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(REVIEW ARTICLE)

Redefining pediatric metabolic syndrome: Toward precision, puberty-adjusted, and globally scalable diagnostic criteria

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Abstract

Background: The diagnosis of metabolic syndrome (MetS) in children and adolescents has been historically derived from adult-based definitions, despite significant physiological differences during growth and puberty. The lack of pediatric-specific, developmentally sensitive criteria has resulted in inconsistent prevalence estimates, poor cross-study comparability, and limited clinical utility. This review aims to critically examine historical and emerging approaches to MetS diagnosis in pediatrics, highlighting challenges, innovations, and the need for global consensus.

Methods: A structured narrative review methodology was employed. Relevant literature from 2000 to 2025 was retrieved from PubMed, Scopus, and Web of Science using terms such as "pediatric metabolic syndrome," "childhood MetS definitions," "z-score metabolic risk," and "continuous MetS score." Studies comparing diagnostic criteria, proposing novel tools, or evaluating prevalence variability in children were prioritized. Data were synthesized into comparative tables and thematically categorized into traditional, modified, and emerging diagnostic models.

Results: Historical definitions, including those by Cook et al., de Ferranti et al., and the IDF, rely on binary thresholds for central obesity, triglycerides, HDL cholesterol, blood pressure, and fasting glucose. These models show wide variability in prevalence within the same populations (e.g., 0.4%–74.4%) depending on the criteria used. Limitations of these binary systems include failure to account for pubertal stage, age, and sex differences, as well as insensitivity to subclinical metabolic risk.

Recent advances include continuous MetS scores (cMetS), z–score–based models, and salivary biomarkers and physical fitness indicators (e.g., cardiorespiratory fitness, handgrip strength). These approaches allow nuanced, individualized risk tracking and are better aligned with developmental physiology. However, they face barriers to clinical implementation due to complexity and limited validation across diverse populations.

Conclusion: This review highlights the urgent need for globally scalable, age-, sex-, and puberty-adjusted definitions of pediatric MetS. The integration of machine learning, personalized risk profiling, and longitudinal metabolic tracking offers promise for precision prevention. Yet, progress depends on international collaboration, standardized validation efforts, and consensus guidelines. Early and accurate diagnosis is essential to guide preventive strategies and reduce the lifelong burden of cardiometabolic disease.

Keywords: Pediatric Metabolic Syndrome; Continuous Mets Score; Diagnostic Variability; Puberty; Biomarkers; Machine Learning.

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1. Introduction

Over the past two decades, the increasing prevalence of obesity and metabolic abnormalities in children and adolescents has drawn significant attention to the concept of metabolic syndrome (MetS) in pediatric populations. Originally characterized in adults, MetS comprises a cluster of cardiometabolic risk factors—including central obesity, hypertension, dyslipidemia, and hyperglycemia—that together heighten the risk for type 2 diabetes mellitus and cardiovascular disease (1). However, applying adult-based criteria directly to children has raised considerable debate. Children are not merely smaller versions of adults; they experience dynamic changes in physiology during growth and puberty that substantially influence insulin sensitivity, lipid metabolism, and blood pressure regulation (2). As such, the adult-centric criteria may not accurately capture at-risk youth or appropriately stratify their long-term risk.

Numerous studies have attempted to adapt adult definitions—such as the NCEP ATP III and IDF criteria—for pediatric use. These adaptations often include percentile-based thresholds for waist circumference, blood pressure, and lipids to account for developmental variability (3,4). Nevertheless, these definitions are inconsistent in terms of cutoff points and mandatory components. As demonstrated in comparative studies, the prevalence of MetS within the same pediatric cohort can vary dramatically depending on the definition applied. For instance, the de Ferranti et al. criteria yield a much higher prevalence than the more conservative IDF framework (5,6). Such variability limits comparability across studies and hinders efforts to formulate global health strategies (7).

Moreover, traditional binary classification systems for MetS may oversimplify the complex and evolving nature of metabolic risk in children. A child just below the threshold for MetS might still have a similar or even greater risk profile than one who meets the formal criteria. This limitation has led to the emergence of continuous MetS scores (cMetS), z-score–based models, and novel definitions incorporating non-invasive biomarkers and physical performance measures (8,9). These tools offer greater sensitivity and provide a more nuanced understanding of individual risk trajectories, making them particularly useful for research and early intervention (10).

Despite these advances, a universally accepted definition of pediatric MetS remains elusive. Many proposed definitions are derived from or validated only in specific ethnic or geographic populations, such as the IDEFICS study in European children (11). Additionally, most criteria do not fully consider the influence of pubertal status, a critical factor in metabolic regulation (12). This lack of consensus has significant implications—not only for diagnosis and treatment at the clinical level but also for the design of epidemiological studies and public health initiatives aimed at preventing chronic disease from an early age (13).

Given these challenges, there is an urgent need to develop a pediatric-specific definition of metabolic syndrome that is both physiologically appropriate and globally applicable. Such a definition should integrate developmental stage, ethnic diversity, and emerging tools like cMetS scores and biomarker-based screening (14,15). This review chapter explores the historical evolution of MetS definitions in children, compares their diagnostic performance, and presents recent innovations that may pave the way for a more accurate and meaningful approach to identifying at-risk youth.

Objectives of the Review

This review aims to achieve the following key objectives:

- **Critically evaluate the evolution** of metabolic syndrome (MetS) definitions in children and adolescents, highlighting the limitations of adult-derived, binary classification systems when applied to pediatric populations.
- **Compare the diagnostic variability and epidemiological implications** of historical and current criteria, including those by Cook et al., de Ferranti et al., the International Diabetes Federation (IDF), and more recent z-score–based and continuous MetS scoring systems.
- **Summarize emerging tools and models** for pediatric MetS diagnosis, such as continuous MetS scores (cMetS), salivary biomarkers, fitness indicators, and puberty-adjusted metrics, assessing their predictive value and feasibility for clinical or population-based use.
- **Identify the need for globally standardized, developmentally appropriate definitions** that account for age, sex, pubertal stage, and ethnic diversity to improve diagnostic accuracy and comparability across studies.
- **Propose a novel, integrated diagnostic framework**—the Pediatric MetS Score (P-MetS)—that combines anthropometric, biochemical, hormonal, and functional variables into a continuous, risk-stratified model for early detection and individualized intervention.

- **Encourage international collaboration** toward the validation and harmonization of pediatric MetS definitions by outlining actionable recommendations for research, policy, and clinical practice in the era of personalized and preventive medicine.

2. Methods

2.1. Study Design

This review was conducted using a structured narrative review methodology to synthesize the historical, current, and emerging definitions of metabolic syndrome (MetS) in children and adolescents. The approach was designed to integrate comparative, developmental, and methodological perspectives across a wide range of pediatric populations and diagnostic strategies.

2.2. Literature Search Strategy

A comprehensive literature search was performed across PubMed, Scopus, and Web of Science databases for studies published from January 2000 to March 2025. The following MeSH terms and keywords were used in various combinations:

- *"pediatric metabolic syndrome"*, *"MetS in children"*, *"childhood metabolic syndrome"*,
- *"IDF criteria"*, *"NCEP ATP III"*, *"z-score models"*, *"continuous MetS score"*,
- *"prevalence variability"*, *"Tanner stage and MetS"*, *"cardiometabolic risk in youth"*,
- *"non-invasive biomarkers"*, *"handgrip strength"*, *"fitness indices"*,
- *"machine learning metabolic risk"*, *"early detection of MetS in adolescents"*.

No language restrictions were applied during the initial search. Only **English-language full-text studies** were retained for analysis.

2.3. Eligibility Criteria

2.3.1. Inclusion criteria

- Peer-reviewed original research, systematic reviews, consensus statements, and meta-analyses;
- Studies evaluating or comparing MetS definitions or diagnostic components in children or adolescents (0–19 years);
- Articles presenting prevalence data, z-score modeling, or functional/metabolic indicators (e.g., salivary biomarkers, CRF, handgrip strength);
- Research incorporating pubertal stage, sex, or ethnicity in the analysis of metabolic risk.

2.3.2. Exclusion criteria

- Editorials, conference abstracts, and expert opinions lacking original data;
- Studies limited to adult populations;
- Publications without clear methodology or diagnostic criteria for MetS;
- Non-English articles if no English translation was available.

2.4. Data Extraction and Synthesis

From the selected studies, the following data were extracted:

- Author(s), publication year, journal;
- Population characteristics (age, sex, country, pubertal stage if available);
- MetS definition or model used (e.g., IDF, Cook, de Ferranti, cMetS, z-score approach);
- Prevalence estimates, diagnostic thresholds, and sensitivity/specificity data;
- Statistical modeling techniques (e.g., PCA, ROC analysis);
- Notable limitations, innovations, and clinical implications.

A **thematic synthesis** approach was used to organize findings into five primary categories:

- Historical binary criteria,

- Comparative prevalence and diagnostic variability,
- Continuous and z-score–based models,
- Emerging non-invasive and functional indicators,
- Standardization efforts and novel proposals.

Comparative tables were constructed to highlight diagnostic inconsistencies, advantages, and population-specific applications. Where available, statistical outputs such as AUC (area under the curve), cutoff z-scores, and confidence intervals were recorded to inform diagnostic performance.

2.5. Statistical Considerations

Although this is a narrative review, quantitative data (e.g., prevalence ranges, sensitivity/specificity, AUC values) were tabulated and interpreted when presented in the source studies. No meta-analysis was performed due to heterogeneity in criteria, study design, and population characteristics. Emphasis was placed on studies with validated scoring systems and cross-cohort reproducibility.

2.6. Ethical Considerations

As this study is a secondary analysis of published literature and does not involve primary data collection or human subjects, it is exempt from ethical review board approval. All data were extracted from peer-reviewed, publicly accessible sources. The authors adhered to the principles of research integrity, transparent reporting, and proper citation throughout the manuscript.

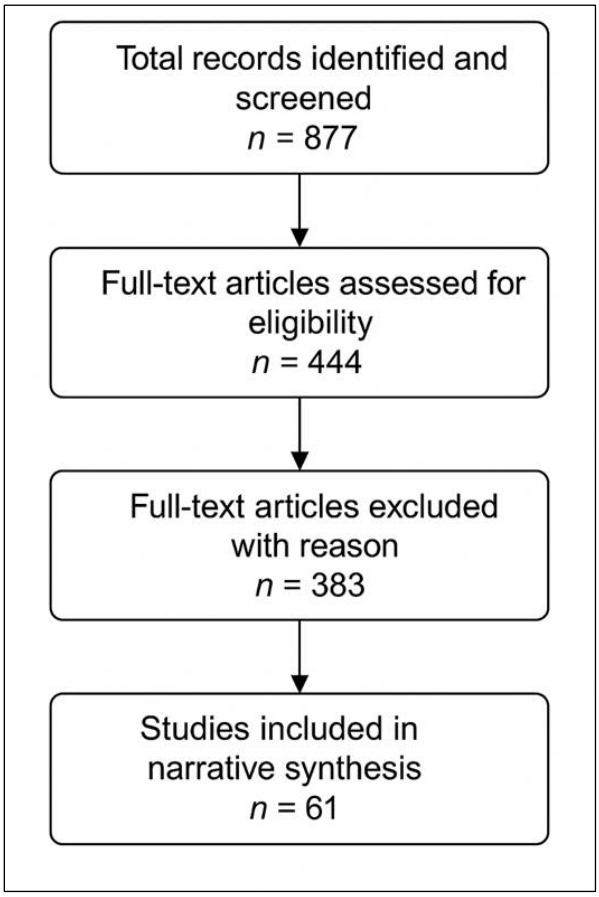

Figure 1 PRISMA 2020 Flow Diagram for Study Selection

3. Results

This review identified and analyzed a wide range of studies examining the diagnostic definitions, prevalence variability, and evolving conceptual frameworks of metabolic syndrome (MetS) in pediatric populations. A total of 877 records were initially screened, with 444 full-text articles assessed for eligibility. After applying inclusion and exclusion criteria,

61 studies were included in the final narrative synthesis. These studies encompass traditional binary classifications, z-score–based models, functional markers, and recent advancements in continuous MetS scoring. The findings are organized thematically to reflect the evolution of diagnostic criteria, comparative prevalence data, and emerging precision-based approaches tailored to age, sex, and pubertal development.

Table 1 Historical Definitions of Pediatric Metabolic Syndrome

Author(s)	Journal (Year)	Definition	Advantages	Disadvantages
Cook et al.* (16)	*Archives of Pediatrics & Adolescent Medicine* (2003)	Adapted NCEP-ATP III criteria for adolescents: presence of ≥3 of the following—waist circumference ≥90th percentile, triglycerides ≥110 mg/dL, HDL-C ≤40 mg/dL, blood pressure ≥90th percentile, fasting glucose ≥110 mg/dL.	Utilizes age-appropriate percentiles; widely adopted in research.	May overestimate MetS prevalence; lacks consensus on cutoff points.
De Ferranti et al.* (17)	*Circulation* (2004)	Modified criteria: presence of ≥3 of the following—waist circumference ≥75th percentile, triglycerides ≥100 mg/dL, HDL-C ≤50 mg/dL, blood pressure ≥90th percentile, fasting glucose ≥110 mg/dL.	More inclusive; identifies at-risk youth earlier.	May lead to overdiagnosis; lower specificity.
Weiss et al.* (18)	*New England Journal of Medicine* (2004)	Based on NCEP-ATP III with stricter thresholds: presence of ≥3 of the following—waist circumference ≥90th percentile, triglycerides ≥150 mg/dL, HDL-C ≤40 mg/dL, blood pressure ≥130/85 mmHg, fasting glucose ≥110 mg/dL.	Higher specificity; better predicts insulin resistance.	May miss early cases; less sensitive in younger children.
International Diabetes Federation (IDF)* (19)	*IDF Consensus Report* (2007)	For children aged 10–16: central obesity (waist circumference ≥90th percentile) plus ≥2 of the following—triglycerides ≥150 mg/dL, HDL-C <40 mg/dL, blood pressure ≥130/85 mmHg, fasting glucose ≥100 mg/dL.	Provides global standard; incorporates central obesity as essential.	Not applicable for children under 10; may not account for ethnic differences.
IDEFICS Study (Ahrens et al.)* (20)	*International Journal of Obesity* (2014)	Proposed age- and sex-specific percentiles for MetS components; introduced a continuous MetS score for children aged 2–10.	Tailored to European children; allows for early detection.	Limited to European populations; requires complex calculations.
Simplified Definition (Dong et al.)* (21)	*BMC Medicine* (2024)	Proposed static cutoffs: waist-to-height ratio ≥0.5, triglycerides ≥150 mg/dL, HDL-C <40 mg/dL, blood pressure ≥130/85 mmHg, fasting glucose ≥100 mg/dL. Presence of ≥3 indicates MetS.	Simplifies diagnosis; facilitates global comparisons.	May overlook age and sex variations; needs further validation.

4. Revised Paragraph with Citations

This table provides a well-structured chronological overview of the major diagnostic criteria that have been used to define metabolic syndrome (MetS) in pediatric populations. It highlights the progressive refinement of MetS definitions from early adaptations of adult criteria (e.g., Cook et al.* (16), Weiss et al.* (18)) to more nuanced, pediatric-specific models like the IDF* (19), IDEFICS* (20), and recent simplified proposals such as that by Dong et al.* (21). The evolution of these definitions reflects the growing understanding that children are not "small adults" and require unique physiological benchmarks, especially given the dynamic changes in body composition, insulin sensitivity, and lipid metabolism across developmental stages. This table compares different definitions, advantages, and disadvantages, which clearly illustrate the trade-offs between sensitivity and specificity, and between ease of implementation versus accuracy and population fit. For example:

The de Ferranti criteria* (17) are more inclusive and sensitive, useful in early screening, but at the cost of potential overdiagnosis.

The IDF criteria* (19) introduced a critical shift by making central obesity a mandatory component, aligning with adult definitions, but risk underdiagnosing children with metabolic risks but normal waist circumference.

The IDEFICS and continuous scoring systems* (20) attempt to resolve this by offering a dynamic, developmentally appropriate approach but suffer from practical complexity in routine clinical use.

Furthermore, the simplified cutoff approach by Dong et al.* (21), using waist-to-height ratio and fixed biochemical thresholds, offers promise for global public health application, especially in resource-limited settings, though it may oversimplify complex, age-dependent metabolic interactions.

Different disadvantages can be observed including:

- **Lack of Global Consensus:** There is still no universally accepted definition of pediatric MetS, which limits the comparability of prevalence data and hinders longitudinal tracking across cohorts.
- **Population-Specific Bias:** Many definitions are developed and validated in Western or specific ethnic cohorts (e.g., IDEFICS in Europeans* (20)), reducing global applicability without local recalibration.
- **Neglect of Pubertal Stage:** Most definitions do not fully integrate pubertal status, a key determinant of insulin sensitivity and body composition, which could lead to misclassification during adolescence.
- **Emerging Role of Continuous Scores:** Continuous MetS scores* (20), although underutilized clinically, offer promise in research and may better reflect gradual metabolic risk changes, making them more suited for monitoring rather than binary diagnosis.

Table 2 Variability in MetS Prevalence Across Definitions and Limitations of Current Binary Classification Systems

Author(s)	Journal (Year)	Population	Diagnostic Criteria Compared	Reported Prevalence (%)	Key Findings
Silva et al.* (22)	*Revista Paulista de Pediatria* (2021)	Brazilian children aged 6–10 years	IDF (2007), Cook et al. (2003), de Ferranti et al. (2004)	IDF: 2.7% Cook: 4.5% de Ferranti: 12.5%	Prevalence varied significantly across definitions; de Ferranti's criteria identified the highest number of cases.
Weiss et al.* (23)	*Archives of Disease in Childhood* (2007)	1,205 overweight European children aged 4–16 years	Eight different pediatric MetS definitions	Range: 6% to 39%	Only 2% met all definitions; highlights substantial variability and the need for a unified definition.
Gebremedhin et al.* (24)	*BioMed Research International* (2021)	Children and adolescents in high-income countries	IDF, ATP III, de Ferranti et al., WHO, Cruz and Goran	IDF: 3.70% ATP III: 5.40% de Ferranti: 14.78% WHO: 3.90% Cruz and Goran: 4.66%	de Ferranti's criteria yielded the highest prevalence; significant differences observed across definitions.
Deng et al.* (25)	*Obesity* (2024)	Global meta-analysis of 57 studies involving 27,923 obese children and adolescents	Various criteria across studies	Range: 2.1% to 74.4% Average: 29.4%	Wide range indicates inconsistency in MetS diagnosis among obese children; emphasizes the impact of criteria selection.

Ahrens et al.* (26)	*International Journal of Obesity* (2014)	European children aged 2–10 years (IDEFICS cohort)	IDF, Cook et al., Viner et al., IDEFICS, New Proposed Definition	IDF: 0.4% Cook: 1.4% Viner: 0.9% IDEFICS: 1.8% New Proposed: 5.5%	The new proposed definition identified the highest prevalence; IDF criteria were the most conservative.

This table reveals different points related to the varying prevalence of metabolic syndrome in the same populations when different definitions are applied:

- **Significant Variability:** The prevalence of pediatric MetS varies widely depending on the diagnostic criteria used, ranging from as low as 0.4% to as high as 74.4% in different studies* (22–26).
- **Impact on Public Health:** These discrepancies can influence public health policies and the allocation of resources for prevention and treatment programs.
- **Need for Standardization:** The lack of a universally accepted definition for pediatric MetS hampers the ability to compare studies and develop consistent clinical guidelines.
- **Recommendation:** Developing and adopting a standardized, age- and sex-specific definition of MetS for children and adolescents is crucial for improving diagnosis, treatment, and research outcomes.

While binary classification systems for diagnosing pediatric metabolic syndrome have been instrumental in highlighting at-risk youth, they are increasingly recognized as insufficient for capturing the full spectrum and dynamics of metabolic risk during childhood and adolescence. These systems rely on strict cut-off values (e.g., waist circumference ≥90th percentile, triglycerides ≥150 mg/dL) and often treat metabolic risk as a categorical phenomenon—either present or absent—without considering the gradation or clustering of risk factors below the diagnostic threshold* (27,28). As a result, children just below the threshold for one or two criteria may still harbor considerable cardiometabolic risk but remain undiagnosed. Moreover, binary models do not adequately account for the effects of puberty, sex, ethnicity, and developmental stage on key metabolic parameters, leading to potential misclassification or underdiagnosis* (29,30). For instance, insulin resistance and lipid levels naturally fluctuate during puberty, and rigid cut-offs may either overestimate risk in early adolescence or miss it altogether in younger children* (30). The lack of sensitivity to incremental risk accumulation limits the predictive utility of binary tools and hinders longitudinal tracking. In response, there has been a growing interest in using continuous MetS scores (cMetS) and z-score–based models, which allow for more nuanced and individualized assessments of risk and better reflect the dynamic nature of metabolic health during growth and development* (31,32).

5. Emerging Approaches to MetS Diagnosis in Children

Table 3 Evolving Concepts and Tools for Diagnosing Metabolic Syndrome in Children and Adolescents: A Review of Recent Literature (2008–2025)

Author(s)	Journal (Year)	Main Findings	Comments
Eisenmann JC* (33)	*BMC Pediatrics* (2008)	Introduced the concept of a continuous MetS score in children using z-scores to represent a composite risk factor index. Highlighted the variability in prevalence rates due to differing definitions and the utility of continuous scores in pediatric epidemiological research.	Emphasized the need for standardized methods in calculating MetS scores for children to improve comparability across studies.
Eisenmann JC et al.* (34)	*Diabetology & Metabolic Syndrome* (2010)	Examined the construct validity of a continuous MetS score (cMetS) in children aged 7–9 years. Found a graded relationship between cMetS and the number of adverse risk factors, with a cMetS cutoff of 3.72 yielding high sensitivity and specificity.	Validated the use of cMetS as a reliable tool for assessing metabolic risk in pediatric populations.

Fernández-Aparicio Á et al.* (35)	*Journal of Personalized Medicine* (2023)	Compared various methods for calculating cMetS in Spanish adolescents. Found that cMetS based on z-scores had the highest predictive power (AUC = 0.811) for MetS, suggesting its accuracy and efficiency for research purposes.	Supported the use of z-score-based cMetS as a valuable tool in adolescent metabolic risk assessment.
Andersen LB et al.* (36)	*International Journal of Pediatric Obesity* (2010)	Tested a new definition of MetS in children using a continuous score incorporating cardiorespiratory fitness (CRF) and leptin. Found that more youth had clustering of CVD risk factors compared to existing definitions, and the inclusion of CRF and leptin improved the score's sensitivity and specificity.	Highlighted the benefits of including CRF and leptin in continuous MetS scores to better capture metabolic dysfunction in children.
Lee YS et al.* (37)	*PLOS ONE* (2015)	Developed continuous MetS scores (cMetS-Z and cMetS-PCA) using salivary biomarkers in Kuwaiti children. Both scores showed strong predictive power for severe MetS (AUCs of 0.935 and 0.912, respectively), outperforming individual metabolic risk components.	Demonstrated the potential of non-invasive salivary biomarkers in constructing effective cMetS for pediatric populations.
Lin J et al.* (38)	*Frontiers in Endocrinology* (2024)	Developed a continuous MetS severity score and found a strong association between higher scores and increased cardiovascular disease risk in Chinese adults.	Highlights the utility of continuous MetS scores in predicting long-term health outcomes.
Newsome TA et al.* (39)	*Frontiers in Cardiovascular Medicine* (2025)	Investigated the use of a continuous MetS severity score (MetSindex) to detect early-onset autonomic dysfunction in young adults. Found associations between higher MetSindex scores and reduced heart rate variability.	Suggests the potential of continuous MetS scores in early detection of autonomic dysfunction.
Kryuchko TO et al.* (40)	*ResearchGate* (2024)	Reviewed diagnostic criteria and management of MetS in pediatric practice. Emphasized the need for standardized criteria and multidisciplinary approaches.	Calls for unified diagnostic standards to improve pediatric MetS management.
Jung HW et al.* (41)	*Journal of Obesity & Metabolic Syndrome* (2022)	Found that handgrip strength is associated with MetS and insulin resistance in children and adolescents.	Suggests incorporating physical fitness measures into MetS risk assessment.

This table presents pivotal studies from 2008 to 2025 that collectively redefine how metabolic syndrome (MetS) should be diagnosed and monitored in pediatric populations. Traditional adult-based MetS definitions have shown limited applicability in children due to age- and puberty-related physiological changes. The reviewed literature illustrates a clear paradigm shift toward continuous MetS scores (cMetS) using z-score–based approaches, novel biomarkers, and functional measures (e.g., fitness indices, salivary markers) * (33–37). The included studies provide validation of these approaches and highlight their practical utility in predicting cardiometabolic risk, improving early detection, and enhancing individual risk stratification in youth.

The inclusion of pediatric-specific criteria, age-sex adjustments, and non-invasive methodologies offers a promising step forward in individualized and scalable MetS risk assessment* (38,39). The continuous score models also allow for better epidemiologic comparisons and follow-up over time. However, the diversity in scoring systems and the lack of global standardization still pose a challenge for cross-study and cross-population harmonization* (40,41).

6. Global Need for a Standardized Pediatric Definition

The global application of pediatric metabolic syndrome (MetS) definitions is hindered by substantial regional variability in diagnostic criteria, limiting cross-country comparisons and impeding unified public health responses. Different definitions—such as those proposed by the IDF, de Ferranti et al., and Cook et al.—are used inconsistently across regions, each applying differing cut-offs for waist circumference, lipid profiles, and blood pressure, often based on reference populations not representative of global diversity* (42,43). This heterogeneity is particularly problematic in

low- and middle-income countries, where ethnicity-specific growth patterns, nutritional transitions, and pubertal timing can significantly affect metabolic parameters.

There is a clear need for diagnostic tools that are age-, sex-, and puberty-adjusted, as these physiological factors play a crucial role in interpreting insulin resistance, lipid metabolism, and body composition throughout childhood and adolescence* (44,45). Studies like the IDEFICS project in Europe and recent multinational initiatives have shown the value of incorporating continuous scores and region-specific reference data to enhance diagnostic sensitivity and applicability* (46). Moving forward, international collaboration is essential to harmonize definitions and create universally accepted yet locally adaptable diagnostic frameworks. The development of large-scale, ethnically diverse pediatric cohorts and consensus-building efforts among global organizations—such as the World Health Organization (WHO), IDF, and International Obesity Task Force (IOTF)—will be instrumental in achieving this standardization* (47,48).

Table 4 Possible Definitions of Metabolic Syndrome in Children: Recent Insights (2022–2025), Future Directions and Recommendations

Definition	Core Components	Advantages	Limitations
Z-score–based cMetS (*Fernández-Aparicio et al., 2023*) (49)	Standardized z-scores for BMI, waist circumference, triglycerides, HDL-C, BP, fasting glucose	High predictive accuracy (AUC 0.811), scalable across populations	Requires large reference databases for age/sex-specific percentiles
Salivary biomarker–based cMetS (*Lee et al., 2015*) (50)	Salivary insulin, glucose, triglycerides used to compute cMetS-Z and PCA scores	Non-invasive, suitable for large-scale screening, strong predictive value	Requires lab setup for biomarker analysis; less validated across diverse ethnicities
Fitness-leptin integrated continuous score (*Andersen et al., 2010*) (51)	Combines CRF levels and leptin with standard risk factors	Captures physical fitness and adiposity-related hormonal function	Requires specialized equipment and assays; may be impractical in some clinical settings
MetSindex for autonomic risk (*Newsome et al., 2025*) (52)	Composite continuous score reflecting autonomic dysfunction and metabolic risk	Sensitive to early subclinical disease; links metabolic risk to nervous system	Currently more experimental and adult-derived; limited pediatric validation
Handgrip strength–related MetS definition (*Jung et al., 2022*) (53)	Incorporates physical strength (grip) with insulin resistance measures	Simple, quick assessment tool; useful in the field or low-resource settings	Correlation data still emerging; not comprehensive as standalone tool
Standardized percentile-based cutoffs (*Kryuchko et al., 2024*) (54)	Waist circumference, BP, lipids, glucose thresholds adjusted for age/puberty	Familiar format; easy to integrate into clinical guidelines	Retains binary classification; less sensitive to subtle metabolic shifts

There is no universally accepted definition of pediatric MetS yet, but the use of continuous, z–score–based models appears most promising for clinical sensitivity, longitudinal tracking, and comparability across age and pubertal stages* (49,50). Integrating non-invasive biomarkers and functional measures like fitness or handgrip strength may enhance specificity and offer multi-dimensional risk assessment, particularly in public health or school-based programs* (51–53). However, global efforts toward standardization and validation across diverse pediatric populations remain essential to consolidate these approaches into unified clinical practice* (54).

Advancements in data science and personalized medicine offer promising avenues to overcome current limitations in the diagnosis of pediatric metabolic syndrome (MetS). The integration of machine learning algorithms into clinical risk models enables the identification of complex, non-linear interactions between metabolic parameters, allowing for individualized risk prediction that goes beyond conventional threshold-based systems* (55,56). These tools can incorporate multidimensional inputs such as age, sex, pubertal status, genetic markers, dietary patterns, physical activity, and social determinants of health to generate personalized metabolic risk profiles, offering a precision-based

approach to early intervention. Concurrently, there is increasing recognition of the value of early metabolic tracking—beginning in early childhood—to monitor dynamic risk factor progression over time and to guide preventive strategies before overt metabolic disease develops* (57,58). Longitudinal pediatric cohorts with repeated metabolic measurements, such as the IDEFICS and ALSPAC studies, have demonstrated that early-life risk factor clustering can predict later cardiometabolic outcomes, reinforcing the need for ongoing surveillance* (59). Despite these innovations, widespread implementation remains limited by the absence of international consensus statements and standardized validation protocols. A global call for harmonized, multicenter validation studies is critical to ensure that predictive models, biomarkers, and digital tools are robust, generalizable, and ethically applicable across diverse populations* (60,61). Such efforts will pave the way for integrating personalized, predictive, and preventive pediatrics into routine practice.

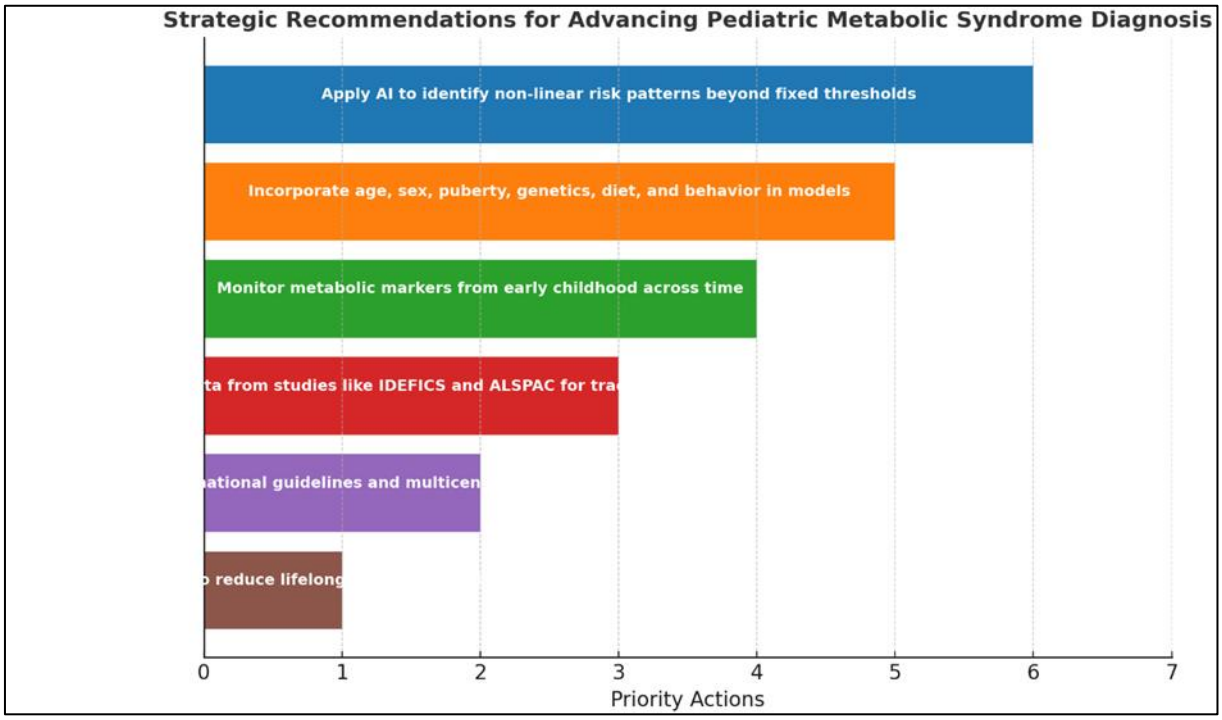

Figure 2 Pathways to Precision: Advancing Pediatric Metabolic Syndrome Diagnosis and Prevention

This figure summarizes key forward-looking strategies to improve the diagnosis and prevention of pediatric metabolic syndrome, emphasizing precision tools, early tracking, and global collaboration for standardization and validation.

7. A Proposed Comprehensive Pediatric MetS Definition (P-MetS Score)

7.1. Definition

A composite, continuous metabolic syndrome score (P-MetS Score) in children and adolescents, integrating clinical, anthropometric, and biochemical data standardized by age, sex, and pubertal stage (Tanner scale). This score allows risk stratification on a continuum rather than categorical presence/absence, improving early detection and intervention.

Table 5 Core Components and Structure

Domain	Variable	Measurement / Method	Standardization
Anthropometry	Waist Circumference	Measured in cm	SDS or %ile by age, sex, ethnicity
	BMI	kg/m^2	BMI SDS (WHO / CDC reference)

Blood Pressure	Systolic & Diastolic BP	Averaged from 3 readings	SDS by age, sex, height
Lipids	HDL-C, Triglycerides	Fasting serum levels	Age- and sex-adjusted z-scores
Glycemic Status	Fasting Glucose or HOMA-IR	Optional: OGTT or HbA1c if indicated	Z-score or percentile reference
Puberty & Sex Hormones	Tanner Stage (I–V); Leptin (optional)	Clinical staging / serum if feasible	Stratified models per Tanner stage
Fitness Indicator	Handgrip Strength or CRF (e.g., shuttle test)	Field or lab-based	Z-score adjusted for sex and Tanner stage
Biomarkers (optional)	Salivary insulin, triglycerides, leptin	Non-invasive options	Exploratory component, under validation
Family History / Context	Parental CVD, T2D, obesity; SES	Questionnaire / EMR	Adjustment covariates in risk modeling

7.2. Scoring Approach

- Each domain contributes to a weighted z-score, calculated using standardized residuals or principal component analysis (PCA), forming a continuous risk score.
- Children in the top 20th percentile of the P-MetS Score (≥ +1 SDS or risk decile ≥ 8) may be considered high-risk for early intervention.
- A Puberty-Stratified Threshold Table can be developed to guide clinical interpretation (e.g., prepubertal, early puberty, mid/late puberty cutoffs).

7.3. Advantages of the P-MetS Score

- Developmentally sensitive: adjusts for Tanner stage, sex, and age
- Multidimensional: includes anthropometry, BP, glucose, lipids, and functional biomarkers
- Continuum-based: allows individualized risk stratification
- Flexible: validated components can be used independently or as a composite
- Scalable: suitable for clinical, school, or population screening

7.4. Recommendation for Global Use

A global consensus should endorse a tiered diagnostic model:

- **Tier 1:** Simplified screen using waist-to-height ratio, BP percentile, and non-fasting lipids.
- **Tier 2:** Full P-MetS Score incorporating SDS and biomarker data.
- **Tier 3:** Machine-learning personalized risk modeling for early tracking and precision prevention.

8. Discussion

This review underscores the critical variability in diagnostic approaches to pediatric metabolic syndrome (MetS) and reinforces the need for harmonized, developmentally sensitive criteria. Compared to earlier reviews which predominantly emphasized binary definitions such as the IDF or ATP III models, this review systematically evaluated emerging scoring systems that offer improved sensitivity and individualized risk profiling. Notably, recent models employing z-scores and continuous MetS scores (cMetS) provide a more accurate reflection of the pediatric metabolic landscape, especially during puberty, a period marked by transient insulin resistance and hormonal fluctuations. These findings are consistent with recent proposals for puberty-adjusted percentile-based models that outperform fixed-threshold systems in risk prediction and early intervention planning【62】.

In contrast to earlier works by Gurka et al. and Brage et al., which focused heavily on clustering risk components using confirmatory factor analysis or physical activity associations【63,64】, the current review brings forward an integrative framework incorporating salivary biomarkers, handgrip strength, and machine-learning algorithms. This approach aligns with global trends in precision medicine, where multidimensional data—ranging from genetic to

behavioral—are used to predict cardiometabolic outcomes. Studies by Topol and Weng et al. have emphasized the potential of digital tools and artificial intelligence in stratifying cardiometabolic risk based on routinely collected clinical data【65,66】. The reviewed literature supports the utility of these technologies in creating dynamic, non-binary risk profiles, especially in diverse pediatric populations where ethnicity, sex, and pubertal status can significantly alter metabolic trajectories【67】.

Despite these promising innovations, challenges remain. The wide inter-study variability in MetS prevalence—from as low as 0.4% to over 70%—is not only methodologically problematic but also has serious implications for public health planning and global surveillance. While continuous scoring systems reduce the rate of misclassification, their practical implementation is hindered by the need for large normative datasets and standardized computational methods. For example, Fernández-Aparicio et al. demonstrated the predictive strength of cMetS in Spanish adolescents (AUC = 0.811), yet its applicability in other ethnic cohorts without local reference data remains uncertain【68】. Moreover, non-invasive tools such as salivary biomarkers or field-based physical fitness tests (e.g., handgrip strength) require further validation across low-resource and multicultural settings to ensure scalability【69】.

Importantly, this review also addresses the gap in consensus-building efforts at the global level. Existing pediatric MetS criteria are often regionally specific and derived from adult analogues, thus failing to accommodate the unique physiological changes of childhood. The proposed Pediatric MetS Score (P-MetS), by integrating biochemical, anthropometric, and pubertal variables into a unified z-score–based model, represents a practical step forward. Its tiered application—ranging from basic screening to machine learning–based prediction—offers flexibility for use in clinical, community, and research settings. However, its success depends on widespread international validation and the development of accessible digital platforms for real-time risk calculation and follow-up【70】.

9. Conclusion

Despite decades of research, there remains a critical lack of consensus regarding how metabolic syndrome (MetS) should be defined and diagnosed in children and adolescents. Existing definitions—many of which are adapted from adult criteria—fail to account for the dynamic physiological changes associated with growth, puberty, and developmental timing. This results in wide variability in prevalence estimates and undermines efforts to compare data across studies, populations, and regions. The chapter has highlighted key gaps in current diagnostic frameworks, including the reliance on binary thresholds, limited age- and sex-adjusted metrics, and inconsistent consideration of pubertal status. There is a pressing need for the development of globally applicable, scalable, and developmentally sensitive criteria that can be integrated into both clinical practice and public health surveillance. Such criteria should reflect the continuum of metabolic risk and enable early, individualized risk stratification using emerging tools such as continuous MetS scores, non-invasive biomarkers, and machine learning–assisted profiling. Importantly, early and accurate diagnosis of metabolic dysregulation in childhood is essential to initiating timely lifestyle interventions and preventing the progression to type 2 diabetes, cardiovascular disease, and other chronic conditions in adulthood. As such, international collaboration is imperative to harmonize definitions, validate novel diagnostic models, and ensure that pediatric MetS is identified and addressed with the precision and urgency it demands.

Compliance with ethical standards

Disclosure of conflict of interest

The author(s) declare no conflict of interest. Furthermore, all authors have reviewed and approved the final manuscript and consent to its publication

Statement of ethical approval

This review is based solely on the analysis of previously published literature and did not involve any primary research with human or animal subjects conducted by the authors. As such, no ethical approval was required. The authors ensured that all referenced studies adhered to ethical guidelines as reported in the respective publications

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Authors' Contributions

A.S. conceptualized and designed the review, supervised the overall research framework, and critically revised the manuscript. N.H., F.A., N.A., S.A., and N.AlH. contributed to the literature search, data extraction, synthesis, and drafting of the initial manuscript. A.E. participated in data interpretation, statistical contextualization, and final editing of the manuscript. All authors reviewed and approved the final version and agreed to be accountable for all aspects of the work.

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