11-1-2017

Inappropriate Use of Homeostasis Model Assessment Cutoff Values for Diagnosing Insulin Resistance in Pediatric Studies

Carrie Fox III
West Virginia School of Osteopathic Medicine

Lourdes Bernardino
West Virginia School of Osteopathic Medicine

Jill Cochran
West Virginia School of Osteopathic Medicine

Mary Essig
West Virginia School of Osteopathic Medicine

Kristie Grove Bridges
West Virginia School of Osteopathic Medicine

HHS Public Access

Author manuscript

J Am Osteopath Assoc. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

J Am Osteopath Assoc. 2017 November 01; 117(11): 689–696. doi:10.7556/jaoa.2017.135.

Inappropriate Use of Homeostasis Model Assessment Cutoff Values for Diagnosing Insulin Resistance in Pediatric Studies

Carrie Fox III, OMS, **Lourdes Bernardino, MD**, **Jill Cochran, MSN, FNP, PhD**, **Mary Essig, MLS**, and **Kristie Grove Bridges, PhD**

Departments of Biomedical Sciences (Student Doctor Fox and Dr Bridges) and Clinical Sciences (Drs Bernardino and Cochran) and the James R. Stookey Library (Ms Essig) at the West Virginia School of Osteopathic Medicine in Lewisburg

Abstract

Background—Assessing pediatric patients for insulin resistance is one way to identify those who are at a high risk of developing type 2 diabetes mellitus. The homoeostasis model assessment (HOMA) is a measure of insulin resistance based on fasting blood glucose and insulin levels. Although this measure is widely used in research, cutoff values for pediatric populations have not been established.

Objective—To assess the validity of HOMA cutoff values used in pediatric studies published in peer-reviewed journals.

Methods—Studies published from January 2010 to December 2015 were identified through MEDLINE. Initial screening of abstracts was done to select studies that were conducted in pediatric populations and used HOMA to assess insulin resistance. Subsequent full-text review narrowed the list to only those studies that used a specific HOMA score to diagnose insulin resistance. Each study was classified as using a predetermined fixed HOMA cutoff value or a cutoff that was a percentile specific to that population. For studies that used a predetermined cutoff value, the references cited to provide evidence in support of that cutoff were evaluated.

Results—In the 298 articles analyzed, 51 different HOMA cutoff values were used to classify patients as having insulin resistance. Two hundred fifty-five studies (85.6%) used a predetermined fixed cutoff value, but only 72 (28.2%) of those studies provided a reference that supported its use. One hundred ten studies (43%) that used a fixed cutoff either cited a study that did not mention HOMA or provided no reference at all. Tracing of citation history indicated that the most commonly used cutoff values were ultimately based on studies that did not validate their use for defining insulin resistance.

Address correspondence to Kristie Grove Bridges, PhD, 400 Lee St N, Lewisburg, WV 24901-1274. kbridges@osteo.wvsom.edu.

Financial Disclosures: None reported.

Author Contributions
All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; Student Doctor Fox and Dr Bridges drafted the article and Dr Cochran, Ms Essig, and Dr Bridges revised it critically for important intellectual content; all authors gave final approval of the version of the article to be published; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conclusion—Little evidence exists to support HOMA cutoff values commonly used to define insulin resistance in pediatric studies. These findings highlight the importance of validating study design elements when training medical students and novice investigators. Using available data to generate population ranges for HOMA would improve its clinical utility.

Keywords

childhood obesity; diabetes; HOMA; insulin resistance

With the increased prevalence of pediatric obesity, there has been much interest in the development of clinical tools for identifying patients at the greatest risk for associated comorbidities. Assessing patients for insulin resistance is one way to identify people who are at a high risk for the development of type 2 diabetes mellitus. However, there is no definitive assessment method, particularly in the pediatric population.[1,2] The euglycemic-hyperinsulinemic glucose clamp technique is considered to be the criterion standard for measurement of insulin resistance.[3] However, this method is time consuming, expensive, and invasive, as it requires infusion of insulin and repeated blood collection. The oral glucose tolerance test (OGTT) is more commonly used to assess insulin resistance in clinical practice and is recommended by the American Diabetes Association as an appropriate screening tool for diabetes risk in asymptomatic adults and children with risk factors such as obesity and family history of diabetes.[4] However, this technique also requires multiple blood collections and takes several hours to complete.[3] Although measures derived from OGTT data such as the Stumvoll metabolic clearance rate and the Matsuda index are believed to be strong predictors of insulin resistance, less invasive and time-consuming methods would be more useful for screening pediatric populations.[5]

Several minimally invasive surrogate measures of insulin resistance using fasting glucose and insulin levels have been developed.[5] These surrogates are not included in current clinical practice guidelines but are widely reported in the research literature.[4] One of the most commonly used measures is the homeostasis model assessment (HOMA) of insulin resistance, which is calculated from fasting insulin and glucose levels (fasting insulin [μIU/mL] × fasting glucose [mg/dL]/405). First introduced by Matthews et al[6] in 1985, HOMA has the advantage of requiring only a single fasting blood test. After its introduction, many investigators began to use HOMA to assess insulin resistance in clinical and epidemiologic studies. A review of these early studies provided recommendations regarding HOMA use and interpretation.[7] The recommendations included the importance of establishing baseline values for different populations, but few large population studies have been completed. Several studies comparing HOMA to euglycemic-hyperinsulinemic clamp in adults have been published, but cutoff values for classifying patients as having insulin resistance have not been clearly established.[5,8,9] While similar studies have been done in the pediatric population, establishing population norms and identifying HOMA cutoff values for these patients has been further complicated by the increase in insulin resistance that occurs naturally during puberty.[2,10–14] The confusion surrounding the assessment of insulin resistance was noted by Rössner et al[15] in 2010, who reiterated the need to establish a standard to avoid research waste. Unfortunately, this goal has not been accomplished, and investigators interested in assessing pediatric insulin resistance continue to use a variety of approaches.[2,16]

In the absence of established HOMA cutoff values for defining insulin resistance in children, some investigators have used a percentile specific to their study population, such as the top quartile or greater than the 85th percentile, as a cut point.[17–20] However, other investigators have used predefined fixed cutoff values.[21–23]

The goal of this review was to assess the use of HOMA cutoff values in the pediatric research literature, including which cutoffs are commonly used and the evidence supporting use of those values. We hope that having a better understanding of how this marker is being used will improve the quality of future research and provide additional impetus for standardizing the assessment of insulin resistance in pediatric populations.

Methods

Literature Search

A literature search was performed in October 2015 and covered studies published January 1, 2010, through the search date. An additional search was later performed to include research published in November and December 2015. The search was limited to articles available in the English language.

The systematic search was conducted using MEDLINE and the following search strategy: ("insulin resistance"[mh] OR insulin resistan*[tiab] OR insulin sensitivity [tiab] OR (resistan* AND insulin*[tiab]) OR metabolic syndr*[tiab])) AND ("Child"[mh:noexp] OR "adolescent"[mh] OR "puberty"[mh:noexp] OR Pediatrics[mh:noexp] OR child[tiab] OR children[tiab] OR adoles*[tiab] OR juvenile*[tiab] OR pediatr*[tiab] OR paediatr*[tiab])) AND (HOMA[tiab] OR "homeostasis model assessment"[tiab] OR HOMA-IR[tiab]).

Screening

Inclusion criteria during the initial review of abstracts were that study participants were aged 18 years or younger and that the study reported measurement of HOMA. Initial review of abstracts was done by K.G.B., and excluded abstracts were divided and reviewed by C.F., L.B., or J.C. A third author who had not already reviewed the abstract made the final decision on any abstracts for which the 2 initial reviewers did not agree. Subsequent review of full-text articles for inclusion was done by C.F., L.B., and K.G.B. with disputed articles reviewed by J.C. Inclusion criteria for the final analysis were confirmation that the study population was aged 18 years or younger and a HOMA score cutoff was used to classify patients as being insulin resistant or not. Studies in which HOMA score was only being compared between groups or correlated to other factors with no use of a cutoff were excluded from further analysis. Studies using HOMA to classify patients as having metabolic syndrome and review articles or comments to the editor were also excluded.

Analysis

Full-text articles were evaluated for HOMA cutoffs used and evidence or citations supporting the use of the cutoff in that population. Each study was classified as using a predetermined cutoff or a cutoff that was a percentile specific to that population (eg, >90th percentile of HOMA in the study population or the top quartile of HOMA in the study population). For studies using a predetermined cutoff, evidence supporting the use of that cutoff was classified as follows:

- No citation for the cutoff was provided.
- The citation referred to a study that used the same cutoff but did not validate the cutoff.
- The references provided did not mention HOMA.
- The citation referred to a study that provided evidence supporting the use of the cutoff in that population.
- The citation referred to a study that did not support the use of the cutoff in that study population (eg, citing a study establishing pubertal cutoffs when the study population was prepubertal, citing a study establishing cutoffs for the diagnosis of metabolic syndrome).

Results

A flowchart summarizing the literature search and screening results is shown in Figure 1. A total of 1360 abstracts were screened for inclusion in the study. Of these abstracts, 424 were excluded because they were not in the pediatric population or did not use HOMA to assess insulin resistance. The remaining 936 full-text articles were obtained and assessed for eligibility. Of these articles, 298 met the criteria for inclusion in the final analysis. Thirty-four studies were excluded at the full-text screening stage because they included patients older than 18 years, 5 were excluded because they were review articles or letters to the editor, and 9 were excluded because they used HOMA to classify patients as having metabolic syndrome. The remaining 590 articles were excluded because they measured HOMA in children but did not use a cutoff to define insulin resistance. Examples included comparing HOMA in different populations, tracking changes in response to an intervention, and correlating HOMA to other factors, such as body mass index.[24–26]

Among the 298 studies included in this review, 51 different HOMA cutoff values ranging from 0.77 to 6.3 were used to classify patients as having insulin resistance (Figure 2). The most frequently used values were 3.16 and 2.5. Forty-three studies (14.4%) used a percentile cutoff specific to the study population. Of the 255 studies (85.6%) that used a predetermined fixed cutoff to define insulin resistance, 72 (28.2%) provided a reference that supported the use of that cutoff in the population. Forty-eight studies (18.8%) provided no reference for their cutoff values, and 62 (24.3%) cited a study that was irrelevant (did not discuss HOMA). Twenty-three articles (9%) cited a study that used the same cutoff value but did not validate it. In addition, 50 studies (19.6%) cited a reference for the HOMA cutoff that clearly did not support the use of that cutoff in their study population (Figure 3). For example, several studies cited the 1985 study by Matthews et al[6] to support the 2.5 cutoff for defining insulin resistance. This study[6] had a small population size, receiver operating characteristic (ROC) curves were not generated, and the authors did not propose 2.5 as a cutoff for diagnosing insulin resistance. That number seems to reflect the study's finding that the median HOMA score for an overnight basal sample was 2.5 in the 6 adult diabetic participants compared with 1.3 in the 6 nondiabetic participants.[6]

The most commonly cited reference for the 3.16 cutoff was Keskin et al.[13] This study compared HOMA to OGTT in 57 pubertal obese children and adolescents. The ROC analysis completed in that study identified 3.16 as the most appropriate cutoff in this population. However, numerous studies cited this article as support for using 3.16 in prepubertal populations despite the fact that insulin resistance is known to increase naturally during puberty.[10,11] The most commonly cited references for the 2.5 cutoff were Valerio et al[27] in 2006, Madeira et al[28] in 2008, and Matthews et al.[6] As described above, the study by Matthews et al[6] did not validate the use of 2.5 as a cutoff value in either adult or pediatric populations. The study by Valerio et al[27] reported the prevalence of insulin resistance in a population of obese children and adolescents in southern Italy. In that study, 2.5 was used as a cutoff for defining insulin resistance in children, and 4.0 was used as a cutoff for adolescents, citing a 2004 study by D'Annunzio et al.[29] Although the authors were contacted, we have been unable to obtain this article. However, an abstract[30] presentation and a later article by the same group[31] reveal the likelihood that these numbers were based on percentiles of HOMA according to Tanner stage in a population of about 100 healthy children. The study by Madeira et al[28] used data from overweight prepubertal children to identify HOMA cutoff values for predicting metabolic syndrome. Although metabolic syndrome and insulin resistance are related, they are not equivalent. Using this study to validate the 2.5 cutoff for diagnosing insulin resistance is not appropriate. Other studies that attempted to establish HOMA cutoffs for identifying metabolic syndrome or assessing cardiovascular risk were also cited by some groups as evidence to support their use in diagnosing insulin resistance.[32,33]

Discussion

Osteopathic medicine emphasizes the importance of disease prevention, which requires appropriate screening to identify patients at the highest risk of disease development and promote early intervention. Assessing obese and overweight pediatric patients for insulin resistance is an approach that may be valuable for the prevention of diabetes and other cardiometabolic diseases. However, standard methods for assessing insulin resistance in children have not been established. In clinical and epidemiologic studies, HOMA is a measurement frequently used to assess insulin sensitivity. Our current review of the pediatric research literature identified a great degree of inconsistency in how HOMA is being used to define insulin resistance and identified extremely limited evidence to support even the most commonly used HOMA cutoff values. Although the difference between 2.5 and 3.16 may not seem significant, the choice of a cutoff value can have a large impact when determining the prevalence of insulin resistance in a population or identifying factors that contribute to its development. For example, in our previous study[34] of overweight and obese Appalachian children, 82% of the patients would have been classified as insulin resistant using 2.5 as a cutoff value, whereas the use of 3.16 would have resulted in a prevalence of 69%. These differences greatly complicate comparisons between studies and impede the development of practice guidelines.

Although inconsistent use of HOMA cutoffs was not surprising, the finding that so few of the selected cutoffs were supported by evidence was unexpected. More than 40% of the articles that used a predetermined cutoff either had no reference for the cutoff or cited an irrelevant study. Many authors simply cited a study that had used the same cutoff but did not seem to review the previous work to ensure that the cutoff was valid for their study population. When tracing back the citation history, many studies that selected 2.5 as a cutoff were ultimately basing its use on the original study by Matthews et al,[6] which described HOMA as a measure of insulin resistance. This study clearly did not attempt to identify a cutoff point, and it provides insufficient information to support widespread use of a specific value for diagnosing insulin resistance in children or adults.

Our findings cast doubt on the quality of study design and adequacy of peer review. Failure to systematically review the literature before designing a study contributes to research waste.[35] This failure seems to be exhibited in the case of HOMA cutoff values. In the training of novice investigators, the importance of working through a citation history to validate elements of study design instead of simply following another group's method should be emphasized. This type of mentorship requires the continued support of research opportunities for osteopathic medical students as we prepare them to advance osteopathic-focused research in the future.

The findings of the current review are limited by the fact that other minimally invasive surrogate measures of insulin resistance, such as the Quantitative Insulin Sensitivity Check Index, were not included. It is possible that the evidence supporting cutoff values for those indices is more substantial. Our review was also limited to articles available in the English language and indexed in PubMed. This approach was used to ensure inclusion only of articles published in journals that have been reviewed by the Literature Selection Technical Review Committee to confirm that they follow best practices, including peer review.[36] Additional evidence supporting the use of specific HOMA cutoffs may be available in excluded journals or unpublished studies. However, as previously noted by Rössner et al,[15] the absence of standard methods for assessing insulin resistance continues to complicate interpretation of and comparisons between studies, thus contributing to research waste. The need to choose a standard surrogate measure and then conduct large population studies to establish sex- and age-specific ranges remains. Given the large number of published studies that assessed HOMA in pediatric patients, it may be possible to generate population ranges for HOMA or other fasting glucose and insulin-based surrogate measures through the sharing of raw data. This approach is more likely to provide clinically useful information than additional studies that compare HOMA or other surrogates with the OGTT or euglycemic-hyperinsulinemic clamp.

Conclusion

Studies using HOMA to diagnose insulin resistance in children used a wide range of cutoff values, most of which are not supported by evidence. These findings imply that inadequate review of the literature before study design is not uncommon and emphasize the importance of training new investigators to validate design components. The results also highlight the need to standardize methods for assessing insulin resistance in children. Given the large number of studies in which HOMA was measured, it may be possible to generate sex- and age-specific population ranges for HOMA or other surrogate measures based on insulin and glucose levels through data sharing.

Acknowledgments

Support: None reported.

We thank Heather Bladen for her assistance in acquiring the full-text articles for this review.

References

1. Levy-Marchal C, Arslanian S, Cutfield W, et al. Insulin resistance in children: consensus, perspective, and future directions. J Clin Endocrinol Metab. 2010; 95(12):5189–5198. DOI: 10.1210/jc.2010-1047 [PubMed: 20829185]
2. Brown RJ, Yanovski JA. Estimation of insulin sensitivity in children: methods, measures and controversies. Pediatr Diabetes. 2014; 15(3):151–161. DOI: 10.1111/pedi.12146 [PubMed: 24754463]
3. Bloomgarden ZT. Measures of insulin sensitivity. Clin Lab Med. 2006; 26(3):611–633. vi. DOI: 10.1016/j.cll.2006.06.007 [PubMed: 16938587]
4. American Diabetes Association. Classification and diagnosis of diabetes. Diabetes Care. 2017; 40(suppl 1):S11–S24. DOI: 10.2337/dc17-S005 [PubMed: 27979889]
5. Otten J, Ahrén B, Olsson T. Surrogate measures of insulin sensitivity vs the hyperinsulinaemic-euglycaemic clamp: a meta-analysis. Diabetologia. 2014; 57(9):1781–1788. DOI: 10.1007/s00125-014-3285-x [PubMed: 24891021]
6. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985; 28(7):412–419. [PubMed: 3899825]
7. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004; 27(6):1487–1495. [PubMed: 15161807]
8. Radikova Z, Koska J, Huckova M, et al. Insulin sensitivity indices: a proposal of cut-off points for simple identification of insulin-resistant subjects. Exp Clin Endocrinol Diabetes. 2006; 114(5):249–256. DOI: 10.1055/s-2006-924233 [PubMed: 16804799]
9. Bonora E, Targher G, Alberiche M, et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care. 2000; 23(1):57–63. [PubMed: 10857969]
10. Pilia S, Casini MR, Foschini ML, et al. The effect of puberty on insulin resistance in obese children. J Endocrinol Invest. 2009; 32(5):401–405. DOI: 10.1007/BF03346475 [PubMed: 19794287]
11. Kurtoğlu S, Hatipoğlu N, Mazıcıoğlu M, Kendirici M, Keskin M, Kondolot M. Insulin resistance in obese children and adolescents: HOMA-IR cut-off levels in the prepubertal and pubertal periods. J Clin Res Pediatr Endocrinol. 2010; 2(3):100–106. DOI: 10.4274/jcrpe.v2i3.100 [PubMed: 21274322]
12. Schwartz B, Jacobs DR, Moran A, Steinberger J, Hong C-P, Sinaiko AR. Measurement of insulin sensitivity in children: comparison between the euglycemic-hyperinsulinemic clamp and surrogate measures. Diabetes Care. 2008; 31(4):783–788. DOI: 10.2337/dc07-1376 [PubMed: 18174496]
13. Keskin M, Kurtoglu S, Kendirci M, Atabek ME, Yazici C. Homeostasis model assessment is more reliable than the fasting glucose/insulin ratio and quantitative insulin sensitivity check index for assessing insulin resistance among obese children and adolescents. Pediatrics. 2005; 115(4):e500–e503. DOI: 10.1542/peds.2004-1921 [PubMed: 15741351]
14. Atabek ME, Pirgon O. Assessment of insulin sensitivity from measurements in fasting state and during an oral glucose tolerance test in obese children. J Pediatr Endocrinol Metab. 2007; 20(2):187–195. [PubMed: 17396435]

15. Rössner SM, Neovius M, Mattsson A, Marcus C, Norgren S. HOMA-IR and QUICKI: decide on a general standard instead of making further comparisons. Acta Paediatr. 2010; 99(11):1735–1740. DOI: 10.1111/j.1651-2227.2010.01911.x [PubMed: 20545928]
16. Andrade, MIS de, Oliveira, JS., Leal, VS., et al. Identification of cutoff points for homeostatic model assessment for insulin resistance index in adolescents: systematic review. Rev Paul Pediatr. 2016; 34(2):234–242. DOI: 10.1016/j.rpped.2015.08.006 [PubMed: 26559605]
17. Baba R, Koketsu M, Nagashima M, Tamakoshi A, Inasaka H. Role of insulin resistance in non-obese adolescents. Nagoya J Med Sci. 2010; 72(3–4):161–166. [PubMed: 20942271]
18. Aristizabal JC, Barona J, Hoyos M, Ruiz M, Marín C. Association between anthropometric indices and cardiometabolic risk factors in pre-school children. BMC Pediatr. 2015; 15(1):170.doi: 10.1186/s12887-015-0500-y [PubMed: 26546280]
19. Urbina EM, Gao Z, Khoury PR, Martin LJ, Dolan LM. Insulin resistance and arterial stiffness in healthy adolescents and young adults. Diabetologia. 2012; 55(3):625–631. DOI: 10.1007/s00125-011-2412-1 [PubMed: 22193511]
20. Choi DP, Oh SM, Lee J-M, et al. Serum 25-hydroxyvitamin D and insulin resistance in apparently healthy adolescents. PLoS One. 2014; 9(7):e103108.doi: 10.1371/journal.pone.0103108 [PubMed: 25072652]
21. Manco M, Morandi A, Marigliano M, Rigotti F, Manfredi R, Maffeis C. Epicardial fat, abdominal adiposity and insulin resistance in obese pre-pubertal and early pubertal children. Atherosclerosis. 2013; 226(2):490–495. DOI: 10.1016/j.atherosclerosis.2012.11.023 [PubMed: 23261169]
22. Karatzi K, Moschonis G, Barouti A-A, Lionis C, Chrousos GP, Manios Y. Dietary patterns and breakfast consumption in relation to insulin resistance in children: the Healthy Growth Study. Public Health Nutr. 2014; 17(12):2790–2797. DOI: 10.1017/S1368980013003327 [PubMed: 24477051]
23. Arshi M, Cardinal J, Hill RJ, Davies PSW, Wainwright C. Asthma and insulin resistance in children. Respirology. 2010; 15(5):779–784. DOI: 10.1111/j.1440-1843.2010.01767.x [PubMed: 20456670]
24. Campos RMS, de Mello MT, Tock L, et al. Aerobic plus resistance training improves bone metabolism and inflammation in adolescents who are obese. J Strength Cond Res. 2014; 28(3): 758–766. DOI: 10.1519/JSC.0b013e3182a996df [PubMed: 24263653]
25. Hsiao F-C, Lin Y-F, Hsieh P-S, et al. Effect of GAS6 and AXL gene polymorphisms on adiposity, systemic inflammation, and insulin resistance in adolescents. Int J Endocrinol. 2014; 2014:674069.doi: 10.1155/2014/674069 [PubMed: 24696684]
26. Díaz M, Bassols J, López-Bermejo A, de Zegher F, Ibáñez L. Metformin treatment to reduce central adiposity after prenatal growth restraint: a placebo-controlled pilot study in prepubertal children. Pediatr Diabetes. 2015; 16(7):538–545. DOI: 10.1111/pedi.12220 [PubMed: 25332100]
27. Valerio G, Licenziati MR, Iannuzzi A, et al. Insulin resistance and impaired glucose tolerance in obese children and adolescents from Southern Italy. Nutr Metab Cardiovasc Dis. 2006; 16(4):279–284. DOI: 10.1016/j.numecd.2005.12.007 [PubMed: 16679220]
28. Madeira IR, Carvalho CNM, Gazolla FM, de Matos HJ, Borges MA, Bordallo MAN. Cut-off point for homeostatic model assessment for insulin resistance (HOMA-IR) index established from receiver operating characteristic (ROC) curve in the detection of metabolic syndrome in overweight pre-pubertal children [article in Portuguese]. Arq Bras Endocrinol Metabol. 2008; 52(9):1466–1473. [PubMed: 19197455]
29. D'Annunzio G, Vanelli M, Meschi F, Pistorio A, Caso M, Pongiglione C. The SIEDP Study Group. Valori normali di HOMA-IR in bambini e adolescenti: studio multicentrico Italiano. Quad Pediatr. 2004; 3:44.
30. D'Annunzio, G., Vannelli, M., Serafino, M., Pistorio, A., Meschi, F., Lorini, R. Values of insulin resistance index by homeostasis model assessment (HOMA-IR) in healthy children and adolescents: an Italian multicenter study; Paper presented at: 64th Scientific Sessions of the American Diabetes Association; 2004; Orlando, FL. Abstract 649-P
31. d'Annunzio G, Vanelli M, Pistorio A, et al. Insulin resistance and secretion indexes in healthy Italian children and adolescents: a multicentre study. Acta Biomed. 2009; 80(1):21–28. [PubMed: 19705616]

32. Tresaco B, Bueno G, Pineda I, Moreno LA, Garagorri JM, Bueno M. Homeostatic model assessment (HOMA) index cut-off values to identify the metabolic syndrome in children. J Physiol Biochem. 2005; 61(2):381–388. [PubMed: 16180336]
33. García Cuartero B, García Lacalle C, Jiménez Lobo C, et al. The HOMA and QUICKI indexes, and insulin and C-peptide levels in healthy children. Cut off points to identify metabolic syndrome in healthy children [in Spanish]. An Pediatr (Barc). 2007; 66(5):481–490. [PubMed: 17517203]
34. Bridges KG, Jarrett T, Thorpe A, Baus A, Cochran J. Use of the triglyceride to HDL cholesterol ratio for assessing insulin sensitivity in overweight and obese children in rural Appalachia. J Pediatr Endocrinol Metab. 2016; 29(2):153–156. DOI: 10.1515/jpem-2015-0158 [PubMed: 26352085]
35. Bhopal RS. Increasing value and reducing waste in biomedical research [correspondence]. Lancet. 2016; 388(10044):562.doi: 10.1016/S0140-6736(16)31216-8
36. FAQ: journal selection for MEDLINE® indexing at NLM. US National Library of Medicine website; https://www.nlm.nih.gov/pubs/factsheets/j_sel_faq.html [Accessed September 15, 2017]

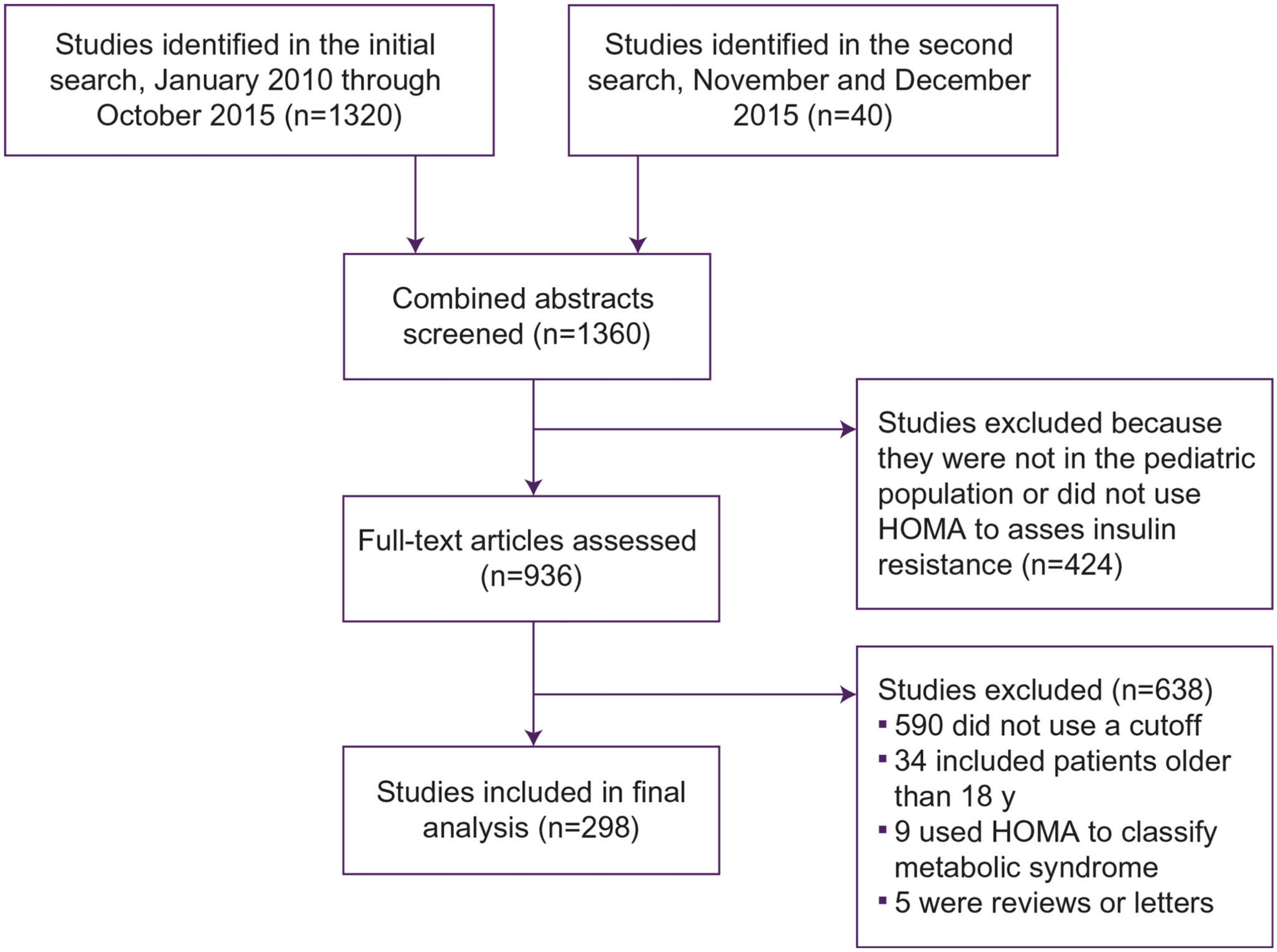

Figure 1.

Flowchart of study selection in a review of pediatric literature in which homeostasis model assessment (HOMA) cutoff values were used to diagnose insulin resistance.

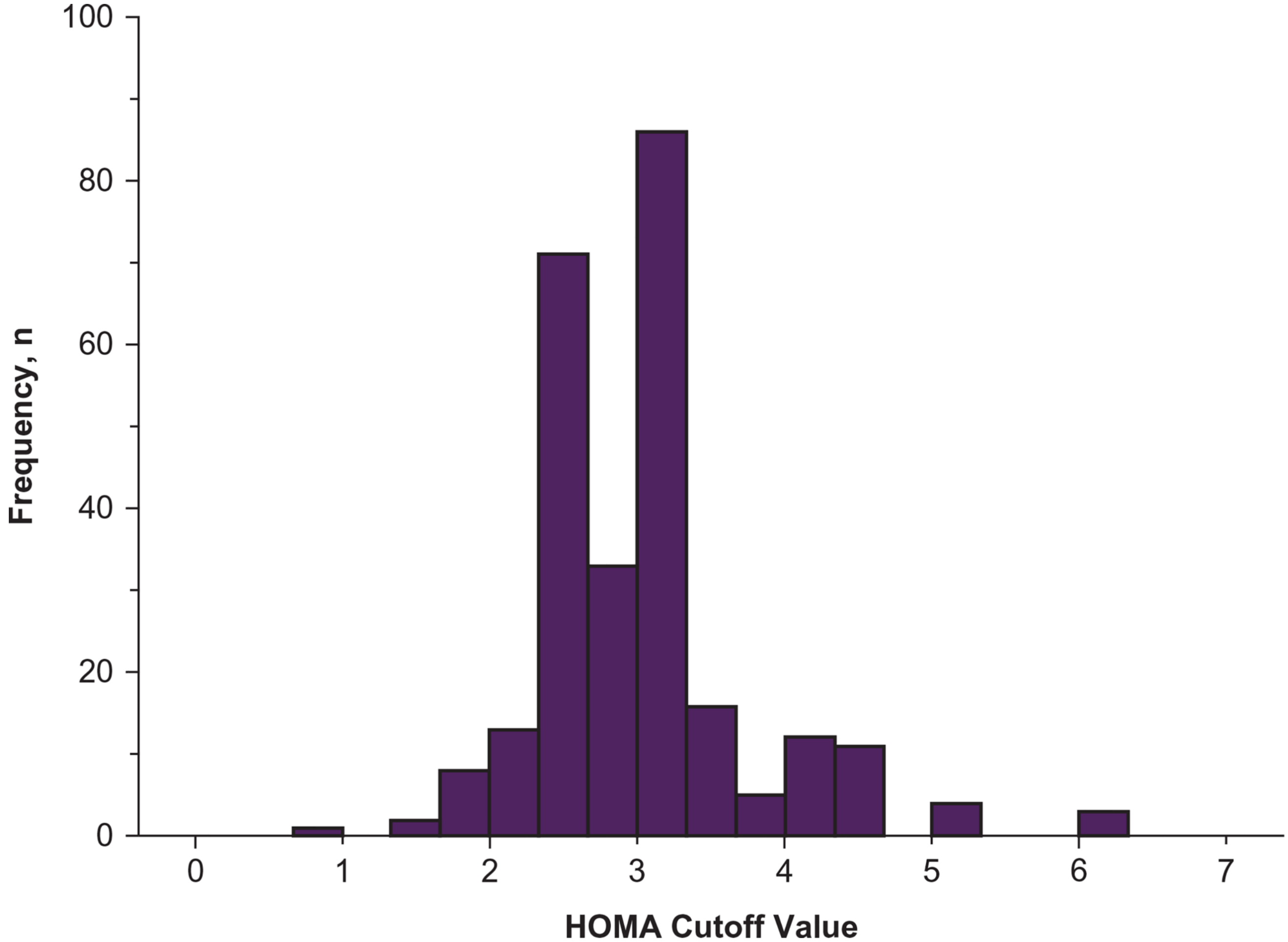

Figure 2.
Frequency and range of pediatric homeostasis model assessment (HOMA) cutoffs (N=298). Fifty-one different cutoff values ranging from 0.77 to 6.3 were used. The most frequently used cutoffs were 3.16 and 2.5.

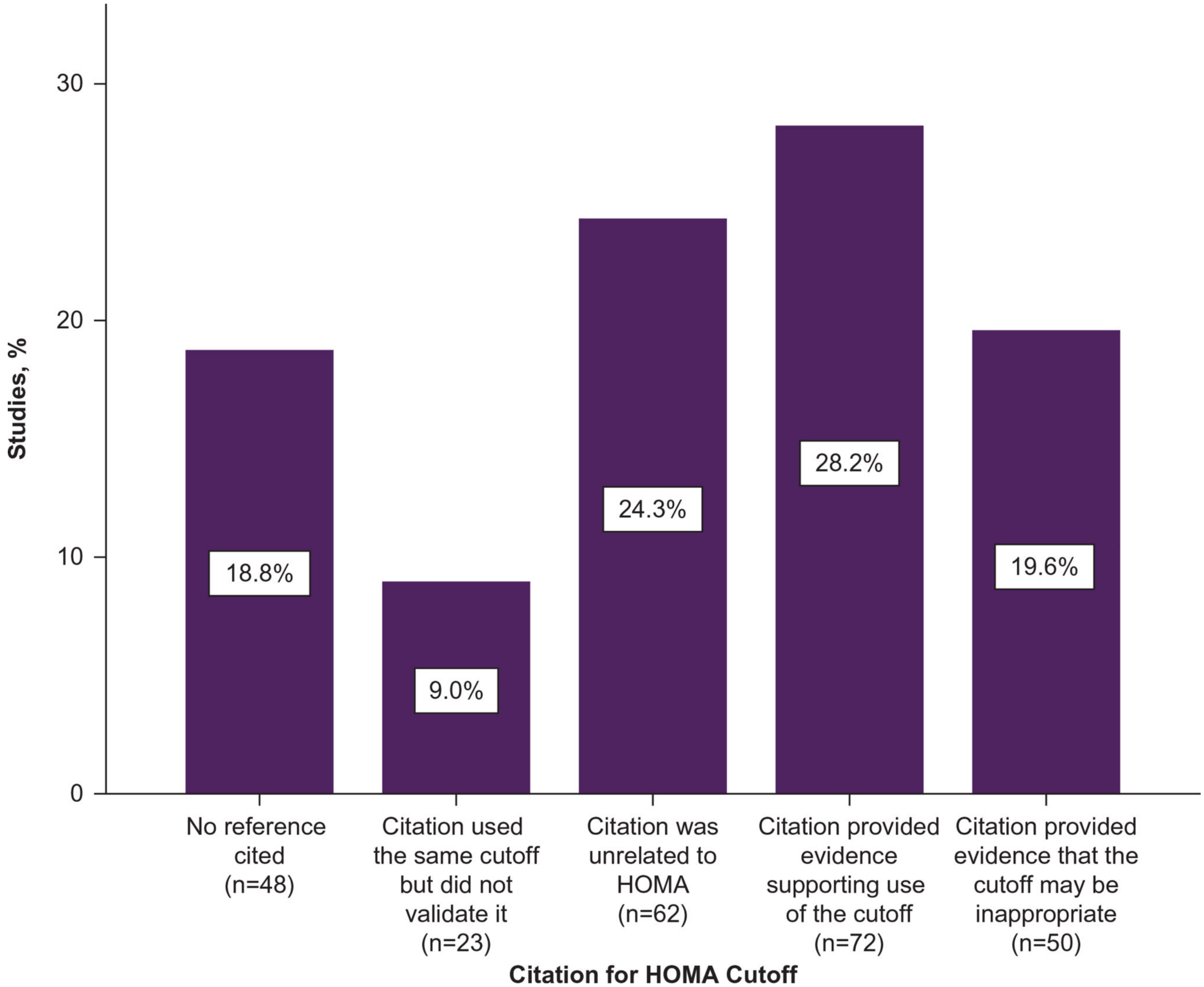

Figure 3.

Assessment of articles that used a fixed cutoff. The majority of studies used a predetermined cutoff value to diagnose insulin resistance (n=255). Citations supporting the use of that cutoff were subsequently evaluated.