

## Research Article

# Prevalence of Metabolic Syndrome among Children and Adolescents in High-Income Countries: A Systematic Review and Meta-Analysis of Observational Studies

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**Introduction.** Metabolic syndrome (MetS) is an assemblage of interconnected cardiovascular risk factors that are prevalent among children and adolescents in high-income countries (HICs). Despite the presence of several studies on the issue, the study findings are incongruent due to the absence of a gold standard diagnostic method of MetS in children. Thus, the findings of the original studies are inconclusive for policy makers and other stakeholders. This systematic review and meta-analysis is aimed at giving conclusive evidence about MetS among children and adolescents in HICs. **Methods.** We conducted searches using electronic databases (PubMed, Scopus, Web of Science, CINAHL (EBSCOhost), EMBASE (Elsevier), and Medline (EBSCOhost)) and other sources (Google Scholar and Google) up to September 2020. Observational studies reporting the prevalence of MetS were eligible in this study. The pooled estimates were computed in fixed and random effect models using six diagnostic methods (IDF, ATP III, de Ferranti et al., WHO, Weiss et al., and Cruz and Goran). Publication bias was verified using funnel plots and Egger's regression tests. Subgroup and sensitivity analysis were performed in case of higher heterogeneities among the included studies. **Result.** In this study, 77 studies with a total population of 125,445 children and adolescents were used in the final analysis. Metabolic syndrome among the overweight and obese population was computed from 28 studies with the pooled prevalence of 25.25%, 24.47%, 39.41%, 29.52%, and 33.36% in IDF, ATP III, de Ferranti et al., WHO, and Weiss et al. criteria, respectively. Likewise, 49 studies were eligible to compute the pooled prevalence of MetS in the general population of children and adolescents. Hence, MetS was found in 3.70% (IDF), 5.40% (ATP III), 14.78% (de Ferranti et al.), 3.90% (WHO), and, 4.66% (Cruz and Goran) of study participants. Regarding the components of MetS, abdominal obesity in the overweight and obese population, and low HDL-C in the general population were the most common components. Besides, the prevalence of MetS among males was higher than females. **Conclusion.** This study demonstrates that MetS among children and adolescents is undoubtedly high in HICs. The prevalence of MetS is higher among males than females. Community-based social and behavioral change communications need to be designed to promote healthy eating behaviors and physical activities. Prospective cohort studies could also help to explore all possible risk factors of MetS and to design specific interventions accordingly.

## 1. Introduction

Metabolic syndrome (MetS) is an assemblage of interconnected cardiovascular risk factors of metabolic origin [1]. Elevated triglycerides (TG), altered glucose metabolism, reduced high-density lipoprotein cholesterol (HDL-C), and elevated blood pressure (BP) and adiposity are the main risk factors [2]. It is primarily caused by insulin resistance due to abnormal cellular metabolism, leading to diabetes mellitus, increased uric acid level, hepatic steatosis, polycystic ovary syndrome, and obstructive sleep apnea [3–8].

The definition of MetS in children and adolescents remains unclear due to the absence of gold standard diagnostic criteria of MetS for the pediatric population [9]. Some of the diagnostic criteria used by studies include the International Diabetes Federation (IDF) criteria [10], the World Health Organization (WHO) criteria [11], the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria modified for age [12], the de Ferranti et al. criteria [13], the Weiss et al. criteria [14], and the Cruz and Goran criteria [15].

Globally, an estimated 3.3% with a range of 0.2% to 38.9% of children and adolescents were expected to live with MetS. The prevalence was considerably higher in the overweight (11.9%) and obese (29.2%) population [9, 16, 17]. Likewise, the prevalence of MetS is remarkably higher in high-income countries (HICs) due to increasing trends of childhood obesity rates [18]. The rise in obesity in the past four decades could be primarily associated with related lifestyle factors such as routine consumption of fructose in the form of soft drinks, juice, and baked goods [19–22]. Thus, obesity increased MetS in children and adolescents from 6% to 39% [23].

Metabolic syndrome has been a global pandemic affecting children and adults [24]. The burden is significantly higher in the developed world posing a high economic burden on the health care system [25]. Cardiovascular and other metabolic complications are also common consequences of MetS in children [26]. In addition, MetS also negatively impacts the mental status and over all cognitive performance of children and adolescents [27]. In spite of the fact that multiple treatment strategies were designed and implemented, the prevalence of MetS remained high in most high-income countries with a remarkable variation among countries [28, 29]. Primary studies substantiated this by showing that the prevalence of MetS in the general population ranged from 0.4% [30] to 24% [31]. Similarly, the prevalence in the obese population ranged from 6% [32] to as high as 55.8% [33]. There is also considerable variation among the diagnostic methods of MetS in the pediatric population [34].

Though comprehensive systematic reviews and meta-analyses are vital for evidence-based decision making, they are scant in HICs where the burden of MetS is undoubtedly higher. Hence, this systematic review and meta-analysis is aimed at determining the pooled prevalence of MetS among children and adolescents in HICs and at giving conclusive evidence about its burden in these countries. The findings will be vital for policy makers and program planners in crafting preventive and treatment measures. The current findings

will be supplementary for assessing the progress of sustainable development goals, specifically, ending all forms of malnutrition by 2030 [35]. In addition, the findings of this study will have a pivotal implication to conduct original studies on a multitude of factors related to high-burden MetS among the pediatric population.

## 2. Methods

**2.1. Data Sources and Eligibility Criteria.** Studies performed in HICs with the aim of identifying MetS among children and adolescents were included in this systematic review and meta-analysis. The eligibility of the studies was verified prior to inclusion to this study using study area, study setups, title, abstract, and full texts. The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guideline [36] was followed in the write-up process of the whole document. We explored national surveys and published and unpublished studies conducted in English. The reference lists of selected articles were also cross-checked for additional articles that were not found using search strings. Studies conducted until September 2020 were searched. Finally, observational studies reporting the prevalence of MetS among children and adolescents conducted both in clinical and community-based setups were included.

Conversely, studies with incomplete or unclear diagnostic methods and studies without full texts were excluded. We communicated with the corresponding authors using email before making the decision to exclude studies without full texts. Letters to editors, conference proceedings, and qualitative studies were also excluded. The EndNote X8 reference manager was used to manage the retrieved articles.

**2.2. Search Strategies and Study Selection Process.** A comprehensive search was performed by three investigators (ZWB, ZT, and TW), independently. Literature searches were conducted for studies published up to September 2020 using databases such as PubMed, Scopus, Web of Science, CINAHL (EBSCOhost), EMBASE (Elsevier), and Medline (EBSCOhost) as well as other sources (Google Scholar and Google). The following key terms were used for searching: (a) *population* (children, child, school age, and adolescent), (b) *exposure* (associated factors and risk factors), (c) *outcome* (metabolic syndrome, MetS, components of metabolic syndrome, and cardiovascular risk factors), (d) *study design* (cohort studies, cross-sectional studies, epidemiology, observational studies, and national health surveys), (e) *study setting* (school, community-based surveys, and health institutions), and (f) *location* (high-income countries, HICs, developed countries, and names of high-income countries). The Boolean search operators “OR” and “AND” were used during the searching process, and the appropriateness of the key terms were checked before conducting the search in each of the explored databases. An example of a search string in PubMed is shown in Table 1.

**2.3. Data Extraction Process.** Data extraction was done by three authors (ZWB, AA, and TW) independently using a standardized data extraction checklist. The extraction



III criteria modified for age, MetS is diagnosed when three of the following criteria are met: TG  $\geq$  110 mg/dl, HDL - C  $\leq$  40 mg/dl, systolic BP or diastolic BP  $\geq$  90th percentile, waist circumference  $\geq$  90th percentile for age and gender, and FG  $\geq$  110 mg/dl [12]. According to de Ferranti et al., MetS is a clustering of at least three of the following criteria: FG  $\geq$  110 mg/dl; HDL - C  $\leq$  50 mg/dl (except in boys aged 15 to 19 years in whom the cut-off point is 45 mg/dl); TG  $\geq$  100 mg/dl; systolic BP  $>$  90th percentile for gender, age, and height; and WC  $>$  75th percentile for age and gender [13]. According to Cruz and Goran, MetS is defined as the presence of at least three of the following abnormalities: abdominal obesity (WC  $>$  90th percentile for age and gender), hypertriglyceridemia (TG  $>$  90th percentile for age and gender), low HDL-C (HDL - C  $>$  10th percentile for age and gender), hypertension (systolic or diastolic blood pressure  $>$  90th percentile adjusted for height, age, and gender), and impaired glucose tolerance [15]. Furthermore, Weiss et al. diagnosed MetS when three or more of the following are obtained: obesity (BMI Z score  $\geq$  2.0), fasting glycemia (glycemia at oral glucose tolerance test of 140-200 mg/dl), elevated BP (BP  $>$  95th centile), low HDL-C (HDL - C  $<$  5th centile), and high TG (TG  $>$  95th centile) [14].

**2.6. Statistical Methods and Analysis.** In this meta-analysis, STATA version 15 (STATA Corporation, College Station Texas) software was used to calculate the pooled estimates. The pooled estimates were computed using both random and fixed effect models. In the presence of high heterogeneity among studies, the pooled estimates were computed using random effect models and were weighted using the inverse variance method. Subgroup analyses were performed using different parameters. The pooled estimates in the general and overweight and obese population were presented separately. For the subgroup analysis, data were extracted based on study continent, study country, and gender of study subjects. The appropriateness of each datum was verified before the analyses. Forest plots, summery tables, and texts were used to present the findings of this study.

**2.7. Publication Bias and Heterogeneity.** Publication bias was assessed using the funnel plot and Egger's regression test at a 5% significant level [40]. Heterogeneity among included studies was explored using the forest plot, the  $I^2$  test, and the Cochrane Q statistics [41]. The  $I^2$  values of 25%, 50%, and 75% were interpreted as low, medium, and high heterogeneity, respectively [42]. In the present meta-analysis, significant heterogeneity was considered when the  $I^2$  value was  $\geq$  50%, with a  $p$  value  $<$  0.05. The possible sources of significant heterogeneity were addressed through subgroup and sensitivity analyses.

### 3. Results

**3.1. Selection of Eligible Studies.** We found 5514 studies in our initial search from reputable databases and grey literature sources. Primarily, 765 studies were duplicated files. A total of 4749 studies were screened using titles and abstracts, and 4648 were removed due to the fact that most of the results

were unrelated to our objective. Finally, the full texts of 101 studies were assessed for eligibility criteria. Of 101 studies, 24 were excluded due to inconsistency of results [43-59], incompleteness of results [60-64], and publications not in English language [65, 66]. Seventy seven studies were included in the current systematic review and meta-analysis, of which 49 [13, 30, 31, 67-112] were used in computing the pooled prevalence of MetS in the general population and 29 [14, 15, 32, 33, 113-136] were used for estimating the pooled prevalence of MetS in overweight and obese study subjects (Figure 1).

**3.2. Characteristics of the Included Studies.** All studies included in this study were cross-sectional studies. Out of the total 77 studies, 49 studies were conducted among the general population of children and adolescents [13, 30, 31, 67-112]. The remaining 28 studies were performed in the overweight and obese population [14, 15, 32, 33, 113-136]. In this review, 125,445 study participants were included, of which 113,742 were from the general population and 11,703 were from the overweight and obese population. In the overweight and obese population, the sample size ranged from 97 [136] to 1241 [119] children. Likewise, the sample size in the general population ranged from 234 [111] to 12,147 [30]. The age range of study subjects in both groups was between 2 and 19 years. Regarding geographic distribution of studies, 34 studies were conducted in Europe, while 23, 16, 2, and 2 studies were conducted in Asia, USA, Canada, and Latin America, respectively. The quality of articles was also assessed using the JBI checklists. Thus, 48 studies were classified under medium quality, and 29 studies had high quality (Tables 2 and 3).

**3.3. Metabolic Syndrome among Overweight and Obese Children and Adolescents.** The pooled prevalence of MetS was estimated using five diagnostic methods (IDF, ATP III, de Ferranti, Weiss, and WHO). In the IDF diagnostic method, thirteen studies [32, 33, 119, 126, 128-132, 134-136] were used to compute the pooled prevalence of MetS (25.25%; 95% CI: 19.31, 31.19;  $I^2 = 97.5\%$ ;  $p \leq 0.001$ ). Regarding the components, abdominal obesity was found to be the most common component (65.62%; 95% CI: 47.09, 84.15;  $I^2 = 99.4\%$ ;  $p \leq 0.001$ ), and high FG level was the least common component (7.64%; 95% CI: 4.81, 10.46;  $I^2 = 97.3\%$ ;  $p \leq 0.001$ ). According to the ATP III method, the pooled prevalence of MetS was computed using 15 eligible studies [32, 113, 115, 116, 118-121, 123-127, 129, 133]. One quarter (24.47%; 95% CI: 19.87, 29.08;  $I^2 = 94.9\%$ ;  $p \leq 0.001$ ) of study subjects were diagnosed with MetS. Regarding the components of MetS, abdominal obesity was the most common component (79.8%; 95% CI: 67.39, 92.23;  $I^2 = 99.5\%$ ;  $p \leq 0.001$ ), and high FG level was the most infrequent component (7.77%; 95% CI: 5.53, 10.02;  $I^2 = 96.3\%$ ;  $p \leq 0.001$ ). The highest pooled prevalence of MetS (39.41%; 95% CI: 34.62, 44.22;  $I^2 = 78.3\%$ ;  $p \leq 0.01$ ) among the overweight and obese population was recorded in the de Ferranti diagnostic criteria, using three eligible studies [32, 115, 119]. Three quarters (75.72%; 95% CI: 67.29, 84.15;  $I^2 = 96\%$ ;  $p \leq 0.001$ ) of children and adolescents were found to have abdominal

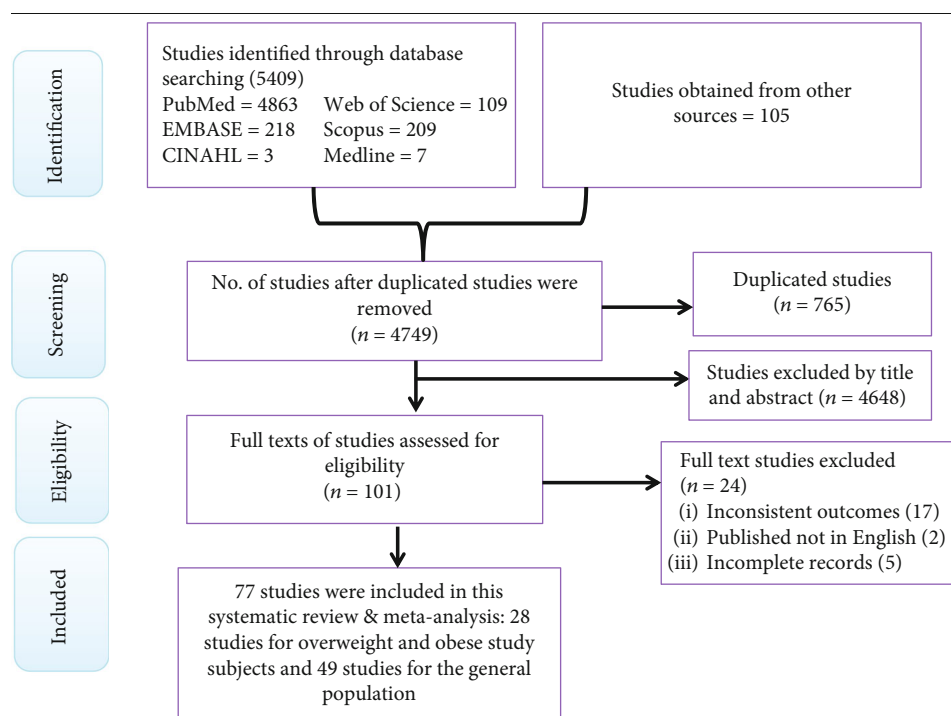


FIGURE 1: PRISMA flow chart showing study selection process.

obesity and only 1.61% (0.34, 2.88, 84.1%;  $p \leq 0.01$ ) of them had high FG level. According to the WHO diagnostic criteria, MetS was found in 29.52% (95% CI: 16.69, 42.35;  $I^2 = 99.1\%$ ;  $p \leq 0.001$ ) of the study population and it was computed from seven eligible studies [32, 114, 117, 119, 121, 122, 129]. In this diagnostic criteria, abdominal obesity (73.41%; 95% CI: 62.73, 84.09;  $I^2 = 99.8\%$ ;  $p \leq 0.001$ ) was the frequent component, whereas high FG was the infrequent one (11.12%; 95% CI: 3.67, 18.57;  $I^2 = 98.7\%$ ;  $p \leq 0.001$ ). Only three studies [14, 15, 32] were used to compute the pooled prevalence of MetS (33.36%; 95% CI: 25.06, 41.65;  $I^2 = 89.9\%$ ;  $p \leq 0.001$ ) in the Weiss diagnostic criteria. Similar to the other diagnostic methods, abdominal obesity (71.48%; 95% CI: 53.87, 89.10;  $I^2 = 93.8\%$ ;  $p \leq 0.001$ ) and high FG level (15.53%; 95% CI: -7.01, 38.07;  $I^2 = 99.1\%$ ;  $p \leq 0.001$ ) were the most and least frequent components, respectively, in the Weiss criteria.

The pooled prevalence of MetS was also estimated among males and females. The prevalence of MetS was relatively higher in males (26.62%) than in females (20.18%) in the IDF method. However, the pooled prevalence was nearly similar among males (24.75%) and females (24.97%) in accordance with the ATP III diagnostic method (Figure 2 and Table 4).

**3.4. Metabolic Syndrome among the General Population of Children and Adolescents.** In the general population of children and adolescents, the pooled prevalence of MetS was computed using the IDF, ATP III, de Ferranti, Cruz and Goran, and WHO diagnostic criteria. The pooled prevalence of MetS was estimated to be 3.70% (95% CI: 2.96, 4.44;  $I^2 =$

97.5%;  $p \leq 0.001$ ) with the IDF diagnostic criteria, which was computed from 23 original studies [30, 73, 74, 77, 79, 81–83, 85, 87, 88, 93, 94, 98–101, 103, 104, 106, 108, 112]. Regarding the components of MetS, low HDL-C was the most prevalent component (23.41%; 95% CI: 14.71, 32.11;  $I^2 = 99.8\%$ ;  $p \leq 0.001$ ), whereas high TG level was the least prevalent component (7.10%; 95% CI: 4.72, 9.48;  $I^2 = 98.4\%$ ;  $p \leq 0.001$ ). Coming to the ATP III diagnostic method, the pooled prevalence of MetS was found to be 6.08% (95% CI: 5.08, 7.07;  $I^2 = 98.2\%$ ;  $p \leq 0.001$ ), and it was estimated from 33 studies [30, 31, 67–72, 74, 76–80, 83, 84, 86, 89–92, 95–98, 100–102, 105, 107–109, 111]. In this diagnostic method, elevated BP was the most common component (21.43%; 95% CI: 16.60, 26.25;  $I^2 = 99.6\%$ ;  $p \leq 0.001$ ) and high FG level (7.16%; 95% CI: 5.22, 9.11;  $I^2 = 99.4\%$ ;  $p \leq 0.001$ ) was the least common component. The highest (14.78%; 95% CI: 11.02, 18.54;  $I^2 = 96.5$ ;  $p \leq 0.001$ ) pooled prevalence of MetS was recorded in the de Ferranti diagnostic criteria, which was computed from four eligible studies [13, 31, 78, 106]. In accordance with the Cruz and Goran diagnostic criteria, the pooled prevalence of MetS was computed from two studies [75, 78], and it was found to be 4.66% (95% CI: 3.29, 6.03;  $I^2 = 76.6\%$ ;  $p \leq 0.01$ ). Elevated BP was the most prevalent component (27.50%; 95% CI: 12.12, 42.89;  $I^2 = 99.0$ ;  $p \leq 0.001$ ) of MetS, and abdominal obesity was the most infrequent component (10.06%; 95% CI: 7.12, 13.00;  $I^2 = 89.6\%$ ;  $p \leq 0.01$ ). Besides, the pooled prevalence of MetS was estimated using the WHO diagnostic method from three studies [68, 79, 110]. Accordingly, 3.90% (95% CI: 0.60, 7.20;  $I^2 = 97.2\%$ ;  $p \leq 0.001$ ) of the study subjects were found to have MetS. The highest component





TABLE 3: Characteristics of studies included to compute the prevalence of metabolic syndrome among the general population in HICs.

Author, year	Country	Sample size	Prevalence in males (%)	Prevalence in females (%)	Age	MetS with diagnostic method (%)					Components of MetS (%)					Quality score
						IDF	ATP III	de Ferranti	Cruz and Goran	WHO	Ab. obesity	Low HDL	High TGL	High FG	High BP	
Cook et al., 2003 [67]	USA	2430	1150 (6.1)	1280 (2.1)	12-19	—	4.2	—	—	—	9.8	23.3	23.4	1.5	4.9	6
de Ferranti et al., 2004 [13]	USA	1960	9.5	8.9	12-19	—	—	9.2	—	—	—	—	—	—	—	6
Goodman et al., 2004 [68]	USA	1513	755 (3.8)	758 (4.7)	—	—	4.2	—	—	8.2	14.5	4.9	4.9	1.7	4.9	5
Agirbashi et al., 2006 [69]	Turkey	1385	690 (3.3)	695 (1.0)	10-17	—	2.2	—	—	—	4.9	13.4	26.7	0.5	15.7	5
DuBose et al., 2006 [70]	USA	375	182 (5)	193 (5)	7-9	—	5	—	—	—	10	5	18	1	37	8
Kim et al., 2007 [71]	Korea Rep.	2165	1081 (9)	1084 (6.5)	12-19	—	7.8	—	—	—	15.9	18.3	26.2	8.4	23	8
Cook et al., 2008 [72]	USA	1826	13.2	5.3	12-19	—	9.4	—	—	—	16.1	22.7	24.2	10.8	10.0	6
Ford et al., 2008 [73]	USA	2014	1058 (6.7)	956 (2.1)	12-17	4.5	—	—	—	—	28.6	22.6	8.9	10.6	3.5	8
Kong et al., 2008 [74]	Hong Kong	1616	786 (1.5)	830 (0.8)	11-16	1.2	2.1	—	—	—	—	—	—	—	—	6
Linardakis et al., 2008 [75]	Greece	1209	786 (2.4)	830 (1.8)	3-17.5	—	—	—	—	—	—	—	—	—	—	6
Pan et al., 2008 [76]	USA	4450	2260 (5.1)	2190 (1.7)	12-9	—	3.5	—	3.9	—	8.5	9.1	10.5	5.1	35.4	6
Pirkola et al., 2008 [77]	Finland	5665	2862 (3.5)	2803 (1.2)	16	2.4	2.1	—	—	—	—	—	—	—	—	8
Seo et al., 2008 [78]	Korea Rep.	3431	1828 (7.7)	1603 (6.1)	10-19	—	6.1	—	—	—	11.5	20.1	29.5	6.6	19.7	8
Cizmecioglu et al., 2009 [79]	Turkey	2491	1828 (14.1)	1603 (16.2)	10-19	—	—	14	—	—	23.7	51.7	37	6.6	19.7	8
Johnson et al., 2009 [80]	USA	2456	1278 (1.7)	1213 (1.5)	10-19	2.3	2.4	—	5.3	2.8	—	—	—	—	—	8
Noto et al., 2009 [81]	Italy	1629	1288 (10.8)	1168 (6.1)	12-19	—	8.6	—	—	—	19.1	19.3	25.6	14.0	6.9	8
Park et al., 2009 [82]	Korea Rep.	4164	859 (0.7)	770 (0.4)	7-14	0.6	—	—	—	—	1	1	1	—	—	6
Al-Isa et al., 2010 [83]	Kuwait	431	2140 (2.9)	2024 (2.3)	10-19	2.6	—	—	—	—	11.3	12.9	11.8	22.7	7.7	7
Di Bonito et al., 2010 [31]	Italy	724	—	431 (14.8)	10-19	14.8	—	—	—	—	31.0	39.6	1.1	9.1	49.4	8
Lee et al., 2010 [84]	Korea Rep.	928	332 (13)	392 (9)	6-16	—	11	24	—	—	—	—	—	—	—	6
Park et al., 2010 [85]	Korea Rep.	664	332 (24)	392 (23)	10-18	—	6.7	—	—	—	9.8	38.6	21.9	2.9	9.3	8
Park et al., 2010 [85]	USA	734	491 (8.5)	437 (4.5)	12-19	2.5	—	—	—	—	8.4	41.1	7.3	3	6.1	6
			414 (7.3)	320 (3.5)	12-19	5.5	—	—	—	—	34.7	21.6	14.2	11.8	4.1	6





TABLE 3: Continued.

Author, year	Country	Sample size	Prevalence in males (%)	Prevalence in females (%)	Age	MetS with diagnostic method (%)				Components of MetS (%)					Quality score		
						IDF	ATP III	de Ferranti	Cruz and Goran	WHO	Ab. obesity	Low HDL	High TGL	High FG		High BP	
	Korea Rep																
Choi et al., 2017 [105]	Korea Rep	3057	1625 (7.0)	1432 (5.2)	10-19	—	6.2	—	—	—	8.9	14.5	19.7	0.5	25.6	8	
Haroun et al., 2017 [112]	UAE	596	308 (12)	288 (10)	10-15.9	3.7	—	—	—	—	17.9	15.1	15.1	15.1	15.1	8	
Kim et al., 2018 [106]	Korea Rep	2314	—	—	12-18	7.8	—	—	—	—	—	—	—	—	—	8	
Stevens et al., 2018 [107]	USA	7464	7.9	4.9	12-15	—	6.5	—	—	—	—	—	—	—	—	8	
Bacopoulou et al., 2019 [108]	Greece	1578	671 (3.4)	907 (2)	12-17	2.6	2.9	—	—	—	9.5	10.7	2.3	25.9	21.8	5	
DeBoer et al., 2019 [109]	USA	4600	2429 (9.9)	2171 (5.5)	12-19	—	7.7	—	—	—	20.9	14.6	21.8	14.9	8.2	8	
Elitok et al., 2019 [110]	Turkey	353	—	—	10-14	—	—	—	—	0.85	14.1	2.5	7.4	1.4	2	6	
Shah et al., 2020 [111]	UAE	234	113 (7.9)	121 (9.9)	6-11	—	8.9	—	—	—	15	47.4	6.8	1.7	20.5	5	

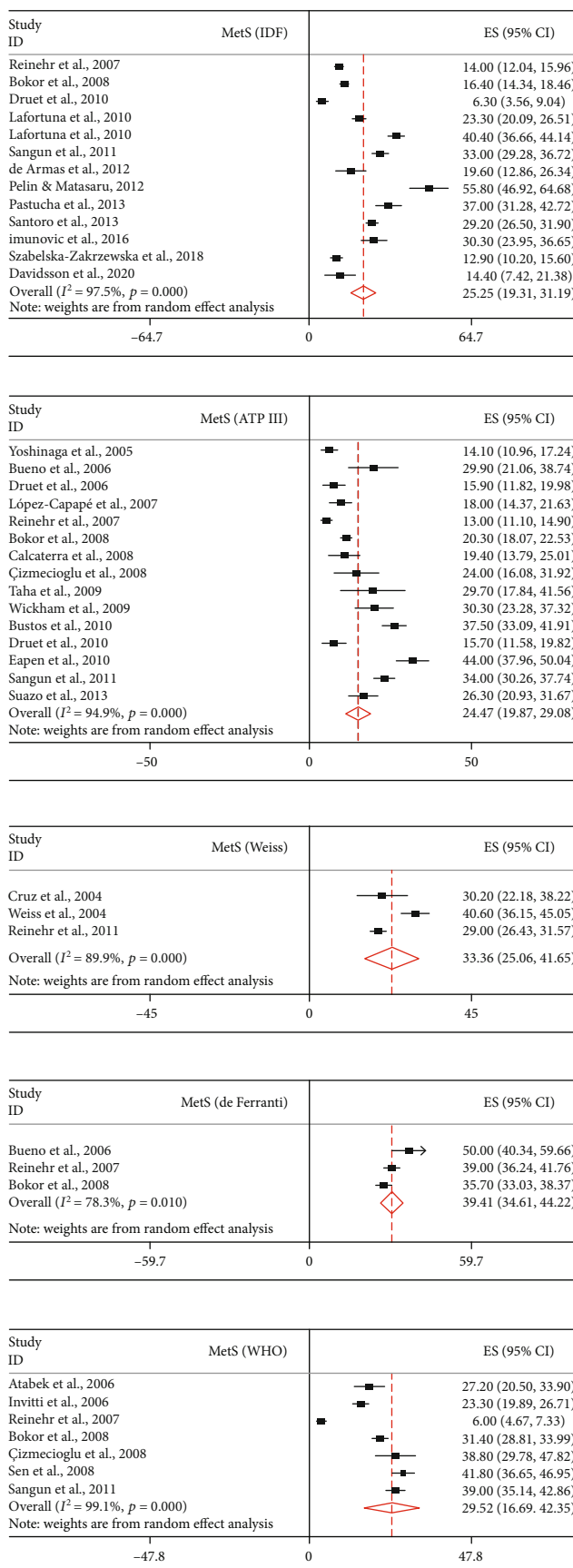


FIGURE 2: The pooled prevalence of MetS among overweight and obese children and adolescents in high-income countries, 2020.

TABLE 4: Pooled prevalence of MetS in overweight and obese children and adolescents in HICs.

Variables	Characteristics	# of studies	Pooled prevalence (95% CI)	Heterogeneity ( $I^2$ (%), $p$ value)	Model
Diagnostic criteria	IDF	13	25.25 (19.31, 31.19)	97.5, $p \leq 0.001$	REM
	ATP III	15	24.47 (19.87, 29.08)	94.9, $p \leq 0.001$	REM
	de Ferranti	3	39.41 (34.62, 44.22)	78.3, $p = 0.010$	REM
	WHO	7	29.52 (16.69, 42.35)	99.1, $p \leq 0.001$	REM
	Weiss	3	33.36 (25.06, 41.65)	89.9, $p \leq 0.001$	REM
Components of MetS (IDF)	Abdominal obesity	5	65.62 (47.09, 84.15)	99.4, $p \leq 0.001$	REM
	Low HDL-C	9	34.77 (26.63, 42.90)	97.5, $p \leq 0.001$	REM
	High TG	10	24.11 (10.61, 37.62)	99.5, $p \leq 0.001$	REM
	High FG	9	7.64 (4.81, 10.46)	97.3, $p \leq 0.001$	REM
	Elevated BP	8	34.80 (22.08, 47.51)	98.9, $p \leq 0.001$	REM
Components of MetS (ATP III)	Abdominal obesity	10	79.81 (67.39, 92.23)	99.5, $p \leq 0.001$	REM
	Low HDL-C	13	29.94 (20.83, 39.05)	98.3, $p \leq 0.001$	REM
	High TG	14	28.43 (16.72, 40.13)	99.2, $p \leq 0.001$	REM
	High FG	13	7.77 (5.53, 10.02)	96.3, $p \leq 0.001$	REM
	Elevated BP	13	30.38 (21.72, 39.04)	98.5, $p \leq 0.001$	REM
Components of MetS (de Ferranti)	Abdominal obesity	2	75.72 (67.29, 84.15)	96.0, $p \leq 0.001$	REM
	Low HDL-C	2	51.24 (45.85, 56.63)	86.5, $p = 0.007$	REM
	High TG	2	47.39 (38.38, 56.41)	95.2, $p \leq 0.001$	REM
	High FG	2	1.61 (0.34, 2.88)	84.1, $p = 0.012$	REM
	Elevated BP	2	35.04 (29.06, 41.02)	90.1, $p = 0.002$	REM
Components of MetS (WHO)	Abdominal obesity	6	73.41 (62.73, 84.09)	99.8, $p \leq 0.001$	REM
	Low HDL-C	4	17.91 (12.30, 23.69)	94.5, $p \leq 0.001$	REM
	High TG	6	31.82 (10.02, 53.63)	99.7, $p \leq 0.001$	REM
	High FG	6	11.12 (3.67, 18.57)	98.7, $p \leq 0.001$	REM
	Elevated BP	5	24.38 (11.79, 36.98)	98.8, $p \leq 0.001$	REM
Components of MetS (Weiss)	Abdominal obesity	2	71.48 (53.87, 89.10)	93.8, $p \leq 0.001$	REM
	Low HDL-C	2	41.48 (-7.16, 90.83)	99.3, $p \leq 0.001$	REM
	High TG	2	34.89 (18.25, 51.53)	94.0, $p \leq 0.001$	REM
	High FG	2	15.53 (-7.01, 38.07)	99.1, $p \leq 0.001$	REM
	Elevated BP	2	23.07 (19.05, 27.10)	31.6, $p = 0.227$	REM
Gender (IDF)	Male	4	26.62 (14.48, 38.75)	97.3, $p \leq 0.001$	REM
	Female	4	20.18 (9.02, 31.14)	94.5, $p \leq 0.001$	REM
Gender (ATP III)	Male	5	24.75 (13.42, 36.07)	93.8, $p \leq 0.001$	REM
	Female	5	24.97 (16.89, 33.06)	85.2, $p \leq 0.001$	REM

REM: random effect model.

(14.42%; 95% CI: 12.82, 16.02) was abdominal obesity, and the lowest one was high FG level (1.63%; 95% CI: 1.06, 2.21), with no heterogeneity among the included studies.

The gender-based distribution of MetS in the general population was also estimated in all diagnostic methods. The pooled prevalence of MetS among males was higher than females in the IDF (3.80%, 2.37%), ATP III (6.61%, 4.65%), and Cruz and Goran (5.53%, 4.22%) diagnostic methods. On the contrary, the pooled prevalence of MetS was lower among males than among females in the de Ferranti

(16.49%, 16.76%) and WHO (2.66%, 3.03%) diagnostic criteria (Figure 3 and Table 5).

*3.5. Subgroup Analysis of the Pooled Prevalence of MetS in the General Population.* The subgroup analyses were performed for the two diagnostic methods (IDF and ATP III) using continents where the original studies were performed. In the IDF diagnostic method, the pooled prevalence of MetS was estimated in three continents (North America, Asia, and Europe). Accordingly, the highest prevalence was recorded

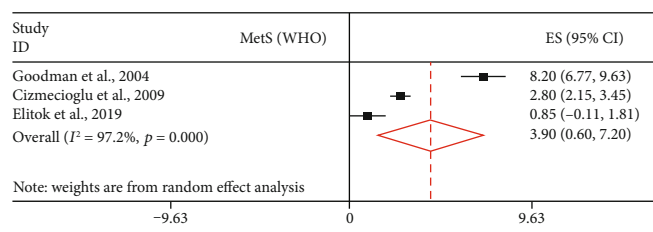
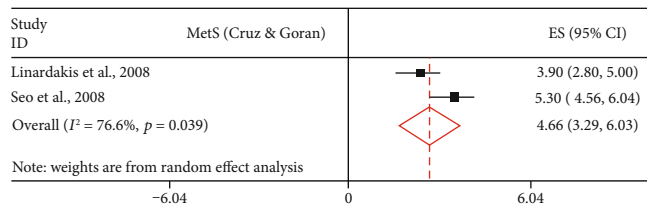
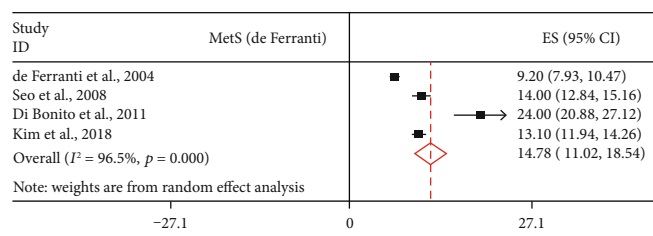
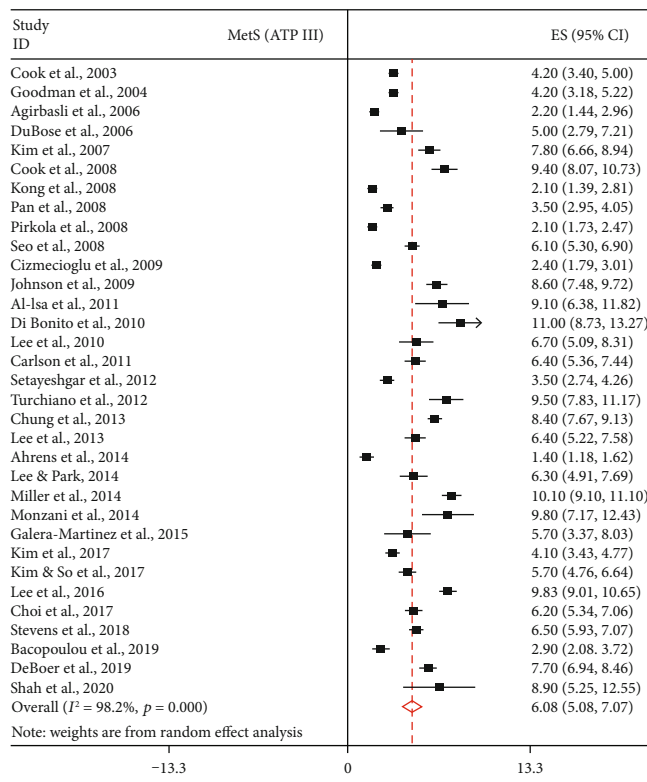
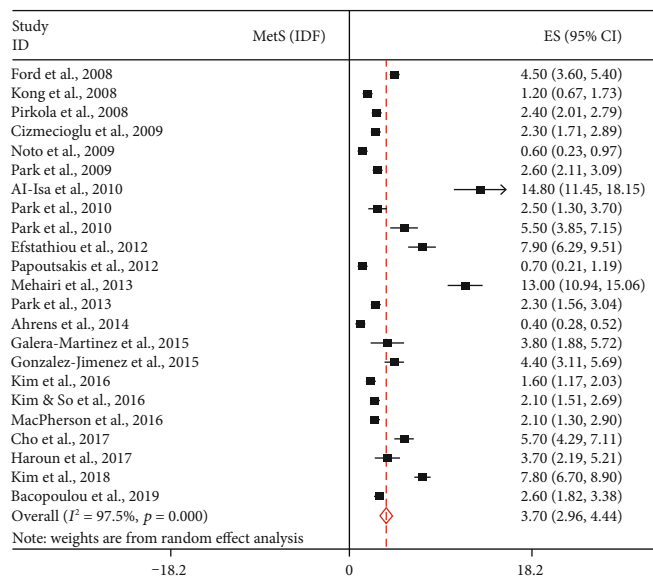


FIGURE 3: The pooled prevalence of MetS among the general population of children and adolescents in high-income countries, 2020.

in Asia, where 4.72% (95% CI: 3.40, 6.04;  $I^2 = 96.7\%$ ;  $p \leq 0.001$ ) of the children and adolescents were found to have MetS. Likewise, the pooled prevalence of MetS in North America and that in Europe were 3.95% (95% CI: 1.95, 5.96;  $I^2 = 90.9\%$ ;  $p \leq 0.001$ ) and 2.54% (95% CI: 1.64, 3.44;  $I^2 = 97\%$ ;  $p \leq 0.001$ ), respectively (Figure 4).

Similarly, the pooled prevalence of MetS was computed for three eligible continents (North America, Asia, and Europe) using the ATP III diagnostic criteria. Thus, 6.79%

(95% CI: 5.40, 8.18;  $I^2 = 96.9\%$ ;  $p \leq 0.001$ ) of the study subjects in North America were diagnosed to have MetS. In Asia, the pooled prevalence of MetS was 6.32% (95% CI: 5.05, 7.58;  $I^2 = 94.9\%$ ;  $p \leq 0.001$ ), and it was 3.84% (95% CI: 2.83, 4.85;  $I^2 = 94.9\%$ ;  $p \leq 0.001$ ) in Europe (Figure 4).

The heterogeneity among the included studies remained significant after subgroup analysis. Hence, the possible sources of heterogeneity were further explored for the two diagnostic methods (IDF and ATP III). Thus, the funnel plots

TABLE 5: The pooled prevalence of MetS and components in the general population in HICs.

Variables	Characteristics	# of included articles	Pooled prevalence (95% CI)	Heterogeneity ( $I^2$ (%), $p$ value)	Model
Diagnostic criteria	IDF	23	3.70 (2.96, 4.44)	97.5, $p \leq 0.001$	REM
	ATP III	33	6.08 (5.08, 7.07)	98.2, $p \leq 0.001$	REM
	de Ferranti	4	14.78 (11.02, 18.54)	96.5, $p \leq 0.001$	REM
	WHO	3	3.90 (0.60, 7.20)	97.2, $p \leq 0.001$	REM
	Cruz and Goran	2	4.66 (3.29, 6.03)	76.6, $p = 0.039$	REM
Gender distribution of MetS (IDF)	Male	19	3.80 (2.90, 4.70)	96.1, $p \leq 0.001$	REM
	Female	20	2.37 (1.77, 2.96)	92.3, $p \leq 0.001$	REM
Gender distribution of MetS (ATP III)	Male	27	6.61 (5.10, 8.13)	98.4, $p \leq 0.001$	REM
	Female	28	4.65 (3.75, 5.54)	98.6, $p \leq 0.001$	REM
Gender distribution of MetS (de F.)	Male	3	16.49 (12.80, 20.17)	88.4, $p \leq 0.001$	REM
	Female	3	16.76 (12.11, 21.41)	92.4, $p \leq 0.001$	REM
Gender distribution of MetS (WHO)	Male	2	2.66 (0.61, 4.72)	86.0, $p = 0.008$	REM
	Female	2	3.03 (-0.11, 6.16)	93.0, $p \leq 0.001$	REM
Gender distribution of MetS (Cruz and Goran)	Male	2	5.53 (3.09, 7.98)	82.8, $p = 0.016$	REM
	Female	2	4.22 (3.27, 5.17)	21.1, $p = 0.260$	FEM
Components MetS (IDF)	Abdominal obesity	14	16.13 (11.47, 20.79)	99.3, $p \leq 0.001$	REM
	Low HDL-C	14	23.41 (14.71, 32.11)	99.8, $p \leq 0.001$	REM
	High TG	13	7.10 (4.72, 9.48)	98.4, $p \leq 0.001$	REM
	High FG	13	10.62 (6.64, 14.59)	99.0, $p \leq 0.001$	REM
	Elevated BP	12	14.56 (10.52, 18.59)	99.2, $p \leq 0.001$	REM
Components MetS (ATP III)	Abdominal obesity	21	16.28 (13.03, 19.53)	99.1, $p \leq 0.001$	REM
	Low HDL-C	21	17.45 (14.43, 20.47)	98.9, $p \leq 0.001$	REM
	High TG	21	19.05 (14.84, 23.26)	99.4, $p \leq 0.001$	REM
	High FG	21	7.16 (5.22, 9.11)	99.4, $p \leq 0.001$	REM
	Elevated BP	21	21.43 (16.60, 26.25)	99.6, $p \leq 0.001$	REM
Components MetS (WHO)	Abdominal obesity	2	14.42 (12.82, 16.02)	0.00, $p = 0.846$	FEM
	Low HDL-C	2	3.78 (1.43, 6.13)	82.8, $p = 0.016$	REM
	High TG	2	5.82 (3.46, 8.19)	64.2, $p = 0.094$	REM
	High FG	2	1.63 (1.06, 2.21)	0.00, $p = 0.672$	FEM
	Elevated BP	2	3.49 (0.65, 6.34)	89.7, $p = 0.002$	REM
Components MetS (Cruz and Goran)	Abdominal obesity	2	10.06 (7.12, 13.00)	89.6, $p = 0.002$	REM
	Low HDL-C	2	10.47 (7.93, 13.02)	85.3, $p = 0.009$	REM
	High TG	2	11.15 (10.25, 12.06)	0.00, $p = 0.383$	FEM
	High FG	2	16.65 (-5.99, 39.28)	99.8, $p \leq 0.001$	REM
	Elevated BP	2	27.50 (12.12, 42.89)	99.0, $p \leq 0.001$	REM

\*Others: underweight and normal weight; REM: random effect model; FM: fixed effect model.

for both diagnostic criteria were presented (Figure 5). The asymmetry of the plots was objectively verified by Egger's regression test, and there was publication bias among the articles included in computing the pooled prevalence of MetS in the IDF ( $p \leq 0.001$ ) and ATP III ( $p \leq 0.001$ ) diagnostic methods. Moreover, sensitivity analyses were performed for both diagnostic methods. This was done to evaluate if the

pooled estimates were altered by the exclusion of any single study. However, none of the studies had significant effects in the pooled estimates (Figure 6).

Finally, the Duval and Tweedie trim and fill analysis, a nonparametric method of accounting for publication bias in meta-analysis, was employed to estimate the pooled prevalence. This was done to estimate the number and outcomes

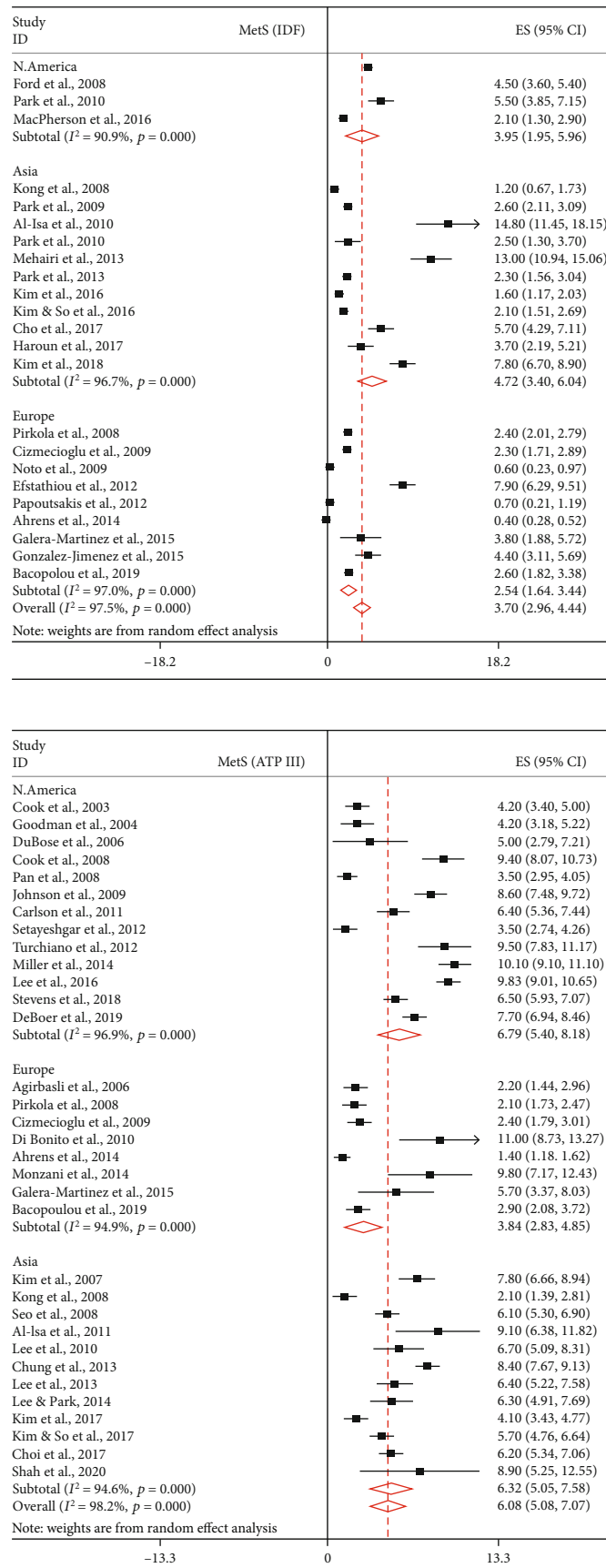


FIGURE 4: Pooled prevalence of MetS based on continent in two diagnostic methods (IDF and ATP III).

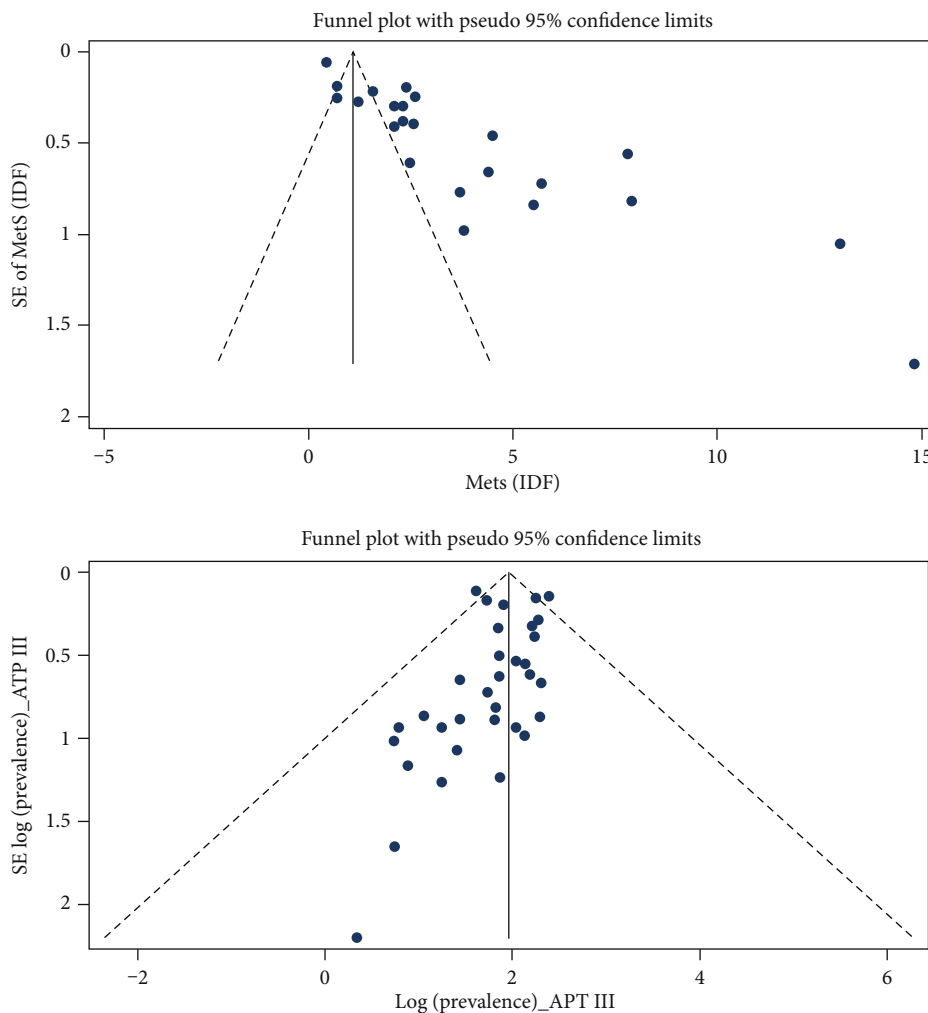


FIGURE 5: Funnel plot for two diagnostic methods (IDF and ATP III).

of missing studies, and adjust the meta-analysis to incorporate the theoretical missing studies. Nevertheless, the pooled prevalence of MetS remained the same (3.70%) using the IDF criteria. However, the pooled prevalence of MetS among the general population of children and adolescents was reduced to 5.40% (95% CI: 4.47, 6.32) in the ATP III diagnostic criteria.

Eventually, the trend of MetS in the general population of children and adolescents in HICs was plotted in a scatter plot based on the prevalence of cases with publication year (2003 to 2020). The trend line implied that there is an increasing trend of cases in three diagnostic methods (IDF, ATP III, and de Ferranti) (Figure 7).

#### 4. Discussion

This is a comprehensive systematic review and meta-analysis, determining the prevalence of metabolic syndrome among children and adolescents in high-income countries. The pooled prevalence of MetS was computed using six diagnostic methods: IDF, ATP III, de Ferranti et al., WHO, Weiss et al., and Cruz and Goran. In the current meta-analysis, 77 studies with a total of 125,445 study participants were

included. Of the total studies, 49 were conducted among the general population of study subjects, and 28 were conducted among overweight and obese population.

This study revealed that the prevalence of MetS among overweight and obese study participants is considerably higher than its prevalence in the general population. The pooled prevalence of MetS in the overweight and obese children and adolescents is as follows: IDF = 25.25%; ATP III = 24.47%; de Ferranti et al. = 39.41%; WHO = 29.52%; and Weiss et al. = 33.36%. Likewise, the pooled prevalence in the general population was 3.70%, 6.08%, 14.78%, 3.90%, 4.66% with the IDF, ATP III, de Ferranti, WHO, and Cruz and Goran diagnostic criteria, respectively. The prevalence in the general population is comparable with findings of a systematic review from Iran, where the prevalence of MetS was 0-8%, 3-16%, and 0-22% in the IDF, ATP III, and de Ferranti criteria, respectively [137]. But, Iranian findings are remarkably lower than the current pooled prevalence of MetS among the overweight and obese population. A possible reason for this disparity may be explained by the fact that overweight and obese children are at greater risk of developing metabolic syndrome as compared to children with normal weight [19]. Furthermore, the higher prevalence of obesity



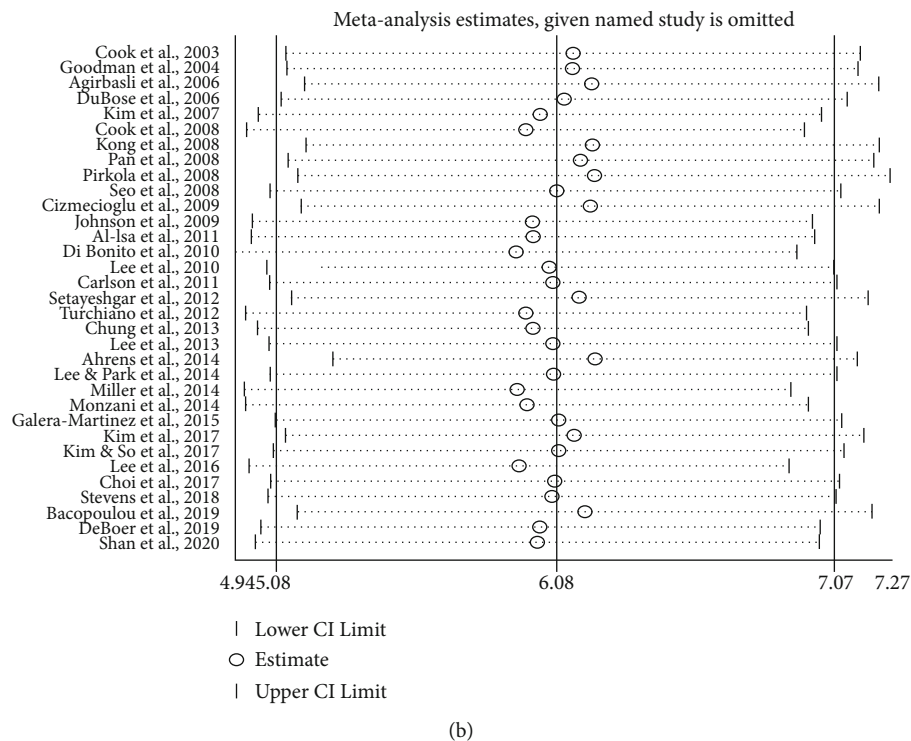
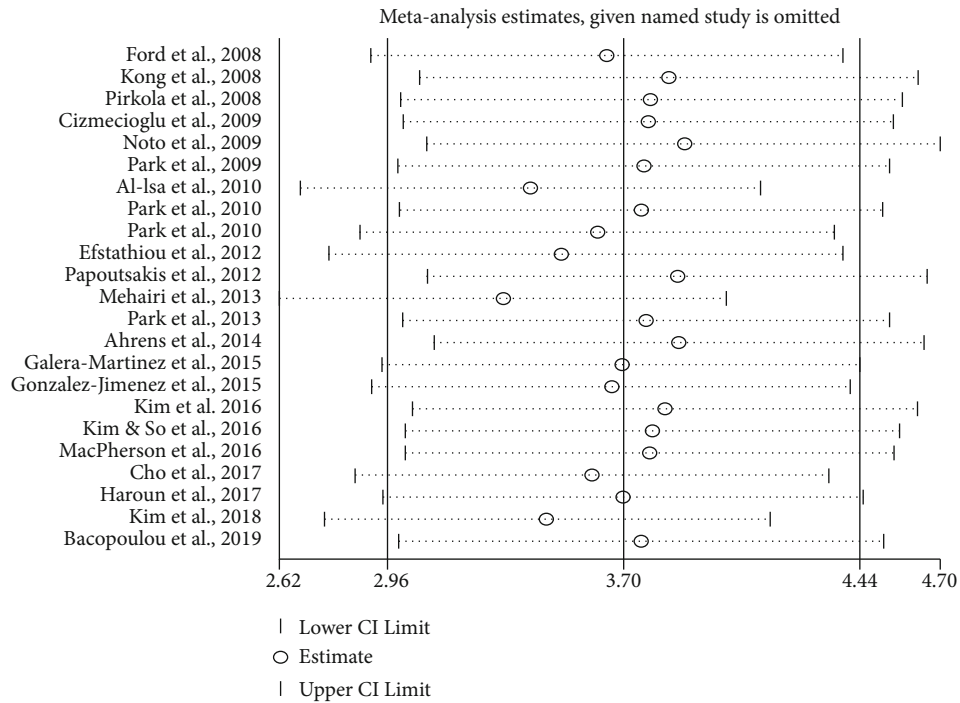


FIGURE 6: Sensitivity analysis of prevalence of MetS in the general population ((a) IDF and (b) ATP III).

in HICs may account for this discrepancy. The current findings are in line with the findings of previous reviews which reported that the prevalence of MetS in the pediatric population ranged from 1.2 to 22.6% in [138] and from 0 to 19.2% in [16]. The median prevalence of MetS in the whole world was 3.3% in 2007 to 2009, which is lower than all the pooled estimates in this meta-analysis [16]. This indicates that the prev-

alence of MetS is on the rise in the developed world. Besides, the present findings are higher than the findings of a meta-analysis in China, where 1.8% (IDF) and 2.6% (ATP III) of the children and adolescents had MetS [139]. The findings of the recent systematic review also revealed that the prevalence of MetS in the pediatric population ranged from 0.3 to 26.4%, with the lower prevalence recorded in the IDF

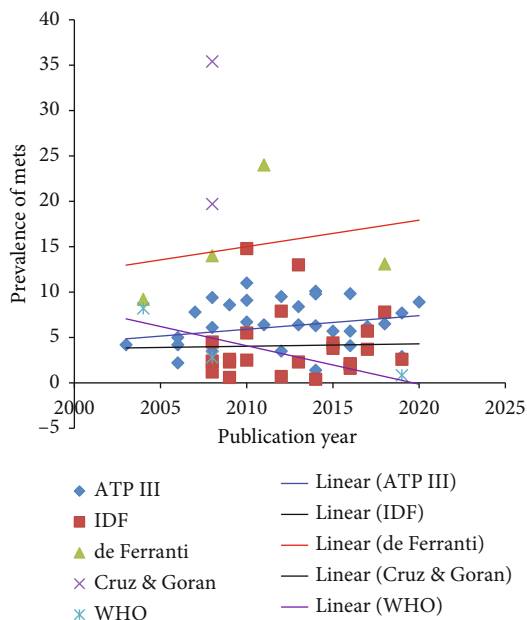


FIGURE 7: Time trend of metabolic syndrome among children and adolescents in HICs from 2003 to 2020.

criteria (0.3-9.5%). But, the prevalence was relatively higher in the de Ferranti et al. criteria (4-26.4%) [140]. Thus, the current findings are in line with the findings in this study. However, the meta-analyses results of the current study are higher than most of the previous findings, which depict that MetS is having an upsurge primarily in the developed world, and it is supported by the findings of the previous reviews [9, 141, 142]. In general, the pooled prevalence of MetS among the obese population is higher in HICs as compared to the low- and middle-income countries, but comparable with the general population [143].

In this study, the pooled prevalence of the components of MetS was also computed using different diagnostic criteria. Abdominal obesity was the most prevalent component of MetS in the overweight and obese population ranging from 65.62% in the IDF criteria to 79.81% in the ATP III criteria. On the other hand, a high level of FG level was the most infrequent component of MetS in the overweight and obese population. The pooled prevalence ranges from 1.61% (de Ferranti et al.) to 15.53% (Weiss et al.). Similarly, the frequent and infrequent components of MetS were computed in the general population. Thus, the most prevalent components include elevated BP (27.50%), low HDL-C (23.41%), high TG level (19.05%), and abdominal obesity (14.42) with the Cruz and Goran, IDF, ATP III, and WHO diagnostic methods, respectively. However, the high FG level is the least frequent component in the ATP III (7.16%) and WHO (1.63%) criteria. Likewise, abdominal obesity and high TG level were the least prevalent components in the Cruz and Goran (10.06%) and IDF (7.10%) criteria. In general, the prevalence of MetS amongst the general population is similar between high-income and low-income countries, whereas the prevalence is not the same amongst obese children in HICs and low-income countries. The pooled prevalence of MetS in

the overweight and obese population was considerably higher among children in HICs. The possible elucidation could be due to a multitude of factors like consumption of unhealthy diets such as diets low in fruit, vegetables, and grains [144, 145]. Moreover, sedentary behavior and lack of physical exercise may also contribute to the rise of MetS in these countries [146].

In most of the diagnostic methods, the prevalence of MetS in males is relatively higher than that in females. The pooled prevalence of MetS in the overweight and obese males is 26.62% (IDF) and 24.75% (ATP III). Likewise, it is 20.18% (IDF) and 24.97% (ATP III) among females. The pooled prevalence of MetS in the general population was computed in both genders using five diagnostic methods. Thus, the pooled prevalence of MetS among males was higher than that among females in the IDF (3.80%, 2.37%), ATP III (6.61%, 4.65%), and Cruz and Goran (5.53%, 4.22%) diagnostic criteria. In contrast, the pooled prevalence of MetS among males was lower compared to that of females in the de Ferranti et al. (16.49%, 16.76%) and WHO (2.66%, 3.03%) diagnostic criteria. In general, males are more highly at risk to have MetS than females both in the original studies and pooled estimates of most diagnostic methods. The current findings are in line with the findings of a meta-analysis in China which showed that males are more highly liable to have MetS than females [139]. The possible justification for gender disparities may be associated with a higher prevalence of obesity in males than females. A higher prevalence of obesity among male children and adolescents may be related to excessive energy intake due to self- and family-imposed perception of being underweight and underestimation of their weight. On the other hand, females control their weight through diet and physical activity due to a self-perception of being overweight [147].

Moreover, the pooled prevalence of MetS in HICs was computed in three continents (Asia, North America, and Europe). Thus, 4.72%, 3.95%, and 2.54% of the study subjects in Asia, North America, and Europe, respectively, are found to have MetS in the IDF criteria. Similarly, the pooled prevalence of MetS in the ATP III criteria is 6.79% (North America), 6.32% (Asia), and 3.84% (Europe). These findings pinpointed that MetS is considerably higher in HICs. This could be associated with a high burden of childhood obesity and consumption of unhealthy diets in these countries [148, 149]. Childhood obesity is not only associated with childhood MetS, but with MetS in adults [150].

Eventually, the number of cases was plotted against the publication year (2003 to 2020), using five diagnostic methods. The trend line revealed that the prevalence of MetS has increased from 2003 to 2020 in all diagnostic criteria. This implies that the prevalence of MetS is increasing in a sustainable manner in the developed world.

The findings of this study may be used by program planners and policy makers to design preventive and treatment strategies against morbidities and mortalities related to MetS. These findings will also help researchers who intend to conduct original researches on multiple factors contributing to a higher burden of MetS in those high-income countries. Nonetheless, there is no specific diagnostic method for MetS,

and this could affect the actual prevalence of MetS in HICs. The other limitation of this study was the exclusion of the following: studies written in non-English language, studies with no full texts, and studies conducted in different study designs and with a different study population. This could cause either under- or overestimation of the pooled prevalence of MetS.

## 5. Conclusion

In conclusion, the current study revealed that the prevalence of MetS among children and adolescents is high in high-income countries with higher proportions among the overweight and obese population. The prevalence is considerably higher in overweight and obese children of Asian countries. Similarly, MetS in the general population of children and adolescents is high in North America. Male children and adolescents are also at greater risk of MetS than females. Metabolic syndrome was diagnosed in underweight, normal weight, overweight, and obese children and adolescents. This implies that MetS is a nonselective problem of children and adolescents in high-income countries. Community-based social and behavioral change communications need to be designed to promote healthy eating behaviors and physical activities. Prospective cohort studies could also help to explore all possible risk factors of MetS and to design specific interventions accordingly.

## Abbreviations

HDL-C:	High-density lipoprotein cholesterol
MetS:	Metabolic syndrome
IDF:	International Diabetic Federation
TG:	Triglyceride
BP:	Blood pressure
FG:	Fasting glucose
WHO:	World Health Organization
BMI:	Body mass index
NCEP-ATP III:	National Cholesterol Education Program Adult Treatment Panel III
WC:	Waist circumference
HICs:	High-income countries
JI:	Juana Brigg's Institute.

## Data Availability

The data that support the review findings of this study are included in the manuscript and supporting files.

## Conflicts of Interest

There are no competing interests.

## Authors' Contributions

ZWB and AA were responsible for analysis, visualization, and writing of the manuscript; ZWB, ZT, AA, and TW made substantial contributions to data acquisition; ZWB, AA, and EGA participated in the data interpretation and made substantial revisions in the first draft; ZWB and TW contributed

to the reception and the design of the work. All authors read and approved the final manuscript.

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## Supplementary Materials

Critical appraisal of cross-sectional studies. (*Supplementary Materials*)

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