RAAS) (Canale *et al.*, 2013).

In this study, body weight, BMI, WC, WHR, and WHtR were significantly higher among subjects with MetS and IR. Body weight is an important indicator of fat mass accumulation and a major determinant of IR (Lee *et al.*, 2006), while WC is considered a more reliable predictor of MetS in the pediatric population than in adults (González-Jiménez *et al.*, 2016). A study in Brazil similarly reported significantly higher BMI, WC, and WHR in adolescents with MetS, as well as significant differences in blood pressure, fasting insulin, HOMA-IR, and triglycerides (Adnan, Rahman and Faridin, 2019). However, their findings regarding FBG and HDL-c differ from those of the present study. Another study in adults showed higher WHR, triglycerides, and LDL-c, and a lower HDL-c level in individuals with MetS, consistent with our findings, although total cholesterol did not differ significantly (Wang *et al.*, 2017).

Scientific evidence has established relationships between insulin, IR, BMI, WC, and WHtR in pediatric obesity (Manios *et al.*, 2008), which aligns with our results. Some authors have identified WC as the strongest anthropometric predictor of IR

(Wedin, Diaz-Gimenez and Convit, 2012), whereas others report that higher BMI is associated with higher HOMA-IR (Gandhe, Lenin and Srinivasan, 2013). Although BMI is not the strongest predictor of cardiovascular disease, it remains an easy, cost-effective method for detecting abnormal body composition and is associated with IR incidence (Lee *et al.*, 2006). Still, complementary anthropometric indicators (including WC, WHR, and WHtR) provide more nuanced assessments of visceral adiposity (Wang *et al.*, 2017). Previous studies have also demonstrated significant differences in BMI, WC, FBG, fasting insulin, HOMA-IR, systolic blood pressure, and lipid parameters between IR and non-IR groups, consistent with the present findings (González-Jiménez *et al.*, 2016).

Prior research evaluating InsuTAG in elderly subjects reported larger AUC values for predicting IR (0.93 vs. 0.88) and MetS (0.79 vs. 0.74) compared to this study (Thota *et al.*, 2017). Similar to our findings, InsuTAG has been shown to correlate with BMI and WC (Thota *et al.*, 2017). Additionally, our study found correlations with body weight, height, lipid profiles, adiponectin, and fasting insulin. Unlike previous findings, InsuTAG did not correlate with age ( $r = -0.063$ ,  $p = 0.316$ ) in this study. We also identified higher cut-off values for predicting IR and MetS ( $> 23.48$  and  $> 23.36$ , respectively) compared to the previous elderly population study ( $> 11.2$ ), which is expected given the different metabolic characteristics of adolescents.

These findings carry meaningful implications in the broader public health context. Beyond its clinical utility, InsuTAG has the potential to function as a practical tool in school-based health screening programs. This is aligned with evidence showing that educational institutions are strongly committed to preventing and managing obesity to support learning and student performance (Restuastuti, Chandra and Batubara, 2020). Integrating InsuTAG into school health activities provides objective data that can be translated into personalized educational materials. Qualitative studies highlight that adolescents respond positively to individualized, non-judgmental health feedback, as it validates their healthy behaviors and

strengthens their autonomy in decision-making (Veiga *et al.*, 2022).

Within a salutogenic framework, early identification of metabolic risk using InsuTAG may enhance metabolic resilience by strengthening adolescents' Sense of Coherence (SoC). Since SoC is positively associated with healthier eating behavior (Veiga *et al.*, 2022), awareness of individual metabolic risk through InsuTAG scoring can improve comprehensibility as one of the key dimensions of SoC, thereby motivating adolescents to adopt better dietary habits. Thus, InsuTAG serves not only as a predictive biomarker of disease risk but also as a potential tool to empower adolescents to develop adaptive coping strategies within an increasingly obesogenic environment.

## CONCLUSION

InsuTAG is a useful indicator for identifying insulin resistance (IR) and metabolic syndrome (MetS). In obese adolescents, the optimal cut-off values are >23.48 for IR and >23.36 for MetS. Beyond its diagnostic value, early detection using InsuTAG contributes meaningfully to salutogenic health promotion. By providing objective risk information, InsuTAG enhances awareness, guides targeted education, and supports sustainable behavioral change, thereby facilitating health maintenance and reducing the long-term risk of cardiovascular complications.

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