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REVIEW

Beyond Cardiometabolic: Health Disorders Risk in Metabolically Healthy Obese Children – A Systematic Review and Meta-Analysis of 19,119 Children

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Background and Objectives: Childhood obesity is associated with both short-term and long-term health complications, yet a new obesity phenotype called metabolically healthy obesity (MHO) has emerged. While MHO is often perceived as a "benign" form of obesity, research specifically examining health disorders risks in children with MHO remains limited. This systematic review and meta-analysis aimed to evaluate health disorders in children with MHO.

Methods: Following PRISMA 2020 guidelines, we systematically searched five databases (PubMed, Scopus, Google Scholar, EBSCO, and ScienceDirect) for observational studies examining MHO children aged 0–18 years. The studies were analyzed using R and R Studio software, with study quality assessed using the Newcastle Ottawa Scale.

Results: Ten studies with a total of 19,119 children were included in this review. Children with MHO demonstrated significantly higher overall health disorders risk compared to MHNW children (pooled OR 2.88, 95% CI [1.64; 5.06]). This trend aligns with the subgroups analysis of left ventricle hypertrophy, hypertension, and kidney damage. However, some of the subgroup analyses showed insignificant results. Additionally, MHO children showed lower risks of experiencing health disorders compared to MUO children (pooled OR 0.56, 95% CI [0.23; 1.34]). The underlying mechanism of the increased health risk is excess adipokines causing systemic inflammation and leading to increased various health risks.

Conclusion: Despite metabolically "healthy" status, children with MHO remain at increased risk for health disorders compared to normal-weight peers. This systematic review and meta-analysis is the first one discussing the health disorders in children with MHO. More studies are required in the future to reinforce these findings in order to produce much more comprehensive insights.

Keywords: children, disorders, metabolically healthy obesity, obesity

Introduction

Childhood obesity has significantly increased in various countries over the past few decades and has become a concerning public health issue. It is estimated that 197 million children aged 0–18 years old are living with obesity in 2022, significantly increased from 11 million in 1975.[1] This trend is further backed up by a recent review, showing one in five children is classified as overweight and obese globally.[2] Unfortunately, this trend cannot be taken lightly. Beyond its high prevalence, childhood obesity also increases the risk of numerous health disorders, such as diabetes mellitus, dyslipidemia, hypertension, non-alcoholic fatty liver disease, obstructive sleep apnea, and polycystic ovary syndrome. Additionally, children with obesity often face negative stigma and reduced quality of life.[3] Therefore, obesity prevention and management through lifestyle and dietary modifications must be implemented as early as possible.

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Childhood obesity is associated with both short-term and long-term health problems that may extend into adulthood. However, a new obesity phenotype known as Metabolically Healthy Obesity (MHO) has recently been gaining attention. MHO in children is characterized by age- and sex-specific body mass index (BMI) categories and the absence of metabolic disorders.[4,5] Due to its healthy metabolic markers, MHO is often perceived as a benign form of obesity and does not increase health disorders.

Interestingly, some studies state that individuals with MHO still have a higher risk of health issues despite their normal metabolic status.[6–15] However, most of the existing literature, including systematic reviews and meta-analyses, has primarily focused on the health risks associated with MHO in adult populations. This causes the health risks of MHO in children to remain underexplored, making it crucial to elaborate on this topic further. Research findings in this younger demographic have also been inconsistent and conflicting, leading to confusion and improper management.

The research question of this systematic-review and meta-analysis is how is the health risk in children with MHO compared to those with MUO (Metabolically Unhealthy Obese) and MHNW (Metabolically Healthy Normal Weight)? To address this issue, this systematic review and meta-analysis were conducted to assess the health risks in children with MHO, comparing them to those with MUO (Metabolically Unhealthy Obese) and MHNW (Metabolically Healthy Normal Weight).

Materials and Methods

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The protocol of our review was registered in the PROSPERO: CRD420251084858.

Data Sources and Literature Search

Our review used five different large electronic databases for obtaining a potential study, including PubMed, Scopus, Google Scholar, EBSCO, and ScienceDirect. The search strategy included the keywords “child” and “metabolically healthy obesity” along with their synonyms. These terms were searched in the title, abstract, and Medical Subject Headings (MeSH) fields using appropriate Boolean operators such as “AND” and “OR” adapted to each database’s specifications for a comprehensive literature search. Detailed search strategies for each database can be found in Table 1.

Table 1 Search Strategy of Pubmed, Scopus, Google Scholar, EBSCO, and ScienceDirect

1a. Search Strategy of PubMed	
#1	((Child*[Title/Abstract]) OR (Pediatric[Title/Abstract]) OR (Adolescen*[Title/Abstract]) OR (Teen*[Title/Abstract]))
#2	((“Metabolically Healthy Obesity”[Title/Abstract]) OR (MHO[Title/Abstract]) OR (“Metabolically Benign Obesity”[Title/Abstract]))
Entry	#1 AND #2 Pubmed
Result [Date]	n = 175 [24/07/25]
1b. Search Strategy of Scopus	
#1	(TITLE-ABS-KEY(child*) OR TITLE-ABS-KEY(pediatric) OR TITLE-ABS-KEY(adolescen*) OR TITLE-ABS-KEY(teen*))
#2	(TITLE-ABS-KEY(“metabolically healthy obesity”) OR TITLE-ABS-KEY(mho) OR TITLE-ABS-KEY(“metabolically benign obesity”))

(*Continued*)

Table 1 (Continued).

Entry	#1 AND #2 Scopus
Result [Date]	n = 285 [24/07/25]
1c. Search Strategy of Google Scholar	
#1	(child OR children OR pediatric OR pediatrics OR adolescence OR adolescent OR adolescents OR teen OR teens OR teenagers OR teenager)
#2	("metabolically healthy obesity" OR MHO OR "metabolically benign obesity")
Entry	allintitle: #1 AND #2 Scholar
Result [Date]	n = 64 [24/07/25]
1d. Search Strategy of EBSCO	
#1	AB (Child* OR Pediatric OR Adolescen* OR Teen*)
#2	AB ("Metabolically Healthy Obesity" OR MHO OR "Metabolically Benign Obesity")
Entry	#1 AND #2 Ebsco
Result [Date]	n = 171 [24/07/25]
1e. Search Strategy of ScienceDirect	
#1	(child OR children OR pediatric OR adolescence OR adolescent OR teenager)
#2	("metabolically healthy obesity" OR MHO OR "metabolically benign obesity")
Entry	Title, abstract, or author-specified keywords #1 AND #2 ScienceDirect
Result [Date]	n = 40 [24/07/25]

Three reviewers independently conducted a comprehensive literature search across five electronic databases: PubMed, Scopus, Google Scholar, EBSCO, and ScienceDirect.

Study Selection

Each of the collected studies' title and abstracts were screened by three reviewers independently. Then, the full text of the studies that met the inclusion and exclusion criteria was retrieved. After that, the full texts were assessed against inclusion and exclusion criteria. The PECO framework was defined as follows:

- Population: children aged 0–18 years;
- Exposure: MHO;
- Comparison: MUO and/or MHNW;
- Outcome: risk of health disorders.

Studies meeting the following criteria were included: (1) full-text availability; (2) observational study (cohort, case control, and cross-sectional); (3) articles published in English; (4) evaluation of the association between MHO and the development of health disorders in children; and (5) reporting of effect estimate and its confidence interval (CI). Exclusion criteria were: (1) in vitro studies; (2) in vivo studies; (3) case reports, reviews, editorials, and commentaries; (4) studies that did not compare MHO with MHNW and/or MUO; (5) articles irrelevant to the research topic; and (6) studies whom full text cannot be retrieved.

Data Extraction and Risk of Bias Assessment

The following data were systematically and independently extracted by three reviewers from each eligible study: (1) first author surname; (2) DOI; (3) publication year; (4) country; (5) study design; (6) MHO definition; (7) age of study population; (8) sample size and proportion for MHO, MUO, and MHNW; (9) investigated health disorders risk. The risk of bias and study quality were independently assessed using the Newcastle-Ottawa Scale (NOS). The results of the NOS are then converted into Agency for Healthcare Research and Quality (AHRQ) standards based on the following criteria: (1) good quality studies are those who obtain 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain; (2) fair quality studies are those who obtain 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain; (3) poor quality studies are those who obtain 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain.

Statistical Analysis

Statistical analyses were performed in R using the meta, metafor, and tidyverse packages following the Cochrane Handbook's recommendations. This review used odds ratios (OR) with corresponding 95% confidence intervals (CI) as the primary measure of association between MHO and health disorders risks. A random-effects model and the inverse variance method were applied for data synthesis. To address and control heterogeneity, subgroup analyses were performed for specific health disorder outcomes. Potential sources of heterogeneity, such as differences in MHO definition, study design, and population characteristics, were explored in detail in the results. Statistical test with $p < 0.05$ considered statistically significant; substantial heterogeneity was defined as $I^2 > 50\%$ and $p < 0.1$, and subgroup analyses were performed for each specific health disorder risk.

Results

Study Selection Result

Eligibility screening was conducted in a stepwise manner as illustrated in the PRISMA flow diagram (see Figure 1). A total of 735 articles were identified from various databases (see Table 1 for details). After removing 424 duplicates, 311 articles were screened based on their titles and abstracts. At this stage, 273 articles were excluded due to irrelevance, inappropriate study designs, or failure to meet the PECO criteria, leaving 38 articles for full-text assessment. Also, 2 articles were unavailable in full text. Of the 36 articles reviewed in full text, 12 were excluded due to wrong outcome, 10 due to wrong population, 1 due to wrong comparator, 1 due to wrong publication type, 1 due to irrelevant topic, and 1 due to no English full-text was available. Consequently, 10 articles were included in the review (see Figure 1 for details).

Characteristic of the Included Study

Our review included studies published at any time, comprising a total sample of 19,119 children aged under 18 years. Among these studies, two used MUO as the comparator group and ten used MHNW as the comparator group. Several health disorders risk were assessed: two studies on diabetes mellitus (DM), two on carotid intima media thickness (CIMT), four on LVH (left ventricular hypertrophy), one on hypertension, one on kidney damage, and one on poor cardiorespiratory fitness (PCRF) (see Table 2). The results of the risk of bias and quality assessments indicated generally good quality across most studies, except for the article by Genovesi et al, which was judged as having poor quality (see Table 3).

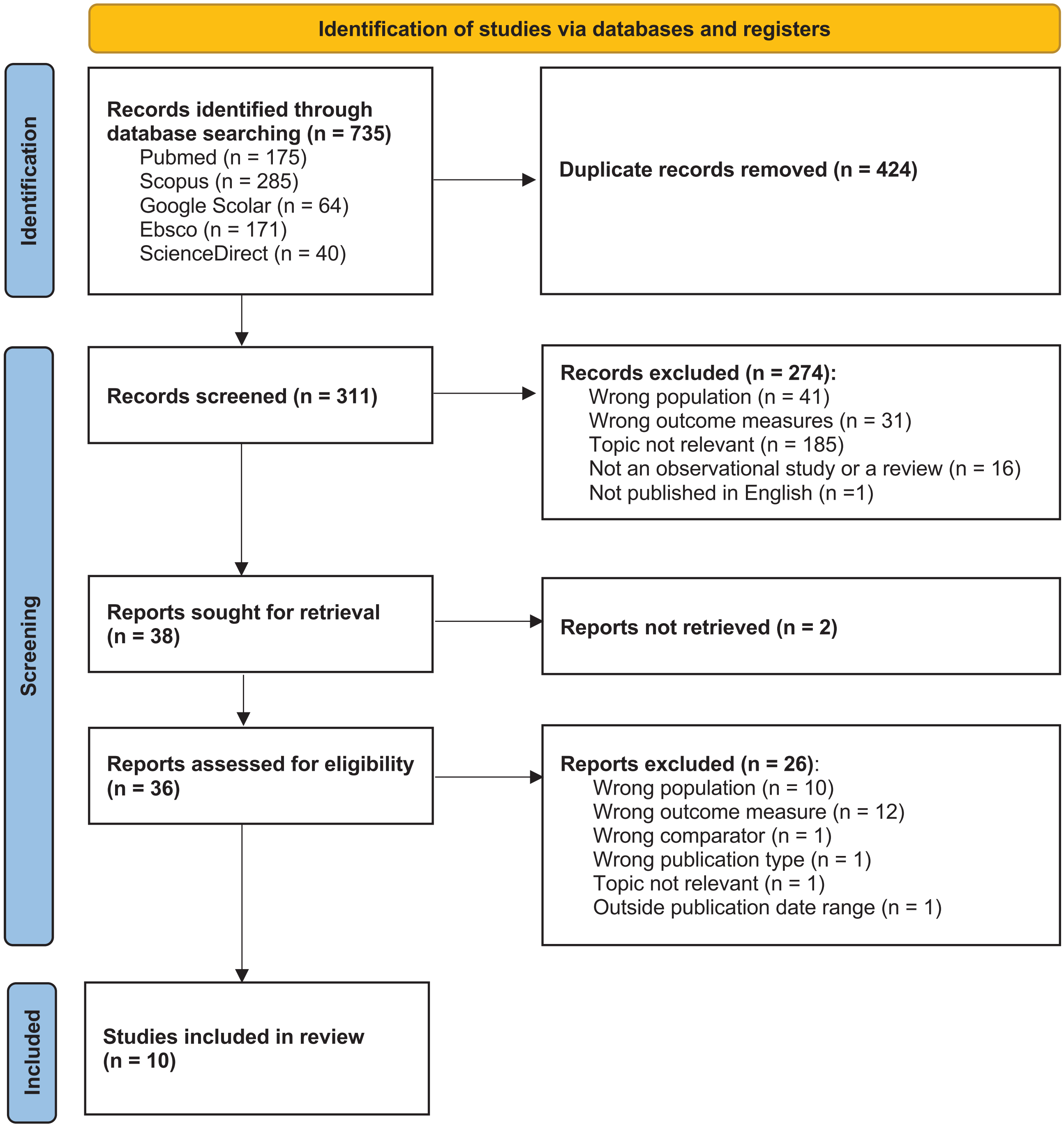

Figure 1 PRISMA Flow Diagram PRISMA figure adapted from Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. Creative Commons.

Association Between MHO and Health Disorders Risk

Ten studies were included in this review to analyze the risk of health disorders in MHO compared to MHNW and/or MUO.[6–15] Participants were classified into MHO, MUO, and MHNW groups based on standardized clinical criteria reported in each study. Because each study applied different modified thresholds and definitions for metabolic health, these variations may contribute to heterogeneity in the pooled estimates.

Despite minimal or absent metabolic abnormalities, children with MHO still show a significantly higher overall risk of developing health disorders than those with MHNW (OR=2.88, 95% CI: 1.64–5.06), with substantial heterogeneity (I^2

 https://doi.org/10.2147/DMSO.S560672

Table 2 Characteristics of Each Study

Reference List Number	First Author Surname	DOI	Publication Year	Country	Study Design	MHO Definition	Age	Total Participants	Population Number			Type of Disorders	Baseline (OR = 1)	Odds Ratio (OR) of MHO Children	95% CI
									MHO	MUO	MHNW				
[7]	Hao	10.2147/DMSO.S484639	2024	China	Cross-sectional	BMI ≥95th percentile, blood pressure >90th percentile, FPG ≥5.6mmol/L, Triglycerides ≥1.7mmol/L, HDL-C ≤1.03mmol/L	7-18	1524	86	122	944	Diabetes Melitus	MHNW	1.12	0.46–2.75
[8]	Tasdighi	10.1016/j.numecd.2021.09.020	2021	Iran	Cohort	Overweight and obese (BMI≥1SD) and exhibit ≤1 cardiometabollic disorders markers	10.9±4.0	1220	130	140	710	Carotid Intima-Media Thickening	MHNW	1.04	0.46–2.35
[12]	Genovesi	10.3389/fendo.2022.1006588	2022	Italy	Cohort	Obese and have systolic blood pressure (SBP) or diastolic blood pressure (DBP) ≥90th percentile, glycaemia ≥100mg/dl, HDL cholesterol ≤40mg/dl, triglycerides ≥100 mg/dl (children <10 years) or ≥130 mg/dl (children ≥10 years)	10.6±2.6	459	191	268	0	Left-Ventricular Hypertrophy	MUO	0.884	0.459–1.751
[6]	Du	10.1016/j.diabres.2022.109884	2022	United States of America	Cross-sectional	Obesity and healthy metabolic status	3-18	3351	141	291	1544	Diabetes Melitus	MHNW	2.35	1.42–3.89
												Left-Ventricular Hypertrophy	MHNW	2.49	1.72–3.63
[10]	Ding	10.1038/jhh.2014.124	2015	China	Cohort	Obesity with none of the five MetS components	6-14	2661	172	297	294	Hypertension	MHNW	3.98	2.71–5.52
[9]	Zhao	10.2337/dc18-1536	2019	Brazil, China, Greece, Italy, Spain	Cross-sectional	NCEP and IDF criteria	6-17	3497	158	362	1393	Carotid Intima-Media Thickening	MHNW	3.91	2.46–6.21

https://doi.org/10.2147/DMSO.S560672

[14]	Di Sessa	10.1038/s41366-023-01379-1	2023	Italy	Cross-sectional	Obese and absence of any of the following risk factors: BP ≥ 95th percentile for age, sex and height in children and BP ≥ 130/80 mmHg in adolescents, fasting plasma glucose ≥ 5.6 mmol/L, triglycerides ≥ 1.13 mmol/L in children and ≥ 1.47 mmol/L in adolescents, HDL-Cholesterol < 1.03 mmol/L	10.72 ± 2.71	396	152	244	0	Kidney Damage	MHNW	1.05	1.00–1.09
[15]	Brand	10.5027/jmh-Vol21-Issue1(2024)art203	2024	Chile	Cross-sectional	Presence of overweight/obesity was used, up to one risk factor for MetS	12-17	274	133	141	0	Poor Cardiorespiratory Fitness	MUO	0.36	0.19–0.67
[11]	Yang	10.1111/dom.15826	2024	China	Cross-sectional	Body weight status is classified based on WHO weight-for-age curve. Metabolic healthy is defined as not having any risk factors for cardiovascular disorders	6-11	2871	227	274	1444	Left-Ventricular Hypertrophy (Concentric Remodelling)	MHNW	2.01	1.23–3.28
												Left-Ventricular Hypertrophy (Eccentric Hypertrophy)	MHNW	6.36	4.03–10.04
												Left-Ventricular Hypertrophy (Concentric Hypertrophy)	MHNW	17.07	7.97–36.58
[13]	Yang	10.1038/s41366-025-01800-x	2025	China	Cross-sectional	Obese based on WHtR and absence of four cardiovascular risk factors: elevated blood pressure, elevated triglycerides, elevated fasting blood glucose, and decreased high-density lipoprotein cholesterol	6 - 11	2866	543	421	1489	Left Ventricular Hypertrophy	MHNW	4.78	3.44–6.64

Table 3 Risk of Bias and Study Quality Assessment

Reference List Number	DOI	Authors	Publication Year	Study Design	NOS Score			Total	Max Score	Quality
					Selection	Comparability	Outcome			
[7]	10.2147/DMSO.S484639	Hao H, Su Y, Feng M.	2024	Cross-sectional	★★★★	★	★★★	8	9	Good
[8]	10.1016/j.numecd.2021.09.020	Tasdighi E, Barzin M, Mahdavi M, et al	2022	Cohort	★★★★	★★	★★	8	9	Good
[12]	10.3389/fendo.2022.1006588	Genovesi S, Tassistro E, Giussani M, et al	2022	Cohort	★★★	★★	★	6	9	Poor
[6]	10.1016/j.diabres.2022.109884	Du T, Fonseca V, Chen W, Bazzano LA.	2022	Cross-sectional	★★★★	★	★★★	8	9	Good
[10]	10.1038/jhh.2014.124	Ding WQ, Yan YK, Zhang MX, et al	2015	Cohort	★★★★	★★	★★	8	9	Good
[9]	10.2337/dc18-1536	Zhao M, López-Bermejo A, Caserta CA, et al	2019	Cross-sectional	★★★★	★	★★★	8	9	Good
[14]	10.1038/s41366-023-01379-1	Di Sessa A, Passaro AP, Colasante AM, et al	2023	Cross-sectional	★★★	★	★★★	7	9	Good
[15]	10.5027/jmh-Vol21-Issue1(2024)art203	Marques KC, Brand C, Sehn AP, et al	2024	Cross-sectional	★★★★	★	★★★	8	9	Good
[11]	10.1111/dom.15826	Yang L, Li M, Wang H, et al	2024	Cross-sectional	★★★★	★	★★★	8	9	Good
[13]	10.1038/s41366-025-01800-x	Yang, L., Li, M., Wang, H., Zhao, M., Magnussen, C. G., Hu, Y., and Xi, B	2025	Cross-sectional	★★★	★★	★★★	8	9	Good

Notes: Stars (★) indicate points awarded by the Newcastle-Ottawa Scale (NOS) for each domain: Selection (maximum 4★), Comparability (maximum 2★), and Outcome (maximum 3★). The total NOS score (maximum 9★) was used to classify study quality: Good (7–9 points), Poor (<7 points).

= 96.6%, p < 0.0001) (Figure 2).[6–15] In contrast, findings from the studies demonstrated that MHO carries a lower overall health disorders risk compared to MUO (OR = 0.56, 95% CI: 0.23–1.34), and accompanied by significant heterogeneity (I^2 = 72.5%, p = 0.0564) (Figure 3).[6–15]

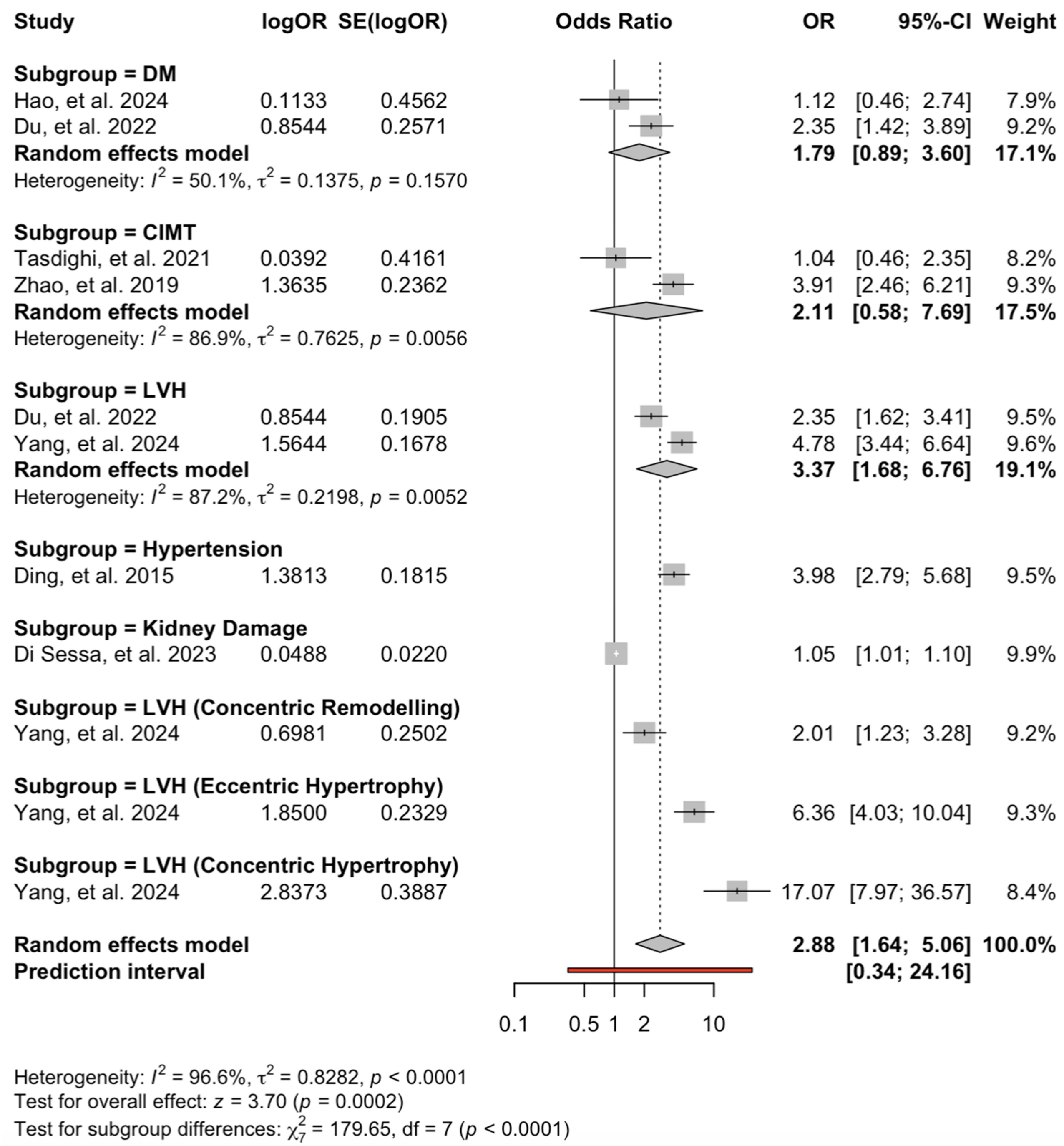

Figure 2 Risk of Cardiometabolic Disorders in MHO vs MHNW Children. Forest plot showing pooled odds ratios (ORs) with 95% confidence intervals (CIs) for various cardiometabolic outcomes in metabolically healthy obese (MHO) compared with metabolically healthy normal weight (MHNW) children. Each subgroup represents a specific outcome analyzed using a random-effects model. Bolded lines denote the pooled summary estimates for each subgroup and the overall meta-analytic summary effect, emphasizing the combined results derived from multiple studies rather than individual estimates. The bold line at the bottom represents the prediction interval, indicating the expected range of effects for future studies based on between-study heterogeneity.

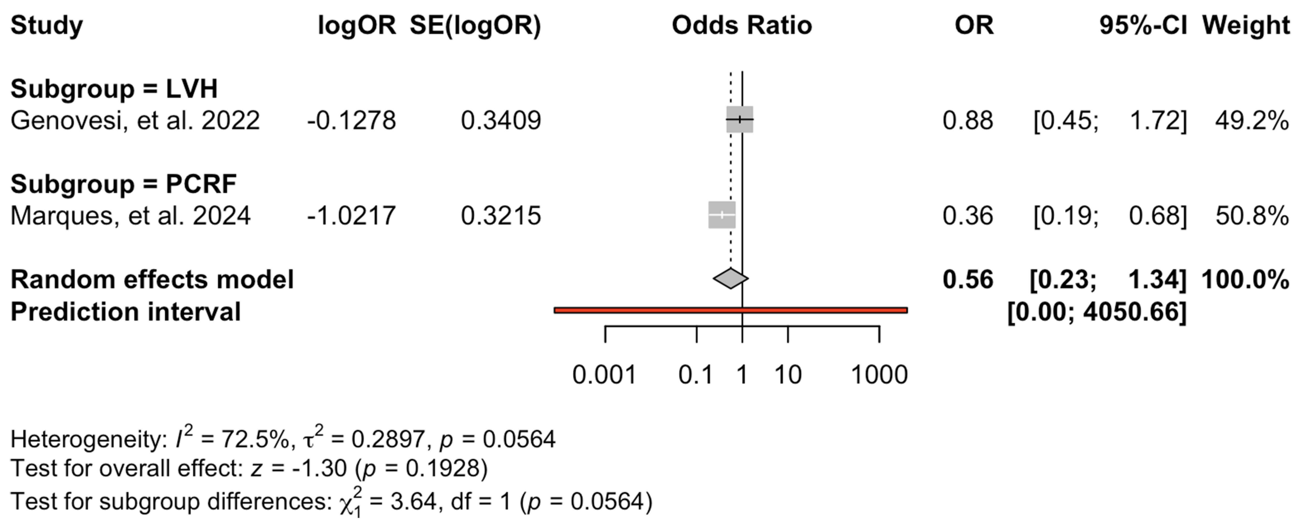

Figure 3 Risk of Cardiometabolic Disorders in MHO vs MUO Children. Forest plot showing odds ratios (ORs) with 95% confidence intervals (CIs) for various cardiometabolic outcomes in metabolically healthy obese (MHO) compared with metabolically unhealthy obese (MUO) children. Each subgroup represents a specific outcome analyzed using a random-effects model. Bolded lines denote the pooled summary estimates for each subgroup and the overall meta-analytic summary effect, emphasizing the combined results derived from multiple studies rather than individual estimates. The bold line at the bottom represents the prediction interval, indicating the expected range of effects for future studies based on between-study heterogeneity.

For further evaluation, subgroup analyses were also performed based on each type of health disorders outcome. Children with MHO showed a higher risk of DM compared to those with MHNW (OR 1.79, 95% CI [0.89–3.60]) (see Figure 2).[6,7]

In studies assessing CIMT, statistical analysis indicated that children with MHO had a higher risk of CIMT thickening compared to those with MHNW (OR 2.11, 95% CI [0.58–7.79]) (see Figure 2).[8,9]

The study focusing on hypertension in children with obesity demonstrated that those with MHO had a higher risk of developing hypertension compared to MHNW children (OR 3.98, 95% CI [2.79–5.68]) (see Figure 2).[10]

Studies evaluating the risk of left ventricular hypertrophy (LVH) were also statistically analyzed. Results showed that children with MHO were at higher risk of developing LVH compared to those with MHNW (OR 3.37, 95% CI [1.68–6.76]) (see Figure 2).[6,11–13] Additionally, a study breaks down the risk of different types of LVH in children with MHO compared to children with MHNW. According to the said study, the risk of MHO children having concentric remodelling, eccentric hypertrophy, and concentric hypertrophy are OR 2.01 (95% CI [1.23–3.28]), OR 6.36 (95% CI [4.03–10.04]), and OR 17.07 (95% CI [7.97–36.57]) respectively.[13] Conversely, the risk of LVH in children with MHO was lower than in those with MUO (OR 0.88, 95% CI [0.45–1.72]) (see Figure 3).[12]

Analysis of the study on kidney damage indicated that children with MHO had a higher risk of kidney damage compared to those with MHO (OR 1.05, 95% CI [1.01–1.10]) (see Figure 2).[14]

Lastly, statistical analysis of the study assessing poor cardiorespiratory fitness (PCRF) showed that children with MHO had a reduced risk of PCRF compared to those with MUO (OR 0.36, 95% CI [0.19–0.68]) (see Figure 3).[15]

Discussion

In general, children with MHO have a higher risk of developing health disorders compared to those with MHNW. On the other hand, children with MHO exhibit a lower risk than those with MUO, which is largely due to more favorable fat distribution and adipokine profiles in the MHO group.[6–15]

A similar pattern among MHO, MUO, and MHNW was also observed across more specific disorders. The main differences lie in the statistical significance of outcomes for each disease. Disorders such as DM, CIMT thickening, and LVH (MHO vs MUO) showed non-significant statistical results.[6–9,12] In contrast, LVH (general and specific types in MHO vs MHNW), hypertension, kidney damage, and PCRF demonstrated statistically significant associations.[6,10,11,13–15]

The risk of diabetes mellitus in children with MHO is influenced by the degree of fat accumulation, particularly visceral fat.[6,7,16] Studies have shown that visceral adipose tissue can produce pro-inflammatory cytokines such as TNF-α and IL-6, which, when present in excess, can lead to systemic inflammation that disrupts insulin signaling in muscle, liver, and adipose tissue.[6,7,16] This systemic inflammation is further exacerbated by adipokine imbalance—characterized by increased leptin levels and decreased adiponectin—resulting in worsened insulin resistance and impaired glucose metabolism.[6,7,16] In contrast, children with MHNW typically have a lower and more evenly distributed fat mass, along with a more balanced adipokine profile, which helps prevent systemic inflammation.[16]

The CIMT thickening risk in MHO children is increased compared to MHNW children due to adipokine imbalance and accumulation of visceral fat. Excess leptin level causes endothelial cell activation, resulting in the expression of cell-adhesive molecules such as VCAM-1 and ICAM-1.[8–10,17–27] The endothelial activation causes inflammation to its cells and reduces nitrate oxide, in which is crucial in vasodilation.[8–10,17–27] Additionally, as mentioned earlier, the accumulation of visceral fat produce pro-inflammatory cytokines such as TNF-α and IL-6, which, when present in excess, cause shear stress to the vascular endothelial.[8–10,17–27] To overcome the stress, the body activates the compensatory mechanisms, which include the hypertrophy of the arteries' intima-media.[8–10,17–27] On the other hand, children with MHNW have a better adipokine profile and fat distribution than MHO children, making them less risked having CIMT thickening.[8–10,17–24,26,27]

Hypertension in MHO children is more common than in MHNW children. Children with MHO have a higher visceral fat than children with MHNW. The higher visceral fat increases the intra-abdominal pressure, resulting in the activation of renal baroreceptors. The baroreceptor activation then causes sodium reabsorption and fluid retention to compensate for the intra-abdominal pressure increase.[10,18,19,21–24,26,27] In addition to that, higher visceral fat also causes MHO children to be more susceptible to endothelial dysfunction and vascular resistance due to the endothelial inflammation. This condition favors the occurrence of hypertension in MHO children.[10,18,19,21–24,26,27] Additionally, high adiposity level also activates renin-angiotensin-aldosterone system (RAAS), aggravating vasoconstriction and hypertension even further.[10,18,19,21–24,26,27] Furthermore, adipokine imbalance also contributes to raising hypertension risk in MHO children.[10,18,19,21–24,26,27] Higher leptin level in MHO children also activates the sympathetic nervous system and increases endothelin-1 production, resulting in vasoconstriction and higher blood pressure.[10,18,19,21–24,26,27]

Compared to MHNW, MHO children have a higher risk of developing LVH, yet lower than MUO children. Children with MHO have a higher visceral fat than children with MHNW. The higher visceral fat increases the intra-abdominal pressure, resulting in the activation of renal baroreceptors. The baroreceptor activation then causes sodium reabsorption and fluid retention to compensate for the intra-abdominal pressure increase. This cascade then causes hypertension, which results in prolonged increase in hemodynamic burden and eventually LVH.[6,11–13,18,19,21–24,26,27] Additionally, high leptin level also causes plasma volume expansion through the activation of the RAAS. This expansion also triggers hypertension and LVH due to an increase in hemodynamic burden.[6,11–13,18,19,21–24,26,27] In addition to that, imbalance adiponectin profile also causes endothelial dysfunction and increased vascular resistance. It then aggravates the heart burden and eventually causes LVH.[6,11–13,18,19,21–24,26,27] Additionally, it has been shown that an increase in leptin-adiponectin ratio has also contributed to LVH incidence in MHO children via complex and various pathways.[6,11–13,18,19,21–24,26,27] In contrast, MHO children have a lower risk of LVH compared to MUO children. As mentioned previously, this phenomenon may be caused by a worse adiponectin profile in MUO children compared to MHO children.[6,11–13,18,19,21–24,26,27] The worse adiponectin profile further aggravates the hemodynamic burden, causing children with MUO to have higher risk of developing LVH.[6,11–13,18,19,21–24,26,27] In addition to that, the atherogenic dyslipidemia in MUO children causes ceramide myocardial accumulation, which is cardiotoxic. Its accumulation impairs myocardial functioning, thus increasing the risk of having LVH further.[6,11–13,18,19,21–24,26,27]

Compared to children with MHO, children with MUO are more susceptible to kidney damage. Greater insulin resistance in MUO children causes a chronic hyperinsulinemic state, triggering the activation of PI3K/Akt/mTOR pathways in kidney tubular cells. The activation induces the hypertrophy of mesangial cells, a rise in glomerulus extracellular matrix synthesis, and activation of Na+/H+ symporter. These cause an increase in the reabsorption of sodium and intraglomerular pressure, making the kidney more susceptible to damage.[14,27–31] Additionally, lipotoxicity, consequent to dyslipidemia, also causes kidney damage. The lipotoxicity increases the accumulation of ceramide in podocyte cells. The accumulation impairs the function of mitochondria and increases oxidative stress, resulting in kidney damage. Although MHO children also experience lipotoxicity, kidney damage is not as significant due to their greater antioxidant activities, such as superoxide dismutase.[14,27–31]

Overall, the theories from various studies show that the risk of health disorders in children with MHO, MUO, and MHNW is affected by lipid distribution and metabolic profile. When one's lipid distribution and metabolic profile becomes unbalanced (eg leptin imbalance, excess visceral fat), a chronic systemic inflammation process is triggered. This inflammation slowly damages the organs leading to an increase in various health risks. Not only that, each adverse effect resulting from MHO may also interact with one another. For instance, an unbalanced metabolic and lipid profile increases the risk of having hypertension which in turn also increases the risk of CIMT, and LVH. Another example is kidney damage which is triggered by DM (insulin resistance state) which is also triggered by dyslipidemia in the first place.

This systematic review and meta-analysis may be the first that discusses the risk of health disorders in children with MHO. However, this review also has several limitations. First, substantial heterogeneity in some subgroups ($I^2 > 50\%$) may affect the stability of pooled estimates. Second, the small number of included studies limits analytical sensitivity and makes the estimated effects tend to be unstable Third, variations in the clinical definitions of MHO, MUO, and MHNW across studies likely contribute to heterogeneity in effect estimates. Nevertheless, with this review, the view of MHO as being "benign", especially in children, can be refuted. In clinical settings, this review may become a guide for pediatric practice by underscoring the need for routine screening of cardiometabolic and non-cardiometabolic risk factors even in obese children without overt metabolic syndrome; it supports early, individualized intervention strategies—including lifestyle modification, nutritional counseling, and regular monitoring—to prevent the progression of subclinical disorders; and it informs pediatric guidelines by highlighting that "healthy obesity" may still confer elevated risks for organ dysfunction and long-term morbidity, thereby guiding clinicians to adopt a more proactive approach in managing all obese pediatric patients. In future research, updating this review to include a greater number of studies and employing standardized phenotype criteria is recommended.

Conclusion

This review shows that children with MHO are at greater risk of health disorders compared to children with MHNW, yet smaller risk than children with MUO. Nevertheless, this result should be interpreted cautiously, considering the high value of heterogeneity and the risk of bias.

Data Sharing Statement

The authors confirm that the data supporting the findings of this study are available within the article.

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Author Contributions

According to CRediT contributorship taxonomy, Richard Christophorus Kurniawan performed the role of conceptualization, data curation, formal analysis, investigation, project administration, software, supervision, visualization, writing—original draft, and writing—review & editing. Frederick Suhamdy performed the role of conceptualization, data curation, formal analysis, investigation, project administration, software, visualization, writing—original draft, and writing—review and editing. Muhammad Makarimal Akhlaq performed the role conceptualization, formal analysis, methodology, resources, validation, and writing—original draft. Eko Fuji Ariyanto performed the role of funding acquisition, supervision, validation, and writing—original draft. All authors have given final approval of the version to be published, have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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