

# ObMetrics: A Shiny app to assist in metabolic syndrome assessment in paediatric obesity

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## Summary

**Objective:** To introduce ObMetrics, a free and user-friendly Shiny app that simplifies the calculation, data analysis, and interpretation of Metabolic Syndrome (MetS) outcomes according to multiple definitions in epidemiological studies of paediatric populations. We illustrate its usefulness using ethnically different populations in a comparative study of prevalence across cohorts and definitions.

**Methods:** We conducted a case study using data from two ethnically diverse paediatric populations: a Hispanic-American cohort ( $N = 1759$ ) and a Hispanic-European cohort ( $N = 2411$ ). Using ObMetrics, we computed MetS classifications (Cook, Zimmet, Ahrens) and component-specific z-scores for each participant to compare prevalences.

**Results:** The analysis revealed significant heterogeneity in MetS prevalence across different definitions and cohorts. According to Cook, Zimmet, and Ahrens's definitions, MetS prevalence in children with obesity was 25%, 12%, and 48%, respectively, in the Hispanic-European cohort, and 38%, 27%, and 66% in the Hispanic-American

**Abbreviations:** BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; IDEFICS, Identification and Prevention of Dietary and Lifestyle-Induced Health Effects in Children and Infants; IDF, International Diabetes Federation; IOTF, International Obesity Task Force; IR, insulin resistance; MetS, metabolic syndrome; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; NHBPEP, National High Blood Pressure Education Program; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; TAG, triacylglycerols; WC, waist circumference.

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cohort. Calculating component-specific z-scores in each cohort also highlighted ethnic-specific differences in lipid metabolism and blood pressure. By automating these complex calculations, ObMetrics considerably reduced analysis time and minimised the potential for errors.

**Conclusion:** ObMetrics proved to be a powerful tool for paediatric research, generating detailed reports on the prevalence of MetS and its components based on various definitions and reference standards. Our case study further provides valuable insights into the challenges of characterising metabolic health in paediatric populations. Future efforts should focus on developing unified consensus guidelines for paediatric MetS. Meanwhile, ObMetrics enables earlier identification and targeted intervention for high-risk children and adolescents.

#### KEYWORDS

adolescent, anthropometry, cardiometabolic risk factors, child, insulin resistance, metabolic syndrome, paediatric obesity

## 1 | INTRODUCTION

Metabolic syndrome (MetS) is a cluster of interrelated metabolic abnormalities commonly found in patients with obesity that significantly increases the risk of developing cardiovascular disease (CVD)<sup>1</sup> and type II diabetes (T2DM).<sup>2</sup> The fundamental components of MetS include increased abdominal adiposity, elevated blood pressure (BP), hyperglycaemia, and dyslipidaemia. To classify an individual as having MetS, disturbances in at least three of these components must be present.<sup>3,4</sup> Recent data underscore the global impact of obesity, revealing an alarming prevalence of this condition within paediatric and adult populations. The high prevalence of paediatric obesity, which affects 107.7 million children,<sup>5,6</sup> is particularly concerning because of its connection with the onset of MetS and future cardiovascular events.<sup>7-12</sup>

The recent commission on obesity has reframed clinical obesity as a systemic disorder marked by organ- and tissue-level dysfunction attributable to excess adiposity, emphasising the need to incorporate metabolic health indicators into clinical decision-making and therapeutic strategies.<sup>13,14</sup> Thus, implementing preventive strategies based on early management of MetS is crucial to mitigate the development of severe health issues later in life in paediatric patients with pre-clinical and clinical obesity.<sup>15,16</sup> Despite the clear necessity of assessing MetS in early life, the absence of an international agreement on the most appropriate definitions of MetS in children and adolescents remains a key limitation, especially given that the definitions applied to adults with MetS cannot be directly extended to the paediatric population.<sup>17</sup> In contrast to the assessment of MetS in adults,<sup>18</sup> paediatricians must utilise cut-off points adjusted by age, sex, height, and ethnicity.<sup>19,20</sup>

Currently, there is no consensus on which components should be included and what weight should they have for the definition of MetS in children or adolescents.<sup>21,22</sup> Some definitions do not consider the evaluation of insulin resistance (IR), which plays a pivotal role in the pathophysiology of the MetS.<sup>23</sup> To date, there is a gap in terms of reference populations of children and adolescents, especially those

representing non-Caucasian ethnicities, largely owing to the substantial human and economic investment required for the data collection in low-middle income countries. Consequently, the published reference tables on existing reference populations are not worldwide representative and are biased toward the North American Caucasian population. This further complicates the scene, demanding the recruitment of large and representative reference populations covering multiple ethnicities and geographic locations.

In this context, several authors have evaluated the prevalence of MetS in study populations of children and adolescents using different classification definitions of MetS, and clarifying which cut-off points and reference tables should be followed. Nowadays, the most widely accepted and utilised definition of MetS is the Zimmet et al. definition (International Diabetes Federation [IDF]),<sup>24,25</sup> which stipulates that diagnosis is only possible after the age of 10 years. Other authors such as Cook et al. (NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III),<sup>26</sup> de Ferranti et al.,<sup>27</sup> Ford et al.,<sup>28</sup> and Viner et al.<sup>29</sup> previously defined the components and their cut-off points for paediatric MetS using percentiles for waist circumference (WC)/body mass index (BMI) and high BP, and static cut-off points for the rest of the components.<sup>30-37</sup> Afterwards, new definitions proposed by Olza et al.<sup>38,39</sup> and Ahrens et al. (Identification and Prevention of Dietary and Lifestyle-Induced Health Effects in Children and Infants study [IDEFICS]),<sup>40</sup> have embraced sex- and age-dependent percentile cut-off points for most or all MetS components. Ahrens et al. also proposed an extension of the Zimmet et al. definition for children below 10 years of age.<sup>40</sup> In addition to MetS classification definitions, there are also definitions, such as those proposed by Ahrens et al. (IDEFICS) and Stravnsbo et al., that allow the calculation of both global MetS z-scores and z-scores for individual MetS components,<sup>40,41</sup> providing robust and comprehensive tools for paediatric research. For more detailed information about available MetS definitions, please visit Table 1. Notice that this work does not seek to solve all the issues raised; rather, it aims to open dialogue among

TABLE 1 Definitions proposed for the metabolic syndrome classification and z-scores in children and adolescents.

| Components of metabolic syndrome  |   |                 |   |  |  |  |   |  |
|-----------------------------------|---|-----------------|---|--|--|--|---|--|
| Definitions                       | Study population  | Age range       | Excess adiposity  | Blood pressure   | Triacylglycerols   | HDL-C  | Glucose   | Insulin resistance   |
| Metabolic syndrome classification |   |                 |   |  |  |  |   |  |
| Cook et al. (2003) (NCEP ATP III) | White, Black, and Mexican American 12–19 years old (N = 2420, NHANES III, 1988–1994)                    | 2–18 years old  | WC ≥90th percentile (age, sex and ethnic-specific, NHANES III)  | SBP or DBP ≥90th percentile (age, sex and height percentile specific, NHBPEP)                  | TAG ≥110 mg/dL (NCEP)  | HDL-C ≤40 mg/dL (NCEP)   | Glucose ≥110 mg/dL (ADA)  | Insulin resistance is not considered   |
| de Ferranti et al. (2004)         | White, Black, and Mexican American 12–19 years old (N = 1960, NHANES III, 1988–1994)                    | 2–18 years old  | WC ≥75th percentile (age, sex and ethnic-specific, NHANES III)  | SBP ≥90th percentile (age, sex and height percentile specific, NHBPEP)                         | TAG ≥100 mg/dL (NCEP)  | HDL-C ≤50 and ≤45 mg/dL for age <15 and ≥15, respectively  | Glucose ≥110 mg/dL  | Insulin resistance is not considered   |
| Ford et al. (2005)                | White, Black, and Mexican American 12–17 years old (N = 1370, NHANES, 1999–2000)                        | 2–18 years old  | WC ≥90th percentile (age, sex and ethnic specific, NHANES III)  | SBP or DBP ≥90th percentile (age, sex and height percentile specific, NHBPEP)                  | TAG ≥110 mg/dL (NCEP)  | HDL-C ≤40 mg/dL (NCEP)   | Glucose ≥100 mg/dL  | Insulin resistance is not considered   |
| Viner et al. (2005)               | White, Black, South Asian, and other or mixed ethnicity 2–18 years old (N = 103, everyone with obesity) | 2–18 years old  | BMI ≥95th percentile (Cole et al. 2000)   | SBP ≥95th percentile (age, sex and height percentile specific, NHBPEP)                         | TAG ≥150 mg/dL   | HDL-C ≤35 mg/dL  | Glucose ≥110 mg/dL or Insulin ≥15 μU/mL ≥30 μU/mL and ≥20 μU/mL for pre-, mid- and postpubertal children, respectively. |  |
| Zimmerman et al. (2007) (IDF)     | It was a report.  | 10–18 years old | WC ≥90th percentile or adult cutoff-points if lower (age ≤16, sex and ethnic-specific, NHANES III) and adult cutoff-points (age >16, sex and ethnic-specific) | SBP or DBP ≥130 or 85 mmHg   | TAG ≥150 mg/dL (NCEP)  | HDL-C ≤40 mg/dL (age ≥16, NCEP) and HDL-C ≤40 mg/dL in males and 50 mg/dL in females (age ≥17, NCEP) | Glucose ≥100 mg/dL (ADA)  | Insulin resistance is not considered   |
| Olza et al. (2011)                | White European (Spanish) 5–10.9 years old (N = 930)   | 4–18 years old  | BMI ≥95th percentile (Cole et al. 2000) (2–18 years old)  | SBP or DBP ≥90th percentile (age, sex and height percentile specific, NHBPEP) (2–18 years old) | TAG ≥90th percentile (age and sex specific) (0–19 years old) | HDL-C ≤10th percentile (age and sex specific) (4–19 years old)                                       | Glucose ≥100 mg/dL  | HOMA-IR ≥2.5 and ≥5.38 for prepubertal (Tanner I) and pubertal children (Tanner II–IV) |

(Continues)

TABLE 1 (Continued)

| Components of metabolic syndrome                              |  |                |  |  |   |       |   |                    |
|---|--|----------------|--|--|---|-------|---|--------------------|
| Definitions   | Study population   | Age range      | Excess adiposity   | Blood pressure   | Triacylglycerols  | HDL-C | Glucose   | Insulin resistance |
| Ahrens et al. (2014) (IDEFICS study, monitoring/action level) | European 2–10.9 years old (N = 18 745, IDEFICS)                      | 3–10 years old | WC ≥90th/95th percentile (age and sex specific, IDEFICS) <sup>23</sup> | SBP or DBP ≥90th/95th percentile (age, height and sex specific, IDEFICS) <sup>23</sup> | TAG ≥90th/95th percentile/HDL-C ≤10th/05th percentile (age and sex specific, IDEFICS) <sup>23</sup> | HDL-C | Glucose/HOMA-IR ≥90th percentile or (age and sex specific, IDEFICS) <sup>23</sup> |                    |
| <b>Metabolic syndrome z-scores</b>                            |  |                |  |  |   |       |   |                    |
| Ahrens et al. (2014) (IDEFICS study)                          | European 2–10.9 years old (N = 18 745, IDEFICS)                      | 3–10 years old | WC z-score   | BP z-score   | Lipid z-score   |       | HOMA-IR z-score   |                    |
| Stravnsbo et al. (2018)                                       | European (Denmark, Estonia, Portugal, Switzerland) and United States | 6–18 years old | WC z-score   | BP z-score   | Lipid z-score   |       | HOMA-IR z-score   |                    |

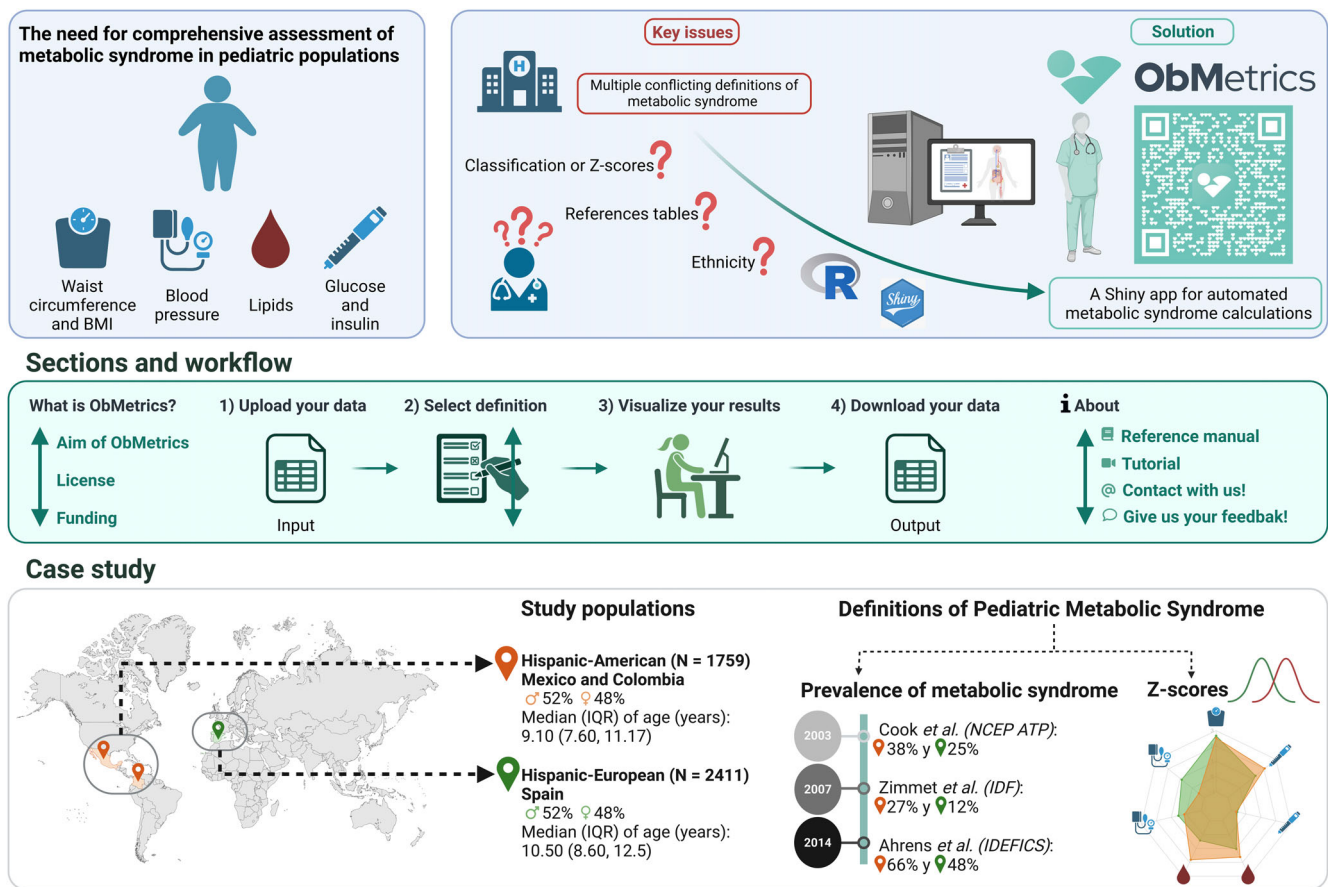
Note: In the definition of Viner et al. (2005), insulin resistance is not assessed directly; instead hyperinsulinaemia is considered. In this same definition, pre-, mid-, and postpubertal children are defined as Tanner I, Tanner II–IV, and Tanner V, respectively. The definition of Zimmet et al. (2007) (IDF) was used with an expanded age range from 2 to 18 years in later works. In this same definition, the presence of obesity is considered a sine qua non-condition for metabolic syndrome and the cut-off points in adults are 94 and 80 cm in males and females. In the case of Mexican American males is 90 cm. Abbreviations: ADA, American Diabetes Association; BMI, body mass index; BP, blood pressure; CoSCIS, Copenhagen School Child Intervention Study; DBP, diastolic blood pressure; EYHS, European Youth Heart Study; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; IDEFICS, Identification and Prevention of Dietary and Lifestyle-Induced Health Effects in Children and Infants; IDF, International Diabetes Federation; KISS, Kinder Sports Studies; NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; NHANES, National Health and Nutrition Examination Survey; NHBPEP, National High Blood Pressure Education Program; PANCS, Physical Activity among Norwegian Children Study; SBP, systolic blood pressure; TAG, triacylglycerols; WC, waist circumference.

paediatric professionals and spotlight key limitations impeding unified MetS definitions.

To the absence of a universally accepted definition for characterising MetS in children and adolescents, numerous studies have reported variable prevalence rates of MetS, even within similar study populations using the same definitions.<sup>3,38–40</sup> Consequently, selecting an appropriate definition requires careful consideration. The challenge lies not only in determining the most suitable definition of MetS but also in deciding whether to adopt the original version or modify it using national reference standards or updated cut-off values. Researchers investigating cardiometabolic risk factors in paediatric populations must therefore navigate a vast body of literature on MetS definitions and reference standards to make an informed choice, a task that demands significant time and expertise. Moreover, the implementation of these definitions often requires programming proficiency to develop computational tools for calculating MetS components. This technical demand, which is not always feasible in clinical settings, increases the risk of coding errors and complicates reproducibility, thereby posing an additional challenge in paediatric research.

In reviewing free or open source software available in the literature for the scientific community, to our knowledge, only the Leibniz Institute for Preventive Research and Epidemiology provides MetS-Score (<https://mets-score.bips.eu/>), an online tool to help paediatricians assess a single definition of MetS in children 3–10 years of age (Ahrens et al., IDEFICS).<sup>40</sup> In addition, this software tool requires entering data for each child one by one, which makes it difficult to use for epidemiological studies on study populations, raising the need for a free software tool that allows researchers to have access to multiple paediatric MetS definitions and z-score calculations to perform analyses in paediatric populations.

In this article, we introduce ObMetrics, a free and user-friendly Shiny application that provides a comprehensive assessment of MetS by calculating both MetS classifications and z-scores in paediatric populations. The app enables users to choose among the most widely recognised international MetS definitions and reference tables (Figure 1). Results are presented in interactive tables and figures that facilitate data interpretation, while an export function allows for streamlined dissemination. Additionally, ObMetrics includes a detailed



**FIGURE 1** Graphical abstract. Overview of the necessity for standardised MetS definitions, with particular attention to conflicting definitions. The central workflow outlines the four main steps: Data input, selection of MetS definitions, visualisation of results, and data export. The case study section demonstrates differences in MetS prevalence across Hispanic-American and Hispanic-European cohorts, highlighting significant ethnic-specific variations in cardiometabolic profiles. This highlights the need for ethnically tailored assessment tools. ObMetrics provides a user-friendly interface, designed to standardise MetS evaluation, with the potential to enhance the comparability and rigor of paediatric obesity research.

review of the original articles describing principal paediatric MetS definitions, providing key details on the impact of ethnicity, age range on each criterion, as well as details on the specific components that are considered in each definition. Finally, ObMetrics features a dedicated 'Best Practices' section in its documentation, providing practical guidance on selecting the most appropriate definition for each specific study. By integrating these capabilities into an accessible Shiny platform, ObMetrics significantly reduces technical barriers and simplifies the assessment of MetS components, enabling researchers to focus on clinical interpretation and generating meaningful insights. Its intuitive interface caters to investigators with limited programming expertise as well as those conducting large-scale hospital cohort studies. Furthermore, ObMetrics has associated a website supported by the public hosting GitHub (see Methods), offering supplementary material ([https://github.com/AlvaroTorresMartos/ObMetrics/tree/main/supplementary\\_material](https://github.com/AlvaroTorresMartos/ObMetrics/tree/main/supplementary_material)) and documentation to enhance usability and promote the advantages of free software. Ultimately, this tool might contribute to the early identification, management, and targeted intervention of high-risk children and adolescents, with the potential to improve health outcomes in this vulnerable population.

## 2 | METHODS

### 2.1 | Description of the Shiny app: ObMetrics

ObMetrics is a free and user-friendly Shiny app for the comprehensive analysis of MetS and its cardiometabolic components in children and adolescents. This app has been developed using the R programming language and is distributed under the terms of the Attribution-NonCommercial-NoDerivatives International licence from Creative Commons (CC BY-NC-ND 4.0). Shiny is an R package specifically designed to facilitate the development of web-based applications directly within the R environment. It is hosted on a secure SSL-encrypted access public server, ensuring cross-platform compatibility and accessibility through any web browser without needing local installation. The official ObMetrics webpage is located at <https://github.com/AlvaroTorresMartos/ObMetrics>. Users can access the Shiny app via a direct link and review the required inputs and their corresponding units (Section 'Usage'). The 'Quick Start' section offers a preview of the app's interface, while 'Documentation' provides detailed instructions on its use. Additional resources, including supplementary materials for this article, software testing logs, and records of beta testing by an expert panel, are also available on the same webpage.

ObMetrics only requires one file as input, a basic spreadsheet (XLSX). To ease the process of data entry, ObMetrics includes a downloadable XLSX template that users can fill with their own data. It conveys several advantages. First, the widespread use and familiarity of spreadsheet software (such as, Microsoft Excel) among healthcare professionals reduces the learning curve and minimises data entry errors. Second, the robust data validation and manipulation features of spreadsheet software allow for data pre-processing and cleaning

prior to import into the Shiny app, enhancing data integrity and reliability.

To facilitate the analysis of the results, ObMetrics provides a series of interactive tables and figures that enable the visual analysis of the results derived from distinct MetS definitions. These visual tools promote a clearer and more intuitive understanding of the data, allowing for rapidly identifying trends and patterns across distinct definitions. The graphical representation of data also enhances comparative analysis, enabling clinical experts to evaluate multiple MetS definitions and make more informed clinical decisions. All figures and tables are available for export in SVG, PNG, JPEG, WEBP, XLSX, and CSV formats, which are widely recognised formats that allow experts to easily filter, sort, and statistically analyse data, as well as share findings with collaborators.

This intuitive and flexible Shiny app enables the calculation of up to seven different MetS classifications and two MetS z-scores definitions for paediatric populations, providing not only the global MetS classification/z-score but also the specific-component classification/z-scores. All the MetS definitions available in ObMetrics have been published in prestigious and peer-reviewed journals internationally recognised by the scientific community (see Tables 1 and S1). Additionally, reference values commonly used for assessing each of the individual MetS components are also included for broader applicability (Table S2).<sup>42-50</sup> Different definitions and reference populations can be combined under a customisable option that allows the user to choose the most appropriate definition for each study population. These features allow experts to perform an exhaustive and standardised assessment of cardiometabolic risk factors, reducing manual workload and potential errors while focusing on the result interpretation. This type of information is particularly useful for paediatricians in making decisions such as prioritising drug treatment or bariatric surgery for patients at the highest cardiometabolic risk.

The app was validated using standard software engineering methodologies to ensure code reliability and stability. Additionally, feedback from a set of expert beta testers in the field was incorporated to optimise functionality, usability, and performance for real-world applications.

The following section presents a use case demonstrating the capabilities of ObMetrics in real-world conditions.

## 3 | CASE STUDY: INTRODUCING ObMetrics WITH EPIDEMIOLOGICAL DATASETS

### 3.1 | Study populations

Data from two paediatric Hispanic cohorts with different geographical and ethnic backgrounds (one from South America and another from South Europe [Spain]) were collected. The Hispanic-American cohort included 1759 participants from Mexico and Colombia. These participants were recruited in four Mexican cities (Monterelos [N = 274], Monterrey [N = 318], Mexico City [N = 308], and Pachuca

[ $N = 655$ ]) and the Colombian city of Medellin ( $N = 204$ ). The Hispanic-European cohort comprised 2411 participants from three Spanish cities: Santiago de Compostela ( $N = 1497$ ), Zaragoza ( $N = 396$ ), and Córdoba ( $N = 518$ ), as part of the GENOBOX study. In both cohorts, anthropometric and biochemical data were collected from participants aged between 3 and 18 years. It is important to note that the Hispanic-American cohort follows an observational study design, whereas the Hispanic-European population is a clinical cohort derived from a hospital setting where the prevalence of overweight and obesity is higher than that reported in the general population. It is acknowledged that ethnic differences between the two cohorts may influence the results. The ethnicity of the American cohort is representative of the general population in each recruiting city.<sup>51</sup> Detailed methodologies for sample collection, as well as anthropometric and biochemical measurements, are described in previous publications.<sup>52–59</sup> The anthropometric and metabolic characteristics of both cohorts are detailed in Table 2.

### 3.2 | Definitions of metabolic syndrome

The prevalence of MetS in two ethnically diverse paediatric populations was evaluated by making use of the definitions proposed by Cook et al. (2003), Zimmet et al. (2007), and Ahrens et al. (2014), which are among the most widely accepted definitions internationally. Each definition applies a specific age range: Cook et al. (2003) for individuals between 2 and 18 years, Zimmet et al. (2007) between 10 and 18 years, and Ahrens et al. (2014) (monitoring level) between 3 and 10 years. Notably, in this study, an extended version of the definition of Zimmet et al. (2007)<sup>40</sup> was used to consider the age range between 3 and 18 years. This experimental design allowed us to analyse the prevalence of MetS using these three definitions in the early childhood subset (ages 3–10 years), and the Cook et al. (2003) and Zimmet et al. (2007) definitions in the adolescence subset (ages 10–18 years) and whole population (ages 3–18 years). Only those participants with complete information necessary to classify MetS status under all three definitions were included. Specific-Mets component z-scores were calculated for individuals aged 6–18 years in both cohorts using the methodology proposed by the National High Blood Pressure Education Program (NHBPEP)<sup>31</sup> for the BP z-scores and by Stavnsbo et al. (2018)<sup>41</sup> for the remaining MetS components. We did not apply any imputation methods because the proportion of missing values was very low (<0.5%). Please note that the BP reference values from Stavnsbo et al. (2018) were not applied in this study, as they do not include the height in the BP z-scores calculation. Details on the calculation of the global MetS and specific-Mets z-score are provided in Table S1.

### 3.3 | Statistical analysis

Categorical variables are presented as both total numbers and percentages, whereas continuous variables are reported as medians with

25th to 75th percentile interquartile ranges. To compare categorical variables, Pearson's Chi-square or Fisher's exact tests were used, and the Wilcoxon rank sum test was used for numerical variables. Cohen's kappa coefficient was calculated to determine the degree of agreement between pairs of definitions in the same cohort. Additionally, Pearson's Chi-square test was used to assess the prevalence differences among children in different cohorts using the same definitions. A  $p$ -value <0.05 was considered statistically significant.

## 4 | RESULTS

### 4.1 | General description of study populations

Our study included 1759 participants in the American cohort and 2411 participants in the European cohort (Table 2). In both populations, nearly 50% of the children were female. The median (interquartile ranges) age was 9.10 (7.60, 11.17) years in the American population and 10.50 (8.60, 12.51) years in the European population. The median (interquartile ranges) BMI z-score was 0.58 (–0.26, 1.85) in the American population and 2.48 (1.59, 3.48) in the European population. Given the higher prevalence of obesity in the European cohort compared with the American, higher values were observed for all cardiometabolic complications, except for plasma triacylglycerols (TAG), which were higher in the American children. To facilitate an accurate interpretation of MetS prevalence and its components, participants were stratified by obesity status.

### 4.2 | Differences in MetS prevalence between cohorts

The MetS prevalence was estimated according to the selected definitions and divided into age groups of early childhood (3–10 years), adolescence (11–18 years), and the whole population (3–18 years), with obesity status determined by BMI according to the International Obesity Task Force (IOTF).<sup>36</sup> Table 3 presents the MetS prevalence in the European and American populations. For the European early childhood subset (3–10 years), the prevalence of MetS in children with overweight was 4.94% (Cook et al., 2003), 2.28% (Zimmet et al., 2007), and 17.49% (Ahrens et al., 2014). On the other hand, the prevalence of MetS in children with obesity was 21.93% (Cook et al., 2003), 6.98% (Zimmet et al., 2007), and 48.04% (Ahrens et al., 2014). In the early childhood American subset (3–10 years), the prevalence of MetS in children with overweight was 8.05% (Cook et al., 2003), 3.36% (Zimmet et al., 2007), and 26.17% (Ahrens et al., 2014). In children with obesity, the prevalence of MetS was 37.42% (Cook et al., 2003), 26.38% (Zimmet et al., 2007), and 66.36% (Ahrens et al., 2014).

In the European adolescence subset (11–18 years), the prevalence of MetS in children with overweight was 9.27% (Cook et al., 2003) and 6.07% (Zimmet et al., 2007), and for children with obesity, it was 28.55% (Cook et al., 2003) and 17.47% (Zimmet et al., 2007). For the American adolescent subset (11–18 years), the prevalence of

TABLE 2 Anthropometric and metabolic characteristics of the study populations.

| Variable        | Whole population (ages 3–18) |   |   | Early childhood (ages 3–10) |      |   | Adolescence (ages 11–18)                            |                      |      |  |   |                      |
|-----------------|------------------------------|---|---|-----------------------------|------|---|---|----------------------|------|--|---|----------------------|
|                 | N                            | Hispanic-American population; N = 1759 <sup>a</sup> | Hispanic-European population; N = 2411 <sup>a</sup> | p-value <sup>b</sup>        | N    | Hispanic-American population; N = 1259 <sup>a</sup> | Hispanic-European population; N = 1341 <sup>a</sup> | p-value <sup>b</sup> | N    | Hispanic-American population; N = 500 <sup>a</sup> | Hispanic-European population; N = 1070 <sup>a</sup> | p-value <sup>b</sup> |
| Sex             | 4170                         |   |   | >0.9                        | 2600 |   |   | 0.03                 | 1570 |  |   | 0.01                 |
| Female          |                              | 912 (51.8%)   | 1252 (51.9%)  |                             |      | 638 (50.7%)   | 737 (55.0%)   |                      |      | 274 (54.8%)  | 515 (48.1%)   |                      |
| Male            |                              | 847 (48.2%)   | 1159 (48.1%)  |                             |      | 621 (49.3%)   | 604 (45.0%)   |                      |      | 226 (45.2%)  | 555 (51.9%)   |                      |
| Age (years)     | 4170                         | 9.10 (7.60, 11.17)                                  | 10.50 (8.60, 12.51)                                 | <0.001                      | 2600 | 8.31 (6.85, 9.44)                                   | 8.90 (7.50, 10.00)                                  | <0.001               | 1570 | 11.91 (11.44, 12.44)                               | 12.84 (11.90, 14.10)                                | <0.001               |
| DBP (mmHg)      | 4170                         | 60 (55, 70)   | 65 (60, 72)   | <0.001                      | 2600 | 60 (52, 65)   | 64 (58, 70)   | <0.001               | 1570 | 65 (60, 70)  | 68 (62, 73)   | <0.001               |
| SBP (mmHg)      | 4170                         | 90 (84, 100)  | 110 (100, 120)                                      | <0.001                      | 2600 | 90 (81, 98)   | 106 (97, 115)                                       | <0.001               | 1570 | 98 (90, 105)                                       | 116 (109, 124)                                      | <0.001               |
| TAG (mg/dL)     | 4170                         | 89 (66, 122)  | 64 (48, 90)   | <0.001                      | 2600 | 87 (64, 119)  | 60 (45, 81)   | <0.001               | 1570 | 97 (72, 128)                                       | 70 (52, 97)   | <0.001               |
| HDL-C (mg/dL)   | 4170                         | 45 (37, 54)   | 49 (41, 59)   | <0.001                      | 2600 | 45 (37, 54)   | 51 (43, 62)   | <0.001               | 1570 | 45 (37, 53)  | 47 (39, 55)   | 0.005                |
| Glucose (mg/dL) | 4170                         | 84 (77, 90)   | 85 (80, 90)   | <0.001                      | 2600 | 84 (78, 89)   | 84 (79, 89)   | 0.03                 | 1570 | 84 (77, 92)  | 87 (81, 92)   | <0.001               |
| Insulin (μU/mL) | 3807                         | 6 (3, 11)   | 11 (6, 17)  | <0.001                      | 2385 | 5 (3, 10)   | 8 (5, 13)   | <0.001               | 1422 | 9 (5, 15)  | 14 (9, 20)  | <0.001               |
| Missing values  |                              | 274   | 89  |                             |      | 158   | 57  |                      |      | 116  | 32  |                      |
| BMI z-score     | 4049                         | 0.58 (−0.26, 1.85)                                  | 2.48 (1.59, 3.03)                                   | <0.001                      | 2480 | 0.62 (−0.24, 1.90)                                  | 2.60 (1.43, 3.30)                                   | <0.001               | 1569 | 0.47 (−0.32, 1.61)                                 | 2.41 (1.70, 2.86)                                   | <0.001               |
| Missing values  |                              | 67  | 54  |                             |      | 67  | 53  |                      |      | 0  | 1   |                      |
| HOMA-IR         | 3807                         | 1.23 (0.68, 2.28)                                   | 2.20 (1.28, 3.48)                                   | <0.001                      | 2385 | 1.06 (0.59, 1.96)                                   | 1.69 (1.03, 2.76)                                   | <0.001               | 1422 | 1.82 (1.07, 3.13)                                  | 2.97 (1.89, 4.31)                                   | <0.001               |
| Missing values  |                              | 274   | 89  |                             |      | 158   | 57  |                      |      | 116  | 32  |                      |
| Obesity status  | 4169                         |   |   | <0.001                      | 2600 |   |   | <0.001               | 1569 |  |   | <0.001               |
| Normal weight   |                              | 1207 (68.6%)  | 494 (20.5%)   |                             |      | 866 (68.8%)   | 316 (23.6%)   |                      |      | 341 (68.2%)  | 178 (16.7%)   |                      |
| Overweight      |                              | 300 (17.0%)   | 586 (24.3%)   |                             |      | 203 (16.1%)   | 273 (20.4%)   |                      |      | 97 (19.4%)   | 313 (29.3%)   |                      |
| Obesity         |                              | 252 (14.4%)   | 1330 (55.2%)  |                             |      | 190 (15.1%)   | 752 (56.1%)   |                      |      | 62 (12.4%)   | 578 (54.1%)   |                      |
| Missing values  |                              | 0   | 1   |                             |      | 0   | 0   |                      |      | 0  | 1   |                      |

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure; TAG, triacylglycerols.

<sup>a</sup>n (%), Median (IQR).

<sup>b</sup>Pearson's Chi-squared test; Wilcoxon rank sum test.

**TABLE 3** Prevalence of metabolic syndrome with the selected definitions in both study populations.

| Early childhood (ages 3–10) |     | Cook (NCEP)                     |                                |                                 |                                 | Zimmet (IDF)                    |                                |                                 |                                 | Ahrens (IDEFICS, monitoring level) |                                    |                                |                                   |        |
|-----------------------------|-----|---------------------------------|--------------------------------|---------------------------------|---------------------------------|---------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------------------------|------------------------------------|--------------------------------|-----------------------------------|--------|
| Variable                    | Sex | American population (N = 1101)  |                                | European population (N = 1284)  |                                 | American population (N = 1101)  |                                | European population (N = 1284)  |                                 | American population (N = 1101)     |                                    | European population (N = 1284) |                                   |        |
|                             |     | No MetS <sup>a</sup> (N = 1021) | Yes MetS <sup>a</sup> (N = 80) | No MetS <sup>a</sup> (N = 1114) | Yes MetS <sup>a</sup> (N = 170) | No MetS <sup>a</sup> (N = 1053) | Yes MetS <sup>a</sup> (N = 48) | No MetS <sup>a</sup> (N = 1228) | Yes MetS <sup>a</sup> (N = 56)  | No MetS <sup>a</sup> (N = 937)     | Yes MetS <sup>a</sup> (N = 164)    | No MetS <sup>a</sup> (N = 889) | Yes MetS <sup>a</sup> (N = 395)   |        |
|                             |     | p-value <sup>b</sup>            | p-value <sup>b</sup>           | p-value <sup>b</sup>            | p-value <sup>b</sup>            | p-value <sup>b</sup>            | p-value <sup>b</sup>           | p-value <sup>b</sup>            | p-value <sup>b</sup>            | p-value <sup>b</sup>               | p-value <sup>b</sup>               | p-value <sup>b</sup>           | p-value <sup>b</sup>              |        |
|                             |     | 0.7                             | 0.019                          | 0.2                             | 0.6                             | 0.2                             | 0.6                            | 0.7                             | 0.040                           |                                    |                                    |                                |                                   |        |
| Female                      |     | 521 (93.04%)                    | 39 (6.96%)                     | 601 (84.77%)                    | 108 (15.23%)                    | 531 (94.82%)                    | 29 (5.18%)                     | 680 (95.91%)                    | 29 (4.09%)                      | 474 (84.64%)                       | 86 (15.36%)                        | 474 (66.85%)                   | 235 (33.15%)                      |        |
| Male                        |     | 500 (92.42%)                    | 41 (7.58%)                     | 513 (89.22%)                    | 62 (10.78%)                     | 522 (96.49%)                    | 19 (3.51%)                     | 548 (95.30%)                    | 27 (4.70%)                      | 463 (85.58%)                       | 78 (14.42%)                        | 415 (72.17%)                   | 160 (27.87%)                      |        |
| Age (years)                 |     | 8.09 (6.56, 8.82)               | 8.66 (7.87, 9.58)              | 8.90 (7.50, 9.96)               | 8.95 (7.50, 10.08)              | 8.09 (6.58, 8.82)               | 9.09 (8.09, 9.61)              | 8.83 (7.50, 10.0)               | 9.45 (7.48, 10.10)              | 8.03 (6.50, 8.73)                  | 8.85 (7.82, 9.70)                  | 8.80 (7.51, 9.90)              | 9.00 (7.45, 10.0)                 | 0.5    |
| Obesity status              |     | <0.001                          | <0.001                         | <0.001                          | <0.001                          | <0.001                          | <0.001                         | <0.001                          | <0.001                          | <0.001                             | <0.001                             | <0.001                         | <0.001                            |        |
| Normal weight               |     | 782 (99.11%)                    | 7 (0.89%)                      | 305 (100.0%)                    | 0 (0.00%)                       | 789 (100.00%)                   | 0 (0.00%)                      | 305 (100.00%)                   | 0 (0.00%)                       | 772 (97.85%)                       | 17 (2.15%)                         | 300 (98.36%)                   | 5 (1.64%)                         | 0.6    |
| Overweight                  |     | 137 (91.85%)                    | 12 (8.05%)                     | 250 (95.06%)                    | 13 (4.94%)                      | 144 (96.64%)                    | 5 (3.36%)                      | 257 (97.72%)                    | 6 (2.28%)                       | 110 (73.83%)                       | 39 (26.17%)                        | 217 (82.5%)                    | 46 (17.49%)                       | 0.036  |
| Obesity                     |     | 102 (62.58%)                    | 61 (37.42%)                    | 559 (78.07%)                    | 157 (21.93%)                    | 120 (73.62%)                    | 43 (26.38%)                    | 666 (93.02%)                    | 50 (6.98%)                      | 55 (33.74%)                        | 108 (66.26%)                       | 372 (51.96%)                   | 344 (48.04%)                      | <0.001 |
| Adolescence (ages 11–18)    |     | Cook (NCEP)                     |                                |                                 |                                 | Zimmet (IDF)                    |                                |                                 |                                 | Ahrens (IDEFICS, monitoring level) |                                    |                                |                                   |        |
| Variable                    | Sex | American population (N = 500)   |                                | European population (N = 1070)  |                                 | American population (N = 479)   |                                | European population (N = 949)   |                                 | American population (N = 500)      |                                    | European population (N = 1070) |                                   |        |
|                             |     | No MetS <sup>a</sup> (N = 462)  | Yes MetS <sup>a</sup> (N = 38) | No MetS <sup>a</sup> (N = 874)  | Yes MetS <sup>a</sup> (N = 196) | No MetS <sup>a</sup> (N = 479)  | Yes MetS <sup>a</sup> (N = 21) | No MetS <sup>a</sup> (N = 949)  | Yes MetS <sup>a</sup> (N = 121) | No MetS <sup>a</sup> (N = 463)     | Yes MetS <sup>a</sup> (N = 10.10%) | No MetS <sup>a</sup> (N = 177) | Yes MetS <sup>a</sup> (N = 0.56%) |        |
|                             |     | p-value <sup>b</sup>            | p-value <sup>b</sup>           | p-value <sup>b</sup>            | p-value <sup>b</sup>            | p-value <sup>b</sup>            | p-value <sup>b</sup>           | p-value <sup>b</sup>            | p-value <sup>b</sup>            | p-value <sup>b</sup>               | p-value <sup>b</sup>               | p-value <sup>b</sup>           | p-value <sup>b</sup>              |        |
|                             |     | 0.10                            | 0.073                          | 0.5                             | 0.2                             | 0.5                             | 0.2                            | 0.2                             | 0.3                             | 0.3                                | 0.3                                | 0.3                            | 0.3                               |        |
| Female                      |     | 258 (94.16%)                    | 16 (5.84%)                     | 432 (83.88%)                    | 83 (16.12%)                     | 264 (96.35%)                    | 10 (3.65%)                     | 463 (89.9%)                     | 52 (10.10%)                     | 463 (89.9%)                        | 52 (10.10%)                        | —                              | —                                 |        |
| Male                        |     | 204 (90.27%)                    | 22 (9.73%)                     | 442 (79.64%)                    | 113 (20.36%)                    | 215 (95.13%)                    | 11 (4.87%)                     | 486 (87.57%)                    | 69 (12.43%)                     | —                                  | —                                  | —                              | —                                 |        |
| Age (years)                 |     | 11.91 (11.46, 12.51)            | 11.65 (11.36, 12.08)           | 12.80 (11.90, 14.08)            | 13.00 (12.00, 14.10)            | 11.91 (11.44, 12.46)            | 11.85 (11.44, 12.30)           | 12.75 (11.81, 14.00)            | 13.60 (12.40, 14.70)            | —                                  | —                                  | —                              | —                                 | <0.001 |
| Obesity status              |     | <0.001                          | <0.001                         | <0.001                          | <0.001                          | <0.001                          | <0.001                         | <0.001                          | <0.001                          | <0.001                             | <0.001                             | <0.001                         | <0.001                            |        |
| Normal weight               |     | 335 (98.24%)                    | 6 (1.76%)                      | 176 (98.88%)                    | 2 (1.12%)                       | 341 (100%)                      | 0 (0%)                         | 177 (99.44%)                    | 1 (0.56%)                       | —                                  | —                                  | —                              | —                                 |        |
| Overweight                  |     | —                               | —                              | —                               | —                               | —                               | —                              | —                               | —                               | —                                  | —                                  | —                              | —                                 |        |

(Continues)



MetS in children with overweight was 7.22% (Cook et al., 2003) and 3.9% (Zimmet et al., 2007), and in children with obesity, it was 40.32% (Cook et al., 2003) and 29.03% (Zimmet et al., 2007). When analysing both age groups (childhood and adolescence) together, the prevalence of MetS in European children with overweight was 7.29% (Cook et al., 2003) and 4.34% (Zimmet et al., 2007). For children with obesity, the MetS prevalence was 24.88% (Cook et al., 2003) and 11.67% (Zimmet et al., 2007). When merging age groups in the American population, the prevalence of MetS in children with overweight was 7.72% (Cook et al., 2003) and 3.25% (Zimmet et al., 2007). For children with obesity, it was 38.22% (Cook et al., 2003) and 27.11% (Zimmet et al., 2007).

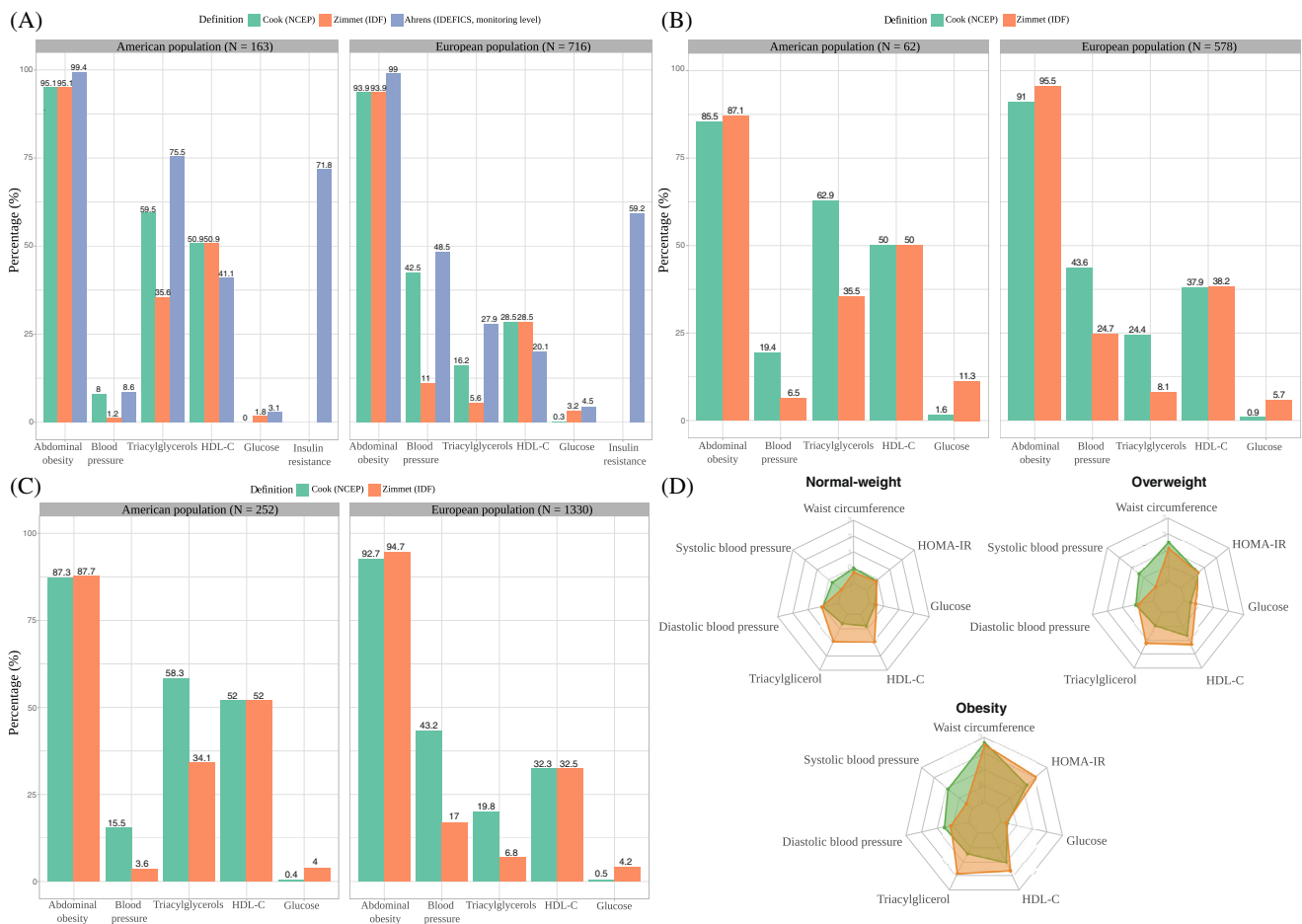
Overall, the prevalence of MetS was predominantly higher in American children with obesity than in their European counterparts across all age groups when the same MetS definition was used. Additionally, the prevalence of MetS increased as age increased in both cohorts within the early childhood subset and the whole population, but not in the adolescent subset (Table 3). This trend was expected, as it has been previously described in the literature.<sup>15,59</sup> Such an increase was less pronounced in the European cohort.

### 4.3 | Between-definitions MetS prevalence differences

The agreement between definitions within the same cohort was evaluated using Cohen's kappa statistic (Table S3). In both cohorts, the agreement (Cohen's kappa coefficient, 95% CI) was moderate between Cook–Zimmet (European cohort: 0.51 (0.45–0.56); American cohort: 0.66 (0.57–0.76)), fair between Cook–Ahrens (European cohort: 0.40 (0.34–0.46); American cohort: 0.31 (0.19–0.42)) and slight between Zimmet–Ahrens (European cohort: 0.13 (0.09–0.17); American cohort: 0.22 (0.13–0.31)) in children with obesity.

### 4.4 | Component-specific analysis of MetS within and between cohorts

Besides evaluating differences in MetS prevalence between cohorts, we also analysed whether children with obesity had different altered MetS components in each population. Our finding revealed differences in the prevalence of elevated BP, elevated TAG, and decreased



**FIGURE 2** Prevalence of MetS Components by Definition in Children with Obesity. The prevalence of MetS components is shown according to different definitions for children with obesity, categorised by age groups: (A) early childhood subset (3–11 years), (B) adolescence subset (11–18 years), and (C) whole population (3–18 years) in both study populations. Panel (D) displays specific MetS components z-scores for children and adolescents aged 6–18 years in both cohorts, differentiated by obesity status. The orange and green lines represent the median z-scores for the American and European cohorts, respectively.

TABLE 4 Specific-Mets components z-scores in both study populations.

| Variable        | American population                  |                                  |                               | European population                 |                                  |                                | Global p-value <sup>c</sup> | Overweight p-value <sup>c</sup> | Obesity p-value <sup>c</sup> |        |        |        |
|-----------------|--------------------------------------|----------------------------------|-------------------------------|-------------------------------------|----------------------------------|--------------------------------|-----------------------------|---------------------------------|------------------------------|--------|--------|--------|
|                 | Normal-weight; N = 1113 <sup>a</sup> | Overweight; N = 295 <sup>a</sup> | Obesity; N = 248 <sup>a</sup> | Normal-weight; N = 510 <sup>a</sup> | Overweight; N = 622 <sup>a</sup> | Obesity; N = 1392 <sup>a</sup> |                             |                                 |                              |        |        |        |
| Age (years)     | 1656                                 | 8.95 (7.79, 11.30)               | 10.25 (8.70, 11.51)           | 9.63 (8.20, 10.98)                  | 2524                             | 10.00 (8.40, 11.88)            | 11.08 (9.50, 13.00)         | 10.60 (8.70, 12.60)             | <0.001                       | <0.001 | <0.001 | <0.001 |
| Sex             | 1656                                 |                                  | 0.02                          | 0.02                                | 2524                             |                                |                             |                                 | 0.003                        | >0.9   | 0.007  | 0.2    |
| Female          | 597 (53.6%)                          | 153 (51.9%)                      | 109 (44.0%)                   | 237 (46.5%)                         | 352 (56.6%)                      | 719 (51.7%)                    |                             |                                 |                              |        |        |        |
| Male            | 516 (46.4%)                          | 142 (48.1%)                      | 139 (56.0%)                   | 273 (53.5%)                         | 270 (43.4%)                      | 673 (48.4%)                    |                             |                                 |                              |        |        |        |
| Height z-score  | 1656                                 | -0.62 (-1.27, 0.04)              | 0.13 (-0.47, 0.65)            | 0.74 (0.02, 1.35)                   | 2524                             | -0.02 (-0.79, 0.60)            | 0.41 (-0.26, 1.04)          | 0.78 (0.13, 1.46)               | <0.001                       | <0.001 | <0.001 | <0.001 |
| WC z-score      | 1656                                 | -0.25 (-0.64, 0.17)              | 1.01 (0.64, 1.42)             | 2.43 (1.93, 3.00)                   | 2459                             | -0.02 (-0.49, 0.46)            | 1.47 (0.99, 1.97)           | 2.66 (2.17, 3.14)               | <0.001                       | <0.001 | <0.001 | <0.001 |
| Missing values  |                                      |                                  |                               |                                     | 10                               | 45                             |                             |                                 |                              |        |        |        |
| DBP z-score     | 1656                                 | 0.10 (-0.52, 0.55)               | 0.25 (-0.25, 0.91)            | 0.39 (-0.16, 0.84)                  | 2440                             | -0.02 (-0.53, 0.48)            | 0.13 (-0.30, 0.64)          | 0.54 (0.04, 1.12)               | <0.001                       | <0.001 | 0.09   | 0.2    |
| Missing values  |                                      |                                  |                               |                                     | 15                               | 23                             |                             |                                 |                              |        |        |        |
| SBP z-score     | 1656                                 | -1.03 (-1.67, -0.29)             | -0.88 (-1.50, -0.29)          | -0.56 (-1.14, -0.06)                | 2435                             | -0.22 (-0.95, 0.54)            | 0.34 (-0.33, 1.06)          | 0.88 (0.23, 1.59)               | <0.001                       | <0.001 | <0.001 | <0.001 |
| Missing values  |                                      |                                  |                               |                                     | 15                               | 24                             |                             |                                 |                              |        |        |        |
| TAG z-score     | 1656                                 | 0.84 (0.13, 1.50)                | 1.03 (0.37, 1.85)             | 1.68 (0.94, 2.51)                   | 2502                             | -0.35 (-0.92, 0.23)            | 0.00 (-0.63, 0.69)          | 0.42 (-0.31, 1.19)              | <0.001                       | <0.001 | <0.001 | <0.001 |
| Missing values  |                                      |                                  |                               |                                     | 1                                | 2                              |                             | 19                              |                              |        |        |        |
| HDL-C z-score   | 1656                                 | -1.02 (-1.70, -0.26)             | -1.32 (-1.87, -0.58)          | -1.61 (-2.04, -1.06)                | 2470                             | 0.19 (-0.39, 1.08)             | -0.64 (-1.27, 0.07)         | -1.03 (-1.55, -0.42)            | <0.001                       | <0.001 | <0.001 | <0.001 |
| Missing values  |                                      |                                  |                               |                                     | 12                               | 11                             |                             | 31                              |                              |        |        |        |
| Glucose z-score | 1656                                 | -0.66 (-1.72, 0.19)              | -0.60 (-1.66, 0.38)           | -0.73 (-1.54, 0.25)                 | 2504                             | -0.62 (-1.36, 0.01)            | -0.61 (-1.34, 0.06)         | -0.61 (-1.30, 0.12)             | 0.5                          | 0.01   | 0.3    | 0.8    |
| Missing values  |                                      |                                  |                               |                                     | 1                                | 4                              |                             | 15                              |                              |        |        |        |
| HOMA-IR z-score | 1382                                 | -0.19 (-1.04, 0.68)              | 0.45 (-0.43, 1.40)            | 2.06 (1.16, 2.88)                   | 2410                             | -0.16 (-0.76, 0.53)            | 0.47 (-0.30, 1.11)          | 1.29 (0.62, 1.89)               | <0.001                       | <0.001 | >0.9   | 0.8    |
| Missing values  |                                      |                                  |                               |                                     | 17                               | 27                             |                             | 70                              |                              |        |        |        |

Abbreviations: DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; SBP, systolic blood pressure; TAG, triacylglycerols; WC, waist circumference.

<sup>a</sup>Median (IQR); n (%).

<sup>b</sup>Kruskal-Wallis rank sum test; Pearson's Chi-squared test. Intra-population comparison.

<sup>c</sup>Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test. Inter-population comparison.

high-density lipoprotein cholesterol (HDL-C) between Europeans and Americans, possibly argued in ethnic differences (Figure 2A–C). To investigate this potential effect of ethnicity on the prevalence of MetS and its individual components, we calculated the MetS z-scores in both study populations (Table 4). Notable differences were observed in all MetS components between individuals with normal weight, overweight, and obesity within each cohort, except for glucose. Similarly, increasing trends were identified in some MetS z-scores within each cohort as the obesity status increased (mainly for diastolic blood pressure [DBP] and homeostatic model assessment for insulin resistance [HOMA-IR]). The HOMA-IR z-score showed the most pronounced increase as the obesity status increased (Table 4). These results reinforce the need to include IR as a component in MetS definitions.

Additionally, there were differences between cohorts in terms of individual MetS z-scores (WC, systolic blood pressure [SBP], TAG and HDL-C), regardless of the obesity status (Figure 2D). The American cohort exhibited a worse lipid profile, as evidenced by elevated TAG and reduced HDL-C z-scores compared with the European cohort, independently of obesity status. The American cohort presented a lower SBP z-score than the European cohort regardless of obesity status, which is responsible for the previously mentioned lower prevalence of altered BP. Notably, American children with obesity showed an unhealthier metabolic profile compared with European children with obesity, as evidenced by their higher TAG z-score, HDL-C z-score, and HOMA-IR z-scores (Table 4 and Figure 2D).

## 5 | DISCUSSION

In the absence of an international consensus for the assessment of MetS in paediatric and adolescent populations, a novel Shiny app named ObMetrics has been developed to enable the calculation of a range of MetS outcomes (including binary and z-score variables) according to definitions available and published to date. Furthermore, ObMetrics offers the flexibility to adopt or create new MetS definitions by allowing users to select different reference standards for each cardiometabolic risk factor, thereby tailoring the criteria to the specific needs of each population.

The variability among MetS definitions and reference tables is a significant challenge in paediatric epidemiological research. The utility of ObMetrics has been demonstrated through a comprehensive case study of MetS prevalences in two ethnically diverse paediatric cohorts. The findings of our case study corroborate the existence of considerable inter-definition and inter-population variation in the prevalence of MetS (Table 3).<sup>60,61</sup> As a main finding from our case study, we found higher MetS prevalence among American children with overweight and obesity compared with their European counterparts, which is in line with previously published studies.<sup>62</sup> Beyond MetS classification, ObMetrics allowed us to compute z-scores permitting the exploration of the distinct metabolic health profiles within each cohort. Particularly, our findings revealed strong between-populations variability in SBP, TAG, and HDL-c components (Table 4

and Figure 2D). These differences might be argued in the different genetic and sociocultural backgrounds of the two study populations and reinforce the necessity to select the most ethnically close reference standard when assessing MetS in a given paediatric population. Interestingly, our study pointed to HOMA-IR as one of the most frequently altered components of MetS in both populations (Figure 2A,D). This trend has been previously confirmed in European populations by different studies,<sup>15,63</sup> which also point to IR as the cornerstone for the development of future cardiometabolic alterations in patients with obesity.<sup>64</sup> This finding is of high importance since, at the moment, the majority of accepted MetS definitions do not consider IR as an altered component of MetS. In the middle of this need, ObMetrics appears to be a powerful tool offering users to move toward definitions considering IR as a crucial alteration of MetS, further offering the possibility to create a customised MetS definition.

Some existing research indicates that paediatric MetS may predict future cardiometabolic disorders,<sup>9,11,12,16</sup> yet it remains unknown whether different MetS definitions offer varying prognostic accuracy. Future investigations should examine the impact of definition choice on predictive capacity, enabling the identification of clinically meaningful cut-points for risk stratification in paediatric populations.

Our study has several notable strengths. The large sample sizes increase statistical power and reliability, allowing robust subgroup analyses based on obesity status and age. Including two ethnically diverse populations allows exploration of inter-cohort differences in MetS prevalence and components, highlighting potential ethnic and regional variations. Using multiple recognised MetS definitions (Cook et al., 2003; Zimmet et al., 2007; Ahrens et al., 2014) adds rigour, enabling comprehensive comparisons and insights into how definitions influence interpreting MetS prevalence in paediatric populations. Altogether, these strengths and our case study results demonstrate the potential of ObMetrics to facilitate the harmonisation of paediatric obesity research and enhance clinical applications.

Likewise, several limitations should be acknowledged. The absence of genetic markers limits our ability to precisely assess ethnic effects and understand genetic predispositions contributing to differences in MetS prevalence between cohorts. Additionally, lacking pubertal development data (Tanner stages) prevented us from testing ObMetrics' utility to capture metabolic differences across pubertal stages.

## 6 | CONCLUSION

ObMetrics emerges as a powerful and user-friendly Shiny app designed to standardise the assessment of MetS in paediatric populations. Given the demonstrated lack of consensus regarding paediatric MetS definitions, ObMetrics further addresses a crucial gap by allowing researchers and clinicians to calculate MetS prevalence and cardiometabolic z-scores across multiple internationally recognised definitions. This capability not only enhances the comparability of paediatric studies but also enables more accurate identification of at-

risk children and adolescents based on ethnically diverse reference standards.

## AUTHOR CONTRIBUTIONS

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## CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose.

## DATA AVAILABILITY STATEMENT

The datasets generated and analysed during the current study are not publicly available due to data regulations and for ethical reasons, considering that this information might compromise research participants' acceptance because our participants only gave their consent for the use of their data by the original team of investigators. However, collaborations for data analyses can be requested by sending a letter to the corresponding author ([caguiler@ugr.es](mailto:caguiler@ugr.es)). The request will then be passed to all the members of the ObMetrics working group for deliberation.

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