Supplementary Online Content

García-Hermoso A, López-Gil JF, Izquierdo M, Robinson Ramírez-Vélez R, Ezzatvar Y. Exercise and insulin resistance markers in children and adolescents with excess weight: a systematic review and network meta-analysis. *JAMA Pediatr*. Published online October 9, 2023. doi:10.1001/jamapediatrics.2023.4038

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Electronic Search Strategy

PubMed (262 results)

((((((("Body Weight"[Mesh]) OR "Overweight"[Mesh]) OR "Obesity"[Mesh])) AND "Child"[Mesh]) OR "Adolescent"[Mesh]) AND (("Exercise"[Mesh]) OR "Resistance Training"[Mesh] OR "Aerobic Exercise"[Mesh]) AND ("Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trial"[Publication Type]) AND "Humans"[Mesh] AND ("Homeostasis Model Assessment"[Mesh] OR "Glucose"[Mesh] OR "Insulin"[Mesh])

EMBASE (16 results)

('body weight'/exp OR 'overweight'/exp OR 'obesity'/exp) AND 'child'/exp OR 'adolescent'/exp AND ('physical exercise'/exp OR 'aerobic exercise'/exp OR 'resistance exercise'/exp) AND ('randomized controlled trial'/exp OR 'controlled clinical trial'/exp) AND 'human'/exp AND ('homeostasis model assessment'/exp OR 'fasting glucose'/exp OR 'fasting insulin'/exp)

Cochrane Controlled Register of Trials (583 results)

((((((("Body Weight"[MeSH Terms]) OR "Overweight"[MeSH Terms]) OR "Obesity"[MeSH Terms])) AND "Child"[MeSH Terms]) OR "Adolescent"[MeSH Terms]) AND (("Exercise"[MeSH Terms]) OR "Resistance Training"[MeSH Terms] OR "Aerobic Exercise"[MeSH Terms]) AND ("Randomized Controlled Trial"[Publication Type] OR "Controlled Clinical Trial"[Publication Type]) AND "Humans"[MeSH Terms] AND ("Homeostasis

Model Assessment"[MeSH Terms] OR "Glucose"[MeSH Terms] OR "Insulin"[MeSH Terms])

Scopus (844 results)

(TITLE-ABS-KEY (("body weight" OR overweight OR obesity) AND child OR adolescent) AND TITLE-ABS-KEY (exercise OR "resistance training" OR "aerobic exercise")) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR EXCLUDE (DOCTYPE , "re")) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA , "NURS")) AND (LIMIT-TO (EXACTKEYWORD , "Homeostasis Model Assessment") OR LIMIT-TO (EXACTKEYWORD , "Insulin") OR LIMIT-TO (EXACTKEYWORD , "randomized controlled trial"))

Web of Science (25 results)

((((AB=("body weight" OR "overweight" OR "obesity")) AND AB=(child OR adolescent)) AND AB=(exercise OR "resistance training" OR "aerobic exercise")) AND AB=("randomized controlled trials" OR "controlled clinical trial")) AND TS=("homeostasis model assessment" OR glucose OR insulin)

CINAHL (13 results)

AB ("body weight" OR "overweight" OR "obesity") AND AB ("child" OR "adolescent") AND AB ("exercise" OR "resistance training" OR "endurance training" OR "aerobic exercise") AND TI "randomized controlled trial" AND AB ("homeostasis model assessment" OR "glucose" OR "insulin")

eTable 1. Table of Characteristics

Study (year) Country	Total n (females) and n groups	Mean age (years)	Exercise modalities	Exercise duration (weeks)	Estimated METs-min per week	Converted METs-min per week	Outcomes
Ben Ounis et al. (2010) [1] Tunisia	n=32 (9) AT: n=16 Control: n=16	12-14	AT	8	2538	2500	Fasting glucose
Benson et al. (2008) [2] New Zealand	n=78 (32) RT: n=37 Control: n= 41	12.2	RT	8	540	500	Fasting insulin, HOMA-IR, fasting glucose
Campos et al. (2014) [3] Brazil	n=42 (28) AT: n=21 AT+RT: n=21	16	AT, CT	48	No control group	No control group	Fasting glucose, fasting insulin, HOMA-IR
Carrel et al. (2005) [4] USA	n=50 (24) AT: n=27 Control: n=23	12	AT	36	783	750	Fasting insulin, fasting glucose
Chae et al. (2010) [5] South Korea	n=38 (17) CT: n=19 Control: n=19	10	CT	12	1755	2000	Fasting insulin, fasting glucose, HOMA-IR
Corte-de-Araujo et al. (2012) [6] Brazil	n=30 (21) ET: n=15 HIT: n=15	10	AT, HIIT	12	No control group	No control group	Serum glucose, insulin, glycated hemoglobin, HOMA-IR
Damaso et al. (2014) [7] Brazil	n=139 (82) AT: n=55 AT+RT: n=61	15-19	AT, CT	48	No control group	No control group	Fasting glucose, fasting insulin, HOMA-IR
Davis et al. (2020) [8] USA	n=175 (107) AT: n=90 Control: n=85	9.7	AT	32	1160	1000	Fasting glucose, fasting insulin, HOMA-IR
Davis et al. (2011) [9] USA	n=26 (26) CT: n=14 Control: n=12	15.8	CT	16	698	750	Fasting glucose, fasting insulin, HOMA-IR, acute insulin response, disposition index
Davis et al. (2012) [10] USA	n=222 (128) low-dose (n=71)	9.4	AT, CT	13	AT_low=800 AT_high=1600	AT_low=750 AT_high=1500	Fasting insulin, fasting glucose, insulin AUC

	high-dose (n=73) Control (n=78)						
de Lira et al. (2017) [11] Brazil	n=84 (NR) High-Intensity Training (n=26) Low-Intensity Training (n=25) Control (n=33)	15	HIIT, AT	12	LIT=749 HIIT=969	LIT=750 HIIT=1000	Fasting glucose, fasting insulin, HOMA-IR
de Souza et al. (2022) [12] Brazil	n=42 (24) karate: n= 20 Control: n=22	12-17	AT	12	1545	1500	Fasting glucose
Dias et al. (2018) [13] Australia	n=99 (53) HIIT: n=33 MICT: n=32 Nutrition advice only: n=34	7-16	AT, HIIT	12	MICT=792 HIIT=840	MICT=750 HIIT=1000	HOMA-IR, fasting glucose
* Farah et al. (2013)[14] and Silva et al. (2015) [15] Brazil	n=43 (10) HIT: n=20 LIT: n=23	13-18	AT	24	No control group	No control group	Fasting glucose, fasting insulin, and HOMA-IR
Faria et al. (2020) [16] Brazil	n=76 (44) MICT: n=24 HIIT: n=26 Control: n=26	16.1	CT, HIIT+RT	12	CT=442 HIIT+RT=386	CT=500 HIIT+RT=500	Fasting insulin, HOMA-IR
Farpour-Lambert et al. (2009) [17] Switzerland	n=44 (16) CT: n=22 Control: n=22	8.9	CT	12	837	750	Fasting insulin, HOMA-IR, fasting glucose
Ferguson et al. (1999) [18] USA	n=73 (53) AT: n=37 Control: n=36	7-11	AT	16	1060	1000	Fasting insulin, fasting glucose
Ghorbanian et al. (2013) [19] Iran	n=30 (0) AT: n=15 Control: n=15	17.3	AT	8	1408	1500	Fasting glucose
González-Ruiz et al. (2021) [20] Colombia	n=120 (81) HIPE: n=30 LIPE: n=30 PLUS: n=30	11-17	CT, HIIT+RT	24	HIPE=1764 LIPE=954 PLUS=1224	HIPE=1500 LIPE=1000 PLUS=1000	Fasting insulin, HOMA-IR, fasting glucose

	Control: n=30						
Grace et al. (2021) [21] South Africa	n=41 (15) CT: n=22 Control: n=19	14	CT	10	398	500	Fasting insulin, HOMA-IR
Jeon et al. (2013) [22] South Korea	n=15 (NR) CT: n = 8 Control: n = 7	13-16	CT	12	710	750	Fasting insulin, HOMA-IR, fasting glucose
Kang et al. (2002) [23] USA	n=59 (54) Lifestyle education: (n=18) Lifestyle education+MIPT: (n=21) Lifestyle education+HIPT: (n=20)	14-15	AT, HIIT	32	Moderate=1032 High=1232	Moderate=1000 High=1500	Fasting insulin, fasting glucose
Karacabey et al. (2009) [24] Turkey	n=40 (0) AT: n=20 Control: n=20	10-12	AT	12	810	750	Fasting insulin
Kelly et al. (2004) [25] USA	n=20 (13) AT: n=10 Control: n=10	10.9	AT	8	1088	1000	Fasting insulin, fasting glucose
Kim et al. (2007) [26] South Korea	n=26 (0) AT: n=14 Control: n=12	17	AT	6	1760	2000	Fasting insulin, HOMA-IR, fasting glucose
Kim et al. (2020) [27] South Korea	n=48 (48) AT: n=24 Control: n=24	14-16	AT	12	2200	2000	Fasting insulin, HOMA-IR, fasting glucose
Koot et al. (2016) [28] The Netherlands	n=51 (29) Inpatient treatment: (n=23) Ambulant treatment: (n=21) Usual care: (n=18)	14.7	AT	24	1160	1000	HOMA-IR
Lee et al. (2013) [29] USA	n=44 (44) AT: n=16 RT: n=16 Control: n=12	14-15	AT, RT	12	AT=1260 RT=774	AT=1500 RT=750	Fasting glucose, fasting insulin, fasting hepatic glucose production, fasting hepatic insulin sensitivity,

							glucose at 2h, insulin at 2h, glucose AUC, insulin AUC, insulin sensitivity
Lee et al. (2019) [30] USA	n=118 (76) AT: n=38 RT: n=40 CT: n=40	12-17	AT, CT, RT	24	No control group	No control group	Fasting glucose, 2h glucose
Lee et al. (2010) [31] South Korea	n=18 (18) AT: n=11 Control: n=7	16.9	AT	12	1232	1500	Fasting insulin, HOMA-IR, fasting glucose
Lee et al. (2012) [32] USA	n=45 (0) AT: n=16 RT: n=16 Control: n=13	14-15	AT, RT	12	AT=1350 RT=1080	AT=1500 RT=1000	Fasting insulin, fasting glucose, 3-h hyperinsulinemiceuglycemic clamp, 2-h hyperglycemic clamp, disposition index
Leite et al. (2022) [33] Brazil	n=94 (NR) AT: n=64 Control: n=30	13.5	AT	12	1486	1500	Fasting insulin, fasting glucose, HOMA-IR, QUICKI
McCormack et al. (2014) [34] USA	n=18 (13) AT: n=10 Control: n=8	13	AT	8	588	500	Fasting insulin, 2-h glucose, HOMA-IR
Meng et al. (2022) [35] China	n=45 (0) HIIT: n = 15 AT: n = 15 Control: n = 15	11.2	AT, HIIT	12	AT=540 HIIT=1000	AT=500 HIIT=1000	Fasting glucose, fasting insulin, HOMA-IR
Meyer et al. (2006) [36] Germany	n=67 (49) AT: n=33 Control: n=34	14.7	AT	24	1170	1000	Fasting insulin, HOMA-IR
Murphy et al. (2009) [37] USA	n=35 (17) AT: n=23 Control: n=12	10.2	AT	12	720	750	Fasting insulin, HOMA-IR, fasting glucose
Park et al. (2012) [38] South Korea	n=29 (15) CT: n = 15 Control: n = 14	12.2	CT	12	1065	1000	Fasting insulin, fasting glucose
Racil et al. (2016) [39] Tunisia	n=68 (68) HIIT: n=23	16.6	HIIT	12	1089	1000	Fasting insulin, HOMA-IR, fasting glucose

	P+HIIIT: n=26 Control: n=19						
Racil et al. (2013) [40] Tunisia	n=34 (34) HIIT: n=11 AT: n=11 Control: n=12	16	AT, HIIT+RT	12	MIIT=800 HIIT=1089	MIIT=750 HIIT=1000	Fasting insulin, HOMA-IR, fasting glucose
Ramezani et al. (2017) [41] Iran	n=60 (0) AT: n=15 RT: n=15 CT: n=15 Control: n=15	10	AT, RT, CT	8	AT=1310 RT=602 CT=956	AT=1500 RT=500 CT=1000	Fasting glucose
Rasooli et al. (2021) [42] Iran	n=40 (0) RT: n=20 Control: n=20	16	RT	8	1200	1000	Fasting glucose, fasting insulin, HOMA-IR
Rosenbaum et al. (2007) [43] USA	n=73 (31) AT: n=49 Control: n=23	13.6	AT	16	261	500	Fasting insulin, fasting glucose, QUICKI, acute insulin response
Salahshoornezhad et al. (2022) [44] Iran	n=62 (62) AT: n=31 Control: n=31	9-12	AT	10	783	750	Fasting glucose
Savoye et al. (2014) [45] USA	n=75 (49) AT: n=38 Control: n=37	10-16	AT	24	780	750	Fasting glucose, fasting insulin, HOMA-IR, 2-h glucose, 2-h insulin
Seo et al. (2019) [46] South Korea	n=103 (40) RT: n=32 Control: n=71	6-16	RT	16	1350	1500	HOMA-IR
Shaibi et al. (2006) [47] USA	n=22 (0) HIIT: n=11 Control: n=11	15	HIIT	16	480	500	Fasting insulin, fasting glucose, insulin sensitivity, acute insulin response, disposition index
Son et al. (2017) [48] South Korea	n=40 (40) CT: n=20 Control: n=20	15	CT	12	1440	1500	Fasting insulin, HOMA-IR, fasting glucose
Sun et al. (2011) [49] China	n=42 (17) AT: n=25 Control: n=17	13.6	AT	10	834	1000	Fasting insulin, HOMA-IR, fasting glucose

TjØnna et al. (2009) [50] Norway	n=54 (14) AIT: n=28 MTG: n=26	14	AT	12	No control group	No control group	Insulin, 2-h insulin, fasting glucose, 2-h post-glucose load, HOMA
Vasconcellos et al. (2016) [51] Brazil	n=20 (6) AT: 10 Control: n=10	12-17	AT	12	1098	1000	Insulin, HOMA-IR, fasting glucose, glucose tolerance (60 min) and glucose tolerance (120 min)
Wong et al. (2008) [52] Singapore	n=24 (0) CT: n=12 Control: n=12	13-14	CT	12	734	750	Fasting glucose
Wong et al. (2018) [53]	n=30 (30) CT: n=15 Control: n=15	15.2	CT	12	819	1000	Fasting insulin, HOMA-IR, fasting glucose
Yetgin et al. (2020) [54] Turkey	n=16 (0) RT: n=8 AT: n=8	16.8	AT, RT	6	No control group	No control group	Glucose, insulin, HOMA-IR
Zehsaz et al. (2016) [55] Iran	n=32 (0) CT: n=16 Control: n=16	10.5	CT	16	721	750	Fasting insulin, HOMA-IR, fasting glucose

AT, Aerobic training; CT, concurrent training; HIIT, high intensity interval training; HIPE, High intensity physical exercise; HOMA-IR, Homeostatic model assessment of insulin resistance; LIPE, low intensity physical exercise; PLUS, combined HIPE and LIPE; QUICKI, quantitative insulin sensitivity check index; RT, resistance training; USA, United States of America.

* Farah et al. (2013) and Silva et al. (2015) analyzed data from the same participants and the same intervention, however, both studies analyzed different outcomes.

eMethods 2. Data Analysis

Effectiveness of exercise types (traditional meta-analysis)

To determine the effect of physical exercise on insulin sensitivity outcomes comparing to a control group, random-effects inverse-variance models with the Hartung-Knapp-Sidik-Jonkman adjustment were used to assess the effects. To determine changes in outcomes (i.e., fasting glucose, fasting insulin, HOMA-IR and 24-h oral glucose tolerance test), the change differences between the exercise and control groups were calculated by using the pooled standard deviation (SD) of change in both groups. In cases where change scores SD were not available, they were estimated from 95% confidence intervals (CI) for either change outcome or intervention effect differences as well as pre-SD and post-SD values. It is important to clarify the following aspects regarding our statistical analyses: (1) meta-analyses were only performed for insulin sensitivity outcomes that were included in five or more studies [56]; (2) to avoid double-counting and following the Cochrane Handbook recommendations, when a study included more than two arms in comparison with a control group, we halved the number of participants in the control group for each of the comparisons [57].

The presence of small-study effects was assessed using the Luis Furuya-Kanamori index (LFK) [58]. A value of −1 indicates no asymmetry, while values between −1 and −2 indicate minor asymmetry, and values greater than −2 indicate major asymmetry [58].

A sensitivity analysis was conducted to assess the robustness of the summarized estimates and to identify whether a specific study contributed to any discrepancies. For this analysis, we systematically excluded one study at a time from the pool of included

studies, conducting the meta-analysis multiple times, with each iteration excluding a different study.

Dose–response meta-analysis

The energy expenditure dose of exercise in terms of METs-min per week was calculated using the Compendium of Physical Activities [59] according to frequency, intensity, type, and duration for each arm. Energy expenditure was classified into seven different groups by approximating the estimated METs-min per week to the closest convenient pre-specified grouping categories of 0 (control group), 500, 750, 1000, 1500, 2000 or 2500 METs-min per week (Supplementary Material 2). Non-linear dose-response meta-analyses were conducted to explore the dose-response association of exercise dose (i.e., METs-min per week) on insulin resistance markers using *drmeta* command following the recommendations by Crippa et al. [60]. We also carried out a sensitivity analysis using only those studies that included children and adolescents with a higher HOMA-IR levels than 3.16 [61].

Network meta-analysis

First, we qualitatively summarize the included randomized clinical trials and RCT in an *ad hoc* table describing direct and indirect comparisons. Second, before conducted the network meta-analysis (NMA), three assumptions were checked [62]: a) to prevent bias in the comparisons, which could lead to heterogeneity and inconsistency, the similarity and comparability of the trials included in the NMA were examined and confirmed. Similarity was assessed by checking whether samples in each exercise type were similar in the baseline distribution of variables understood as effect modifiers (i.e., sex, age); b) to ensure that the study-related conditions were homogenous, the absence of

heterogeneity in the results of pairwise comparisons was confirmed. The size and clinical relevance of heterogeneity was determined by the τ^2 statistic rated as low degree of clinical relevance (<0.04), moderate (0.04 to 0.14), or substantial (0.14 to 0.40) [63]; c) consistency and transitivity were checked to ensure that no relevant discrepancies exist between direct and indirect evidence. The similarity assumption was determined using the node-splitting method [64].

To perform the NMA, the next steps were followed: we assessed the strength of the available evidence using a network geometry graph to display the evidence in the network for insulin resistance outcomes. In these figures, the size of the nodes was proportional to the number of participants in trials who received the intervention specified in the node, the thickness of continuous line connecting nodes proportional to number of trials directly comparing the two intervention [65].

Comparative evaluation of the interventions effect on fasting glucose, insulin, and HOMA-IR were conducted through a random effects pairwise meta-analysis [66] and a frequentist NMA [67] for comparisons between interventions and control. We assessed heterogeneity using the I^2 statistic, ranging from 0% to 100% [68]. Based on the values of I^2, we categorized heterogeneity as not important (0% to 30%), moderate (30% to 60%), substantial (60% to 75%), or considerable (75% to 100%) [68]. Similarly, the corresponding *p* values were considered.

Rankograms were established to indicate the probability that each treatment is the best available intervention. Furthermore, we estimated the surface under cumulative ranking (SUCRA) [65] for each intervention. The SUCRA assigns a value ranging from 0 to 1 to each intervention in the rankogram, which allows them to be ranked. A SUCRA value of approximately 0 denotes the worst available intervention, while a value of approximately 1 indicates the best available intervention. SUCRA condenses the

information about the effectiveness of each intervention into a single value, simplifying the complex results of network meta-analysis into just a few numbers. The significance of the SUCRA is highest when there is a consistent difference in preference between consecutive ranks across the entire rating scale. However, SUCRA scores were reported as percentages, for clarity.

eMethods 3. Excluded Studies and Reasons for Exclusion

Reason for exclusion: Duplicated data

Ackel-D'Elia, C., Carnier, J., Bueno Jr, C. R., Campos, R. M. D. S., Sanches, P. D. L., Clemente, A. P. G., ... & Dâmaso, A. R. (2013). Effects of different physical exercises on leptin concentration in obese adolescents. International journal of sports medicine, 164-171.

Bharath, L. P., Choi, W. W., Cho, J. M., Skobodzinski, A. A., Wong, A., Sweeney, T. E., & Park, S. Y. (2018). Combined resistance and aerobic exercise training reduces insulin resistance and central adiposity in adolescent girls who are obese: randomized clinical trial. European journal of applied physiology, 118, 1653-1660.

de Mello, M. T., de Piano, A., Carnier, J., Sanches, P. D. L., Correa, F. A., Tock, L., ... & Damaso, A. R. (2011). Long-term effects of aerobic plus resistance training on the metabolic syndrome and adiponectinemia in obese adolescents. The journal of clinical hypertension, 13(5), 343-350.

Deldin, A., Kuk, J. L., & Lee, S. (2019). Influence of sex on the changes in regional fat and skeletal muscle mass in response to exercise training in adolescents with obesity. Childhood obesity, 15(3), 216-222.

Inoue, D. S., De Mello, M. T., Foschini, D., Lira, F. S., Ganen, A. D. P., Campos, R. M. D. S., ... & Dâmaso, A. R. (2015). Linear and undulating periodized strength plus

aerobic training promote similar benefits and lead to improvement of insulin resistance on obese adolescents. Journal of Diabetes and its Complications, 29(2), 258-264.

Tenório, T. R., Balagopal, P. B., Andersen, L. B., Ritti-Dias, R. M., Hill, J. O., Lofrano-Prado, M. C., & Prado, W. L. (2018). Effect of low-versus high-intensity exercise training on biomarkers of inflammation and endothelial dysfunction in adolescents with obesity: A 6-month randomized exercise intervention study. Pediatric exercise science, 30(1), 96-105.

Walsh, J. J., Bonafiglia, J. T., Goldfield, G. S., Sigal, R. J., Kenny, G. P., Doucette, S., ... & Gurd, B. J. (2020). Interindividual variability and individual responses to exercise training in adolescents with obesity. Applied Physiology, Nutrition, and Metabolism, 45(1), 45-54.

Walsh, J. J., D'Angiulli, A., Cameron, J. D., Sigal, R. J., Kenny, G. P., Holcik, M., ... & Goldfield, G. S. (2018). Changes in the Brain-Derived Neurotrophic Factor Are Associated with Improvements in Diabetes Risk Factors after Exercise Training in Adolescents with Obesity: The HEARTY Randomized Controlled Trial. Neural Plasticity, 2018, 7169583-7169583.

Wong, A., Sanchez-Gonzalez, M. A., Son, W. M., Kwak, Y. S., & Park, S. Y. (2018). The effects of a 12-week combined exercise training program on arterial stiffness, vasoactive substances, inflammatory markers, metabolic profile, and body composition in obese adolescent girls. Pediatric Exercise Science, 30(4), 480-486.

Reason for exclusion: No information on the outcome of interest

Abassi, W., Ouerghi, N., Nikolaidis, P. T., Hill, L., Racil, G., Knechtle, B., ... & Bouassida, A. (2022). Interval training with different intensities in overweight/obese adolescent females. International Journal of Sports Medicine, 43(05), 434-443.

Aguilar-Cordero, M. J., Rodríguez-Blanque, R., Leon-Ríos, X., Expósito Ruiz, M., García García, I., & Sánchez-López, A. M. (2020). Influence of physical activity on blood pressure in children with overweight/obesity: a randomized clinical trial. American Journal of Hypertension, 33(2), 131-136.

Alberga, A. S., Farnesi, B. C., Lafleche, A., Legault, L., & Komorowski, J. (2013). The effects of resistance exercise training on body composition and strength in obese prepubertal children. The Physician and sports medicine, 41(3), 103-109.

Alberga, A. S., Prud'Homme, D., Kenny, G. P., Goldfield, G. S., Hadjiyannakis, S., Gougeon, R., ... & Sigal, R. J. (2015). Effects of aerobic and resistance training on abdominal fat, apolipoproteins and high-sensitivity C-reactive protein in adolescents with obesity: the HEARTY randomized clinical trial. International journal of obesity, 39(10), 1494-1500.

Alberga, A. S., Prud'homme, D., Sigal, R. J., Goldfield, G. S., Hadjiyannakis, S., Phillips, P., ... & Kenny, G. P. (2016). Effects of aerobic training, resistance training, or both on cardiorespiratory and musculoskeletal fitness in adolescents with obesity: the HEARTY trial. Applied physiology, nutrition, and metabolism, 41(3), 255-265.

Alves, A. S. R., Venancio, T. L., Honorio, S. A. A., MARTINS, J., & Manuel, C. (2019). Multicomponent training with different frequencies on body composition and physical fitness in obese children. Anais da Academia Brasileira de Ciências, 91.

Barros, T. A., do Prado, W. L., Tenório, T. R., Ritti-Dias, R. M., Germano-Soares, A. H., Balagopal, B. P., ... & Freitas-Dias, R. (2021). Cardiovascular Effects of Aerobic Exercise With Self-Selected or Predetermined Intensity in Adolescents With Obesity. Pediatric Exercise Science, 33(3), 125-131.

Berntsen, S., Mowinckel, P., Carlsen, K. H., Lødrup Carlsen, K. C., Pollestad Kolsgaard, M. L., Joner, G., & Anderssen, S. A. (2010). Obese children playing towards an active lifestyle. International Journal of Pediatric Obesity, 5(1), 64-71.

Bouamra, M., Zouhal, H., Ratel, S., Makhlouf, I., Bezrati, I., Chtara, M., ... & Chaouachi, A. (2022). Concurrent Training Promotes Greater Gains on Body Composition and Components of Physical Fitness Than Single-Mode Training (Endurance or Resistance) in Youth With Obesity. Frontiers in Physiology, 13, 1-16.

Carnier, J., de Mello, M. T., Ackel-ĎElia, C., Corgosinho, F. C., da Silveira Campos, R. M., de Lima Sanches, P., ... & Dâmaso, A. R. (2013). Aerobic training (AT) is more effective than aerobic plus resistance training (AT+ RT) to improve anorexigenic/orexigenic factors in obese adolescents. Appetite, 69, 168-173.

Chang, C., Liu, W., Zhao, X., Li, S., & Yu, C. (2008). Effect of supervised exercise intervention on metabolic risk factors and physical fitness in Chinese obese children in early puberty. Obesity reviews, 9, 135-141.

Chen, F. T., Chen, S. R., Chu, I. H., Liu, J. H., & Chang, Y. K. (2017). Multicomponent exercise intervention and metacognition in obese preadolescents: A randomized controlled study. Journal of Sport and Exercise Psychology, 39(4), 302-312.

Chen, S. R., Tseng, C. L., Kuo, S. Y., & Chang, Y. K. (2016). Effects of a physical activity intervention on autonomic and executive functions in obese young adolescents: A randomized controlled trial. Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association, 35(10), 1120-1125.

Chuensiri, N., Suksom, D., & Tanaka, H. (2018). Effects of high-intensity intermittent training on vascular function in obese preadolescent boys. Childhood Obesity, 14(1), 41-49.

Comeras-Chueca, C., Villalba-Heredia, L., Perez-Lasierra, J. L., Marín-Puyalto, J., Lozano-Berges, G., Matute-Llorente, Á., ... & Casajús, J. A. (2022). Active Video Games Improve Muscular Fitness and Motor Skills in Children with Overweight or Obesity. International Journal of Environmental Research and Public Health, 19(5), 2642.

Cvetković, N., Stojanović, E., Stojiljković, N., Nikolić, D., Scanlan, A. T., & Milanović, Z. (2018). Exercise training in overweight and obese children: Recreational

football and high-intensity interval training provide similar benefits to physical fitness. Scandinavian journal of medicine & science in sports, 28, 18-32.

Elloumi, M., Makni, E., Ounis, O. B., Moalla, W., Zbidi, A., Zaoueli, M., ... & Tabka, Z. (2011). Six-minute walking test and the assessment of cardiorespiratory responses during weight-loss programmes in obese children. Physiotherapy Research International, 16(1), 32-42.

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Reason for exclusion: Not enough information on the type of exercise

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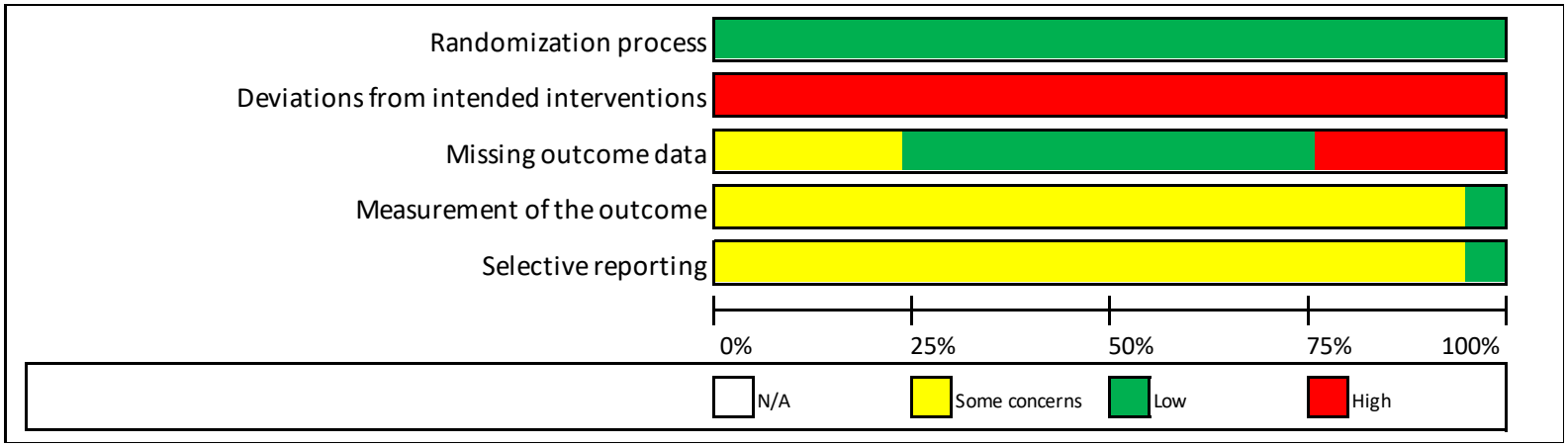
eTable 2. Results of the Cochrane Risk-of-Bias Tool for Randomized Controlled Trials (RoB-2)

All studies were deemed to be at low risk of bias for the "randomization process" domain since we only included randomized studies. Inversely, the domain "Deviations from intended interventions" was rated to be at high risk of bias in all studies due to the impossibility of blinding participants and people delivering the intervention to group assignment in the exercise interventions. For the rest of the items, most studies were considered to have some concerns regarding risk of bias.

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selective reporting	Overall
Ben Ounis et al. (2010) [1]	Low	High	Low	Some concerns	Some concerns	Some concerns
Benson et al. (2008) [2]	Low	High	High	Some concerns	Some concerns	High
Campos et al. (2014) [3]	Low	High	High	Some concerns	Some concerns	High
Carrel et al. (2005) [4]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Chae et al. (2010) [5]	Low	High	Low	Some concerns	Some concerns	Some concerns
Corte-de-Araujo et al. (2012) [6]	Low	High	High	Some concerns	Some concerns	High
Damaso et al. (2014) [7]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Davis et al. (2020) [8]	Low	High	High	Some concerns	Some concerns	High
Davis et al. (2011) [9]	Low	High	High	Some concerns	Some concerns	High
Davis et al. (2012) [10]	Low	High	Some concerns	Low	Low	Low
de Lira et al. (2017) [11]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
de Souza et al. (2022) [12]	Low	High	High	Some concerns	Some concerns	High

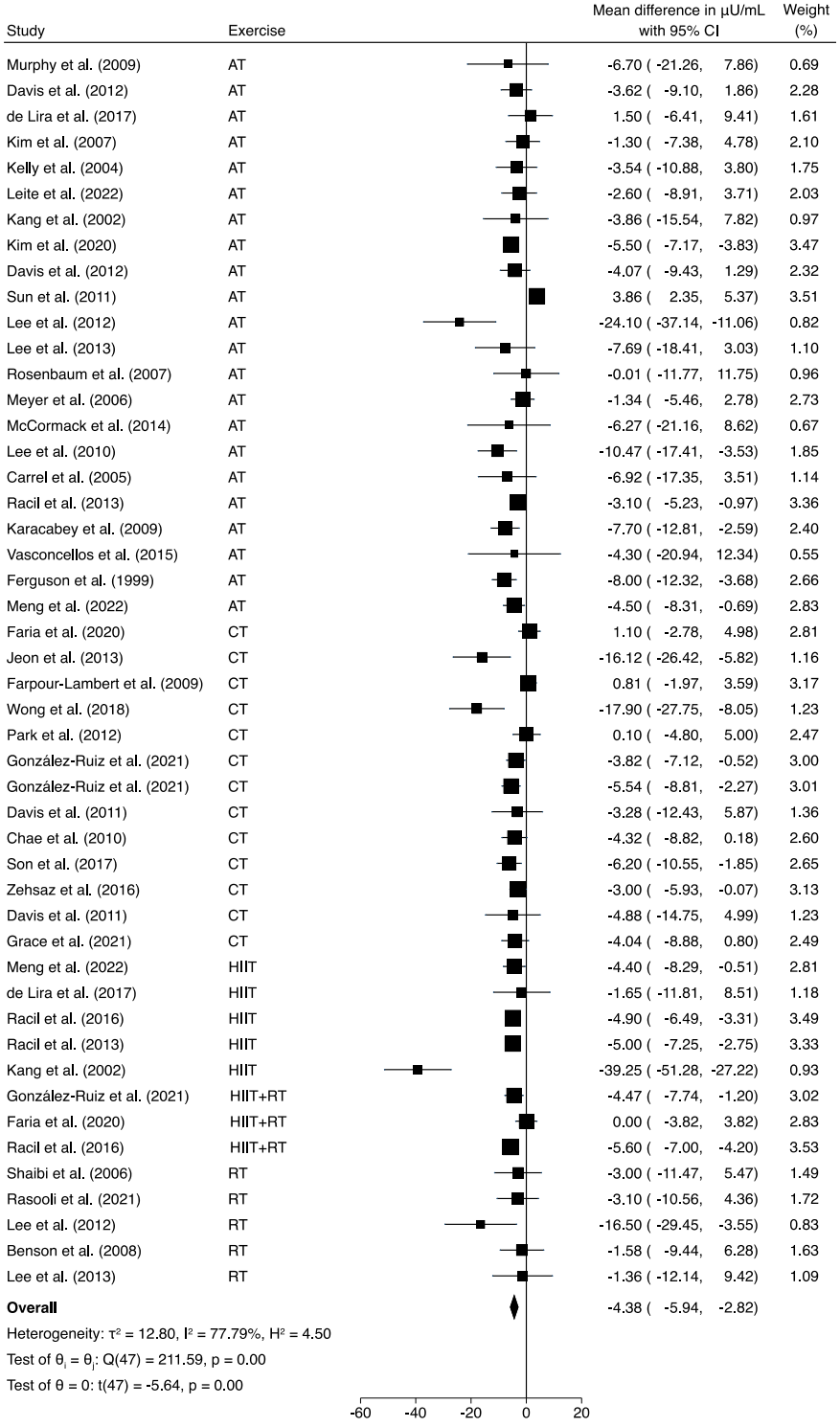
Dias et al. (2018) [13]	Low	High	High	Some concerns	Some concerns	High
Farah et al. (2013)[14] and Silva et al. (2015) [15]	Low	High	High	Some concerns	Some concerns	High
Faria et al. (2020) [16]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Farpour-Lambert et al. (2009) [17]	Low	High	Low	Low	Low	Low
Ferguson et al. (1999) [18]	Low	High	Low	Some concerns	Some concerns	Some concerns
Ghorbanian et al. (2013) [19]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
González-Ruiz et al. (2021) [20]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Grace et al. (2021) [21]	Low	High	High	Some concerns	Some concerns	High
Jeon et al. (2013) [22]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Kang et al. (2002) [23]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Karacabey et al. (2009) [24]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Kelly et al. (2004) [25]	Low	High	Low	Some concerns	Some concerns	Some concerns
Kim et al. (2007) [26]	Low	High	Low	Some concerns	Some concerns	Some concerns
Kim et al. (2020) [27]	Low	High	Low	Some concerns	Some concerns	Some concerns
Koot et al. (2016) [28]	Low	High	High	Some concerns	Some concerns	High
Lee et al. (2013) [29]	Low	High	Low	Some concerns	Some concerns	Some concerns
Lee et al. (2019) [30]	Low	High	High	Some concerns	Some concerns	High
Lee et al. (2010) [31]	Low	High	Low	Some concerns	Some concerns	Some concerns
Lee et al. (2012) [32]	Low	High	Low	Some concerns	Some concerns	Some concerns
Leite et al. (2022) [33]	Low	High	High	Some concerns	Some concerns	High
McCormack et al. (2014) [34]	Low	High	Low	Some concerns	Some concerns	Some concerns
Meng et al. (2022) [35]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Meyer et al. (2006) [36]	Low	High	Low	Some concerns	Some concerns	Some concerns

Murphy et al. (2009) [37]	Low	High	Low	Some concerns	Some concerns	Some concerns
Park et al. (2012) [38]	Low	High	Low	Some concerns	Some concerns	Some concerns
Racil et al. (2016) [39]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Racil et al. (2013) [40]	Low	High	Low	Some concerns	Some concerns	Some concerns
Ramezani et al. (2017) [41]	Low	High	Low	Some concerns	Some concerns	Some concerns
Rasooli et al. (2021) [42]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Rosenbaum et al. (2007) [43]	Low	High	High	Some concerns	Some concerns	High
Salahshoornezhad et al. (2022) [44]	Low	High	Low	Some concerns	Some concerns	Some concerns
Savoye et al. (2014) [45]	Low	High	High	Some concerns	Some concerns	Some concerns
Seo et al. (2019) [46]	Low	High	High	Some concerns	Some concerns	High
Shaibi et al. (2006) [47]	Low	High	Low	Some concerns	Some concerns	Some concerns
Son et al. (2017) [48]	Low	High	Low	Some concerns	Some concerns	Some concerns
Sun et al. (2011) [49]	Low	High	Low	Some concerns	Some concerns	Some concerns
TjØnna et al. (2009) [50]	Low	High	Some concerns	Some concerns	Some concerns	Some concerns
Vasconcellos et al. (2016) [51]	Low	High	Low	Low	Low	Low
Wong et al. (2008) [52]	Low	High	Low	Some concerns	Some concerns	Some concerns
Wong et al. (2018) [53]	Low	High	Low	Some concerns	Some concerns	Some concerns
Yetgin et al. (2020) [54]	Low	High	Low	Some concerns	Some concerns	Some concerns
Zehsaz et al. (2016) [55]	Low	High	Low	Some concerns	Some concerns	Some concerns



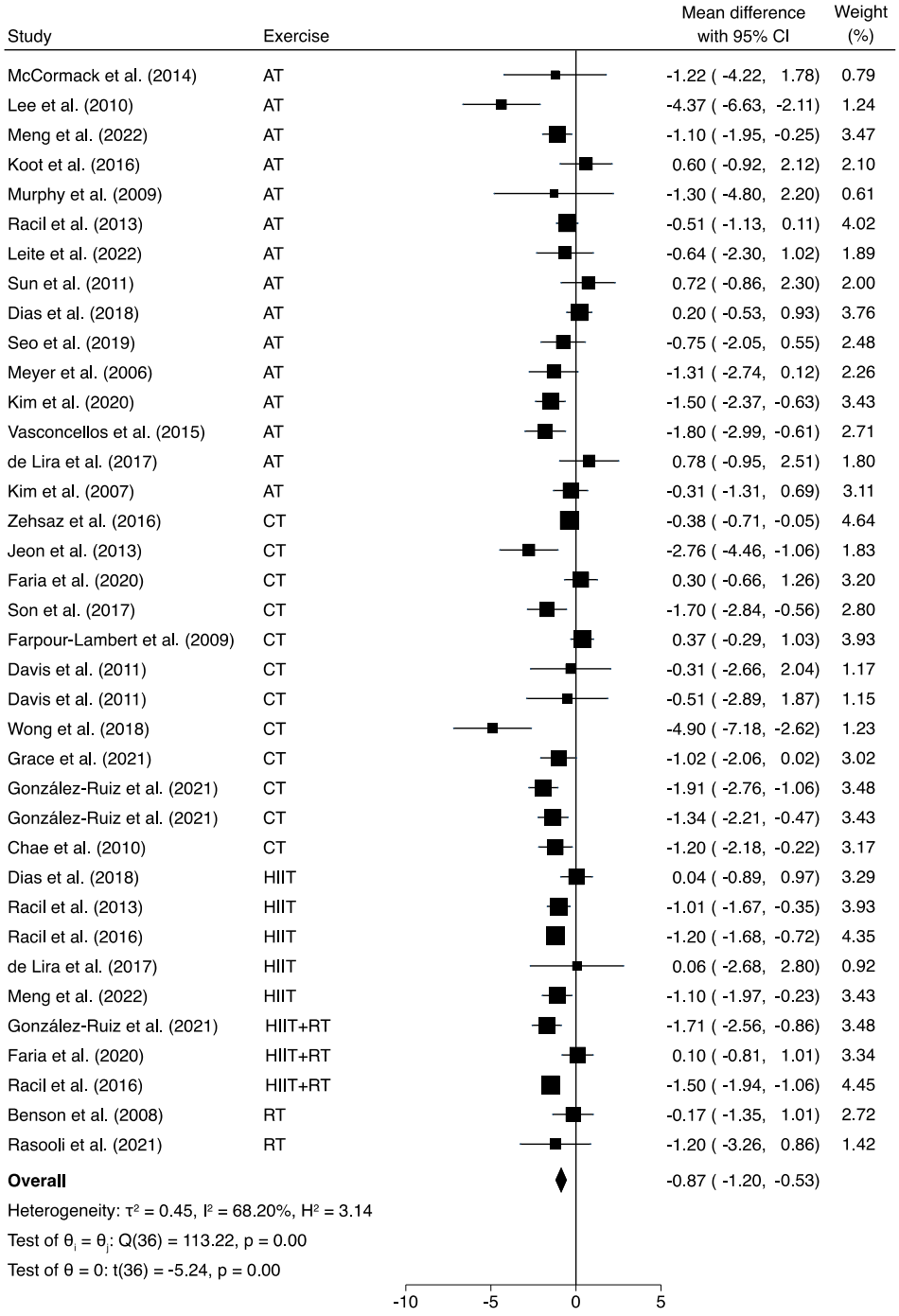
eFigure 1. Effect of Exercise Programs on Fasting Insulin in Children and Adolescents With Excess Weight

AT, aerobic training; CT, concurrent training; HIIT, high-intensity interval training; HIIT+RT, high-intensity interval training and resistance training; RT, resistance training.



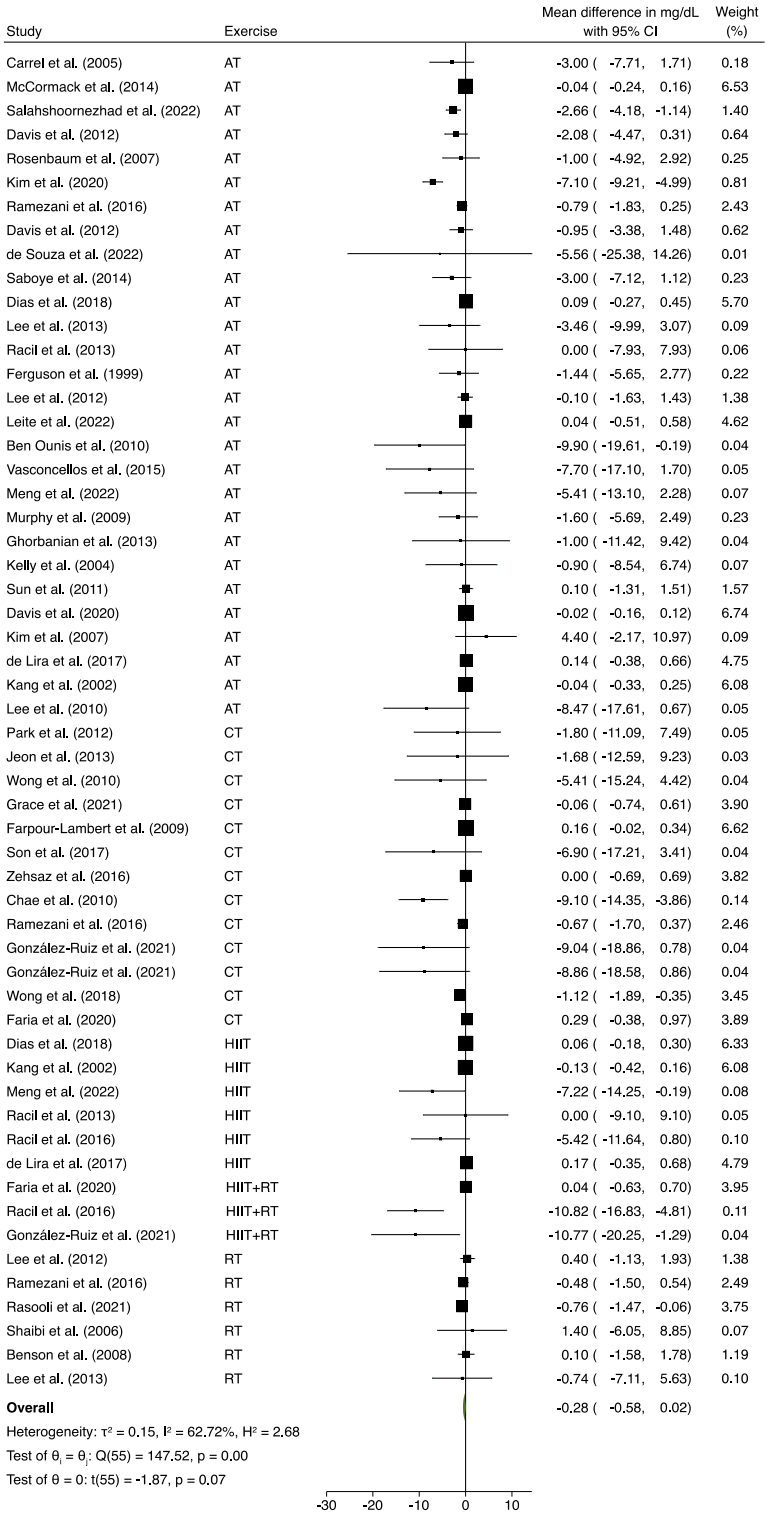
eFigure 2. Effect of Exercise Programs on Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) in Children and Adolescents With Excess Weight

AT, aerobic training; CT, concurrent training; HIIT, high-intensity interval training; HIIT+RT, high-intensity interval training and resistance training; RT, resistance training.



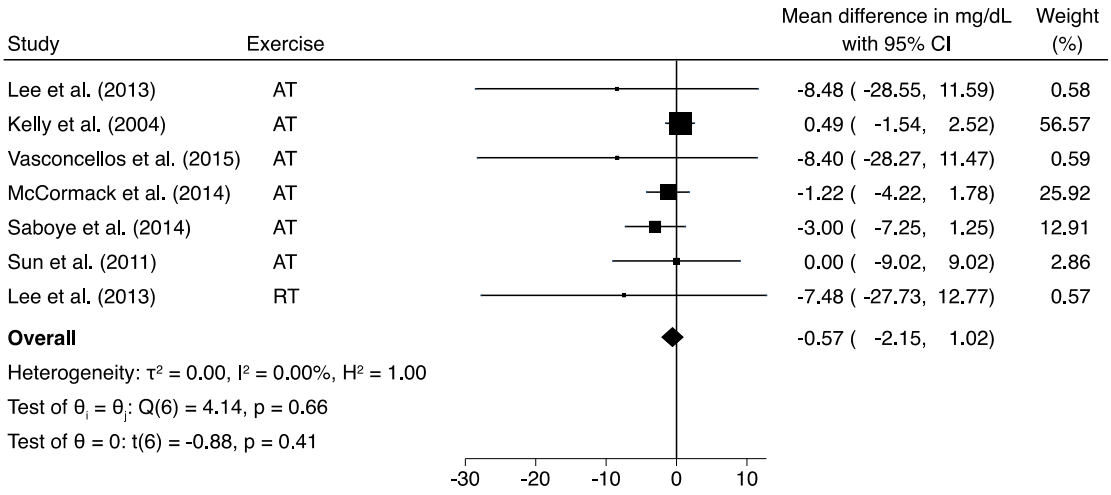
eFigure 3. Effect of Exercise Programs on Fasting Glucose in Children and Adolescents With Excess Weight

AT, aerobic training; CT, concurrent training; HIIT, high-intensity interval training; HIIT+RT, high-intensity interval training and resistance training; RT, resistance training.



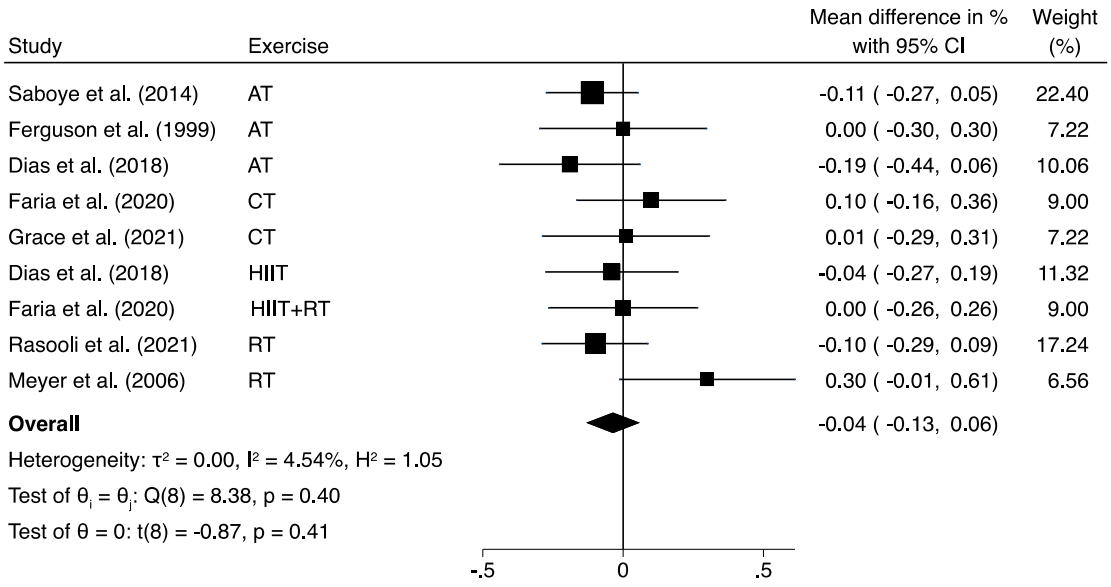
eFigure 4. Effect of Exercise Programs on 2-Hour Oral Glucose Tolerance in Children and Adolescents With Excess Weight

AT, aerobic training; RT, resistance training.

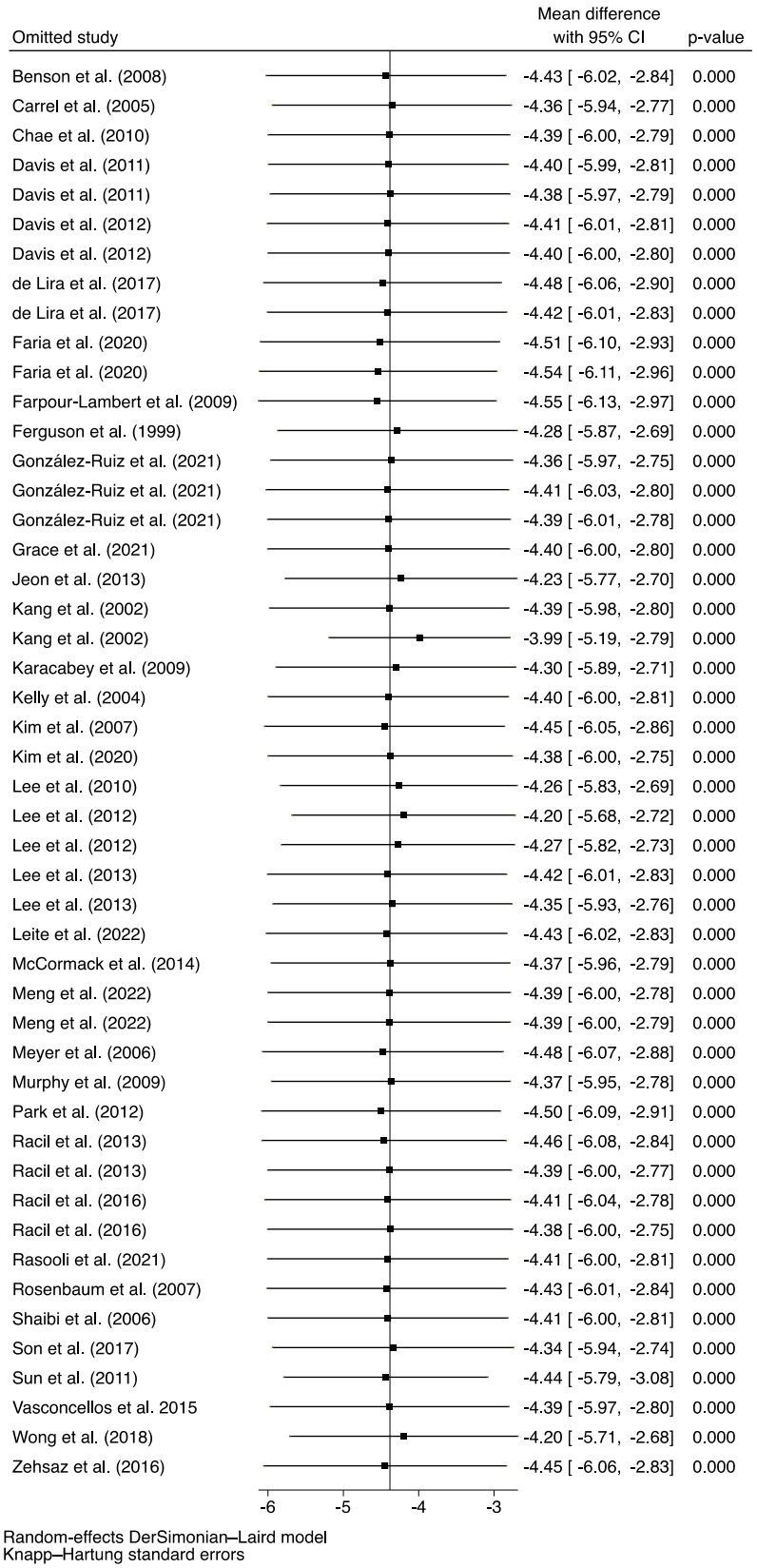


eFigure 5. Effect of Exercise Programs on Glycated Hemoglobin in Children and Adolescents With Excess Weight

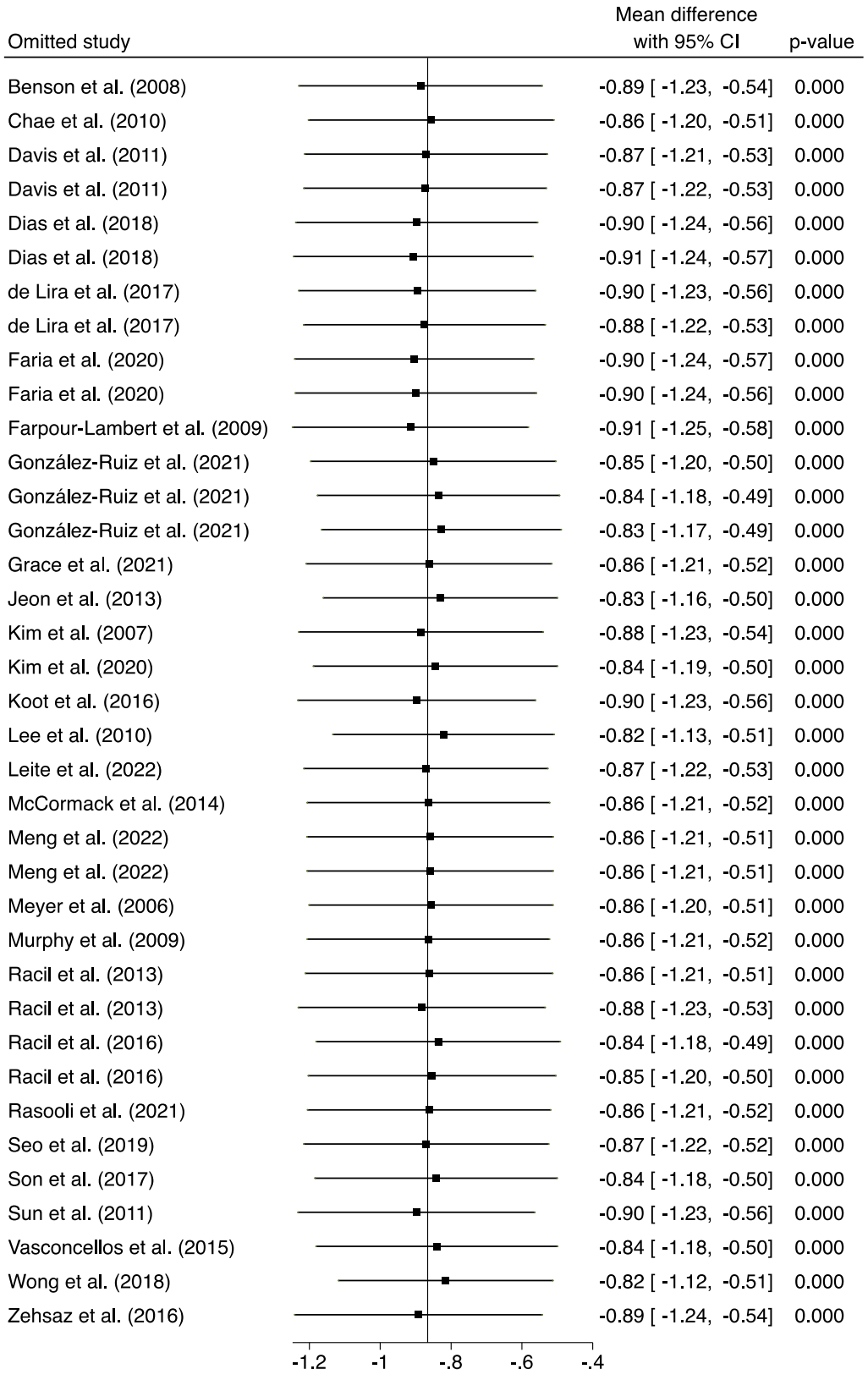
AT, aerobic training; CT, concurrent training; HIIT, high-intensity interval training; HIIT+RT, high-intensity interval training and resistance training; RT, resistance training



eFigure 6. Sensitivity Analyses Once Each Study Was Excluded for Fasting Insulin

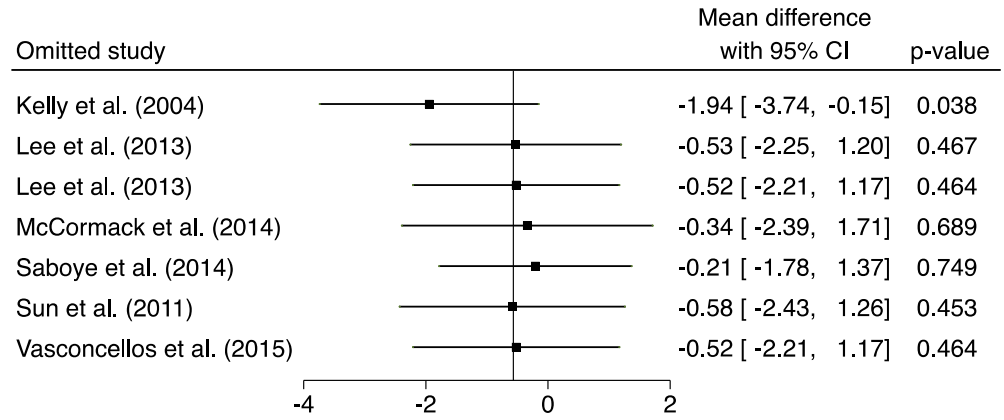


eFigure 7. Sensitivity Analyses Once Each Study Was Excluded for Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)



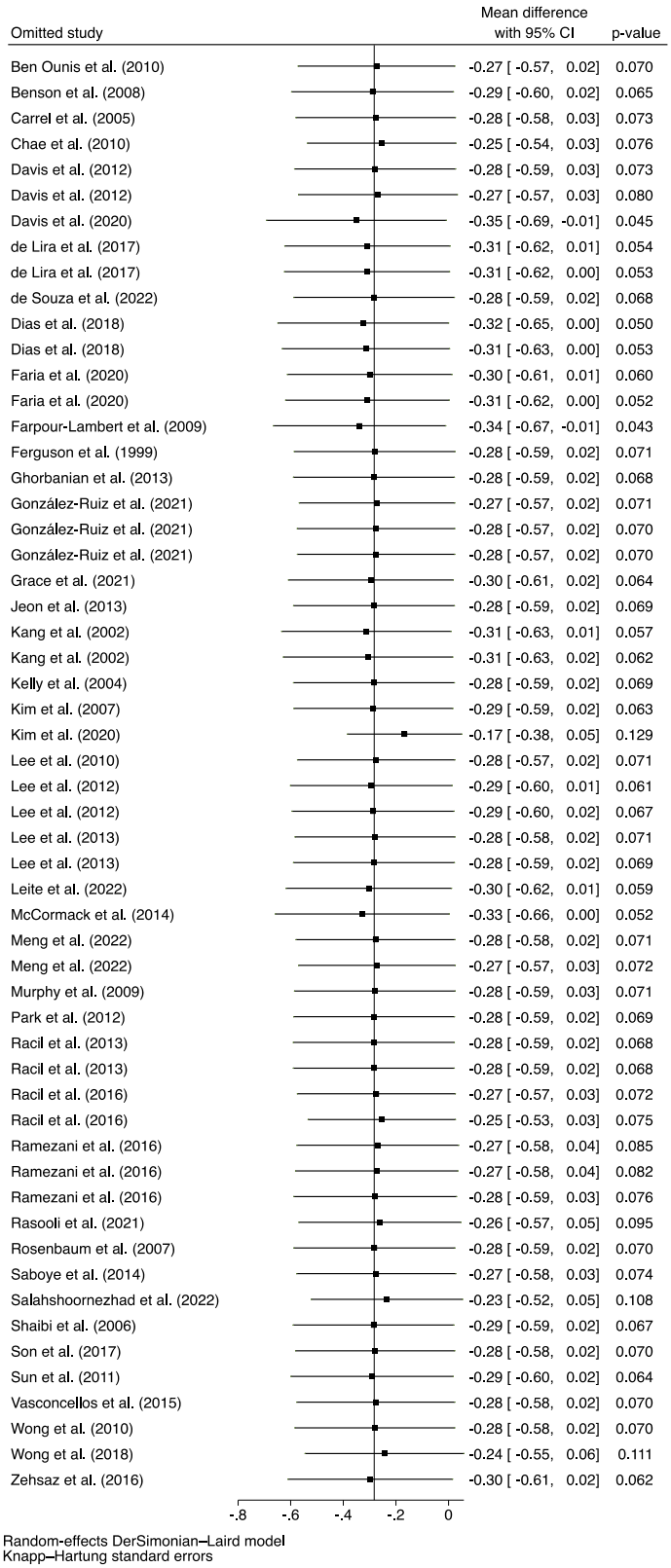
Random-effects DerSimonian–Laird model
Knapp–Hartung standard errors

eFigure 8. Sensitivity Analyses Once Each Study Was Excluded for 2-Hour Oral Glucose Tolerance

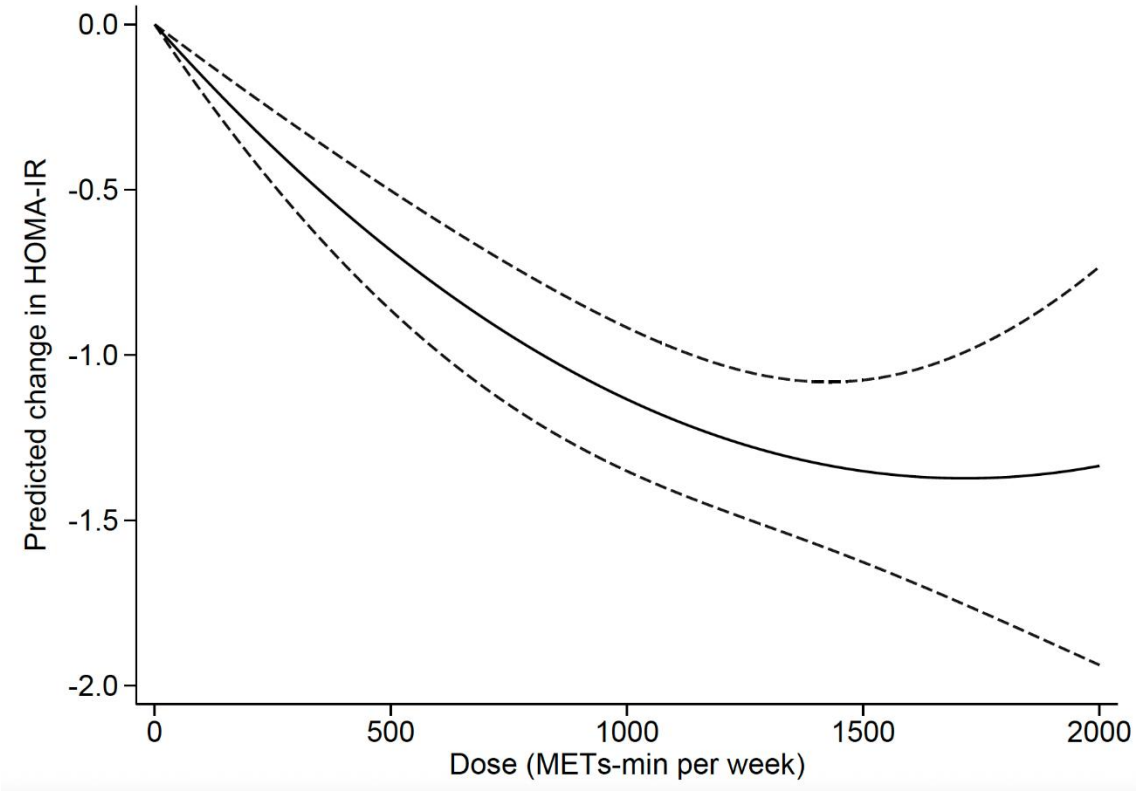


Random-effects DerSimonian–Laird model
Knapp–Hartung standard errors

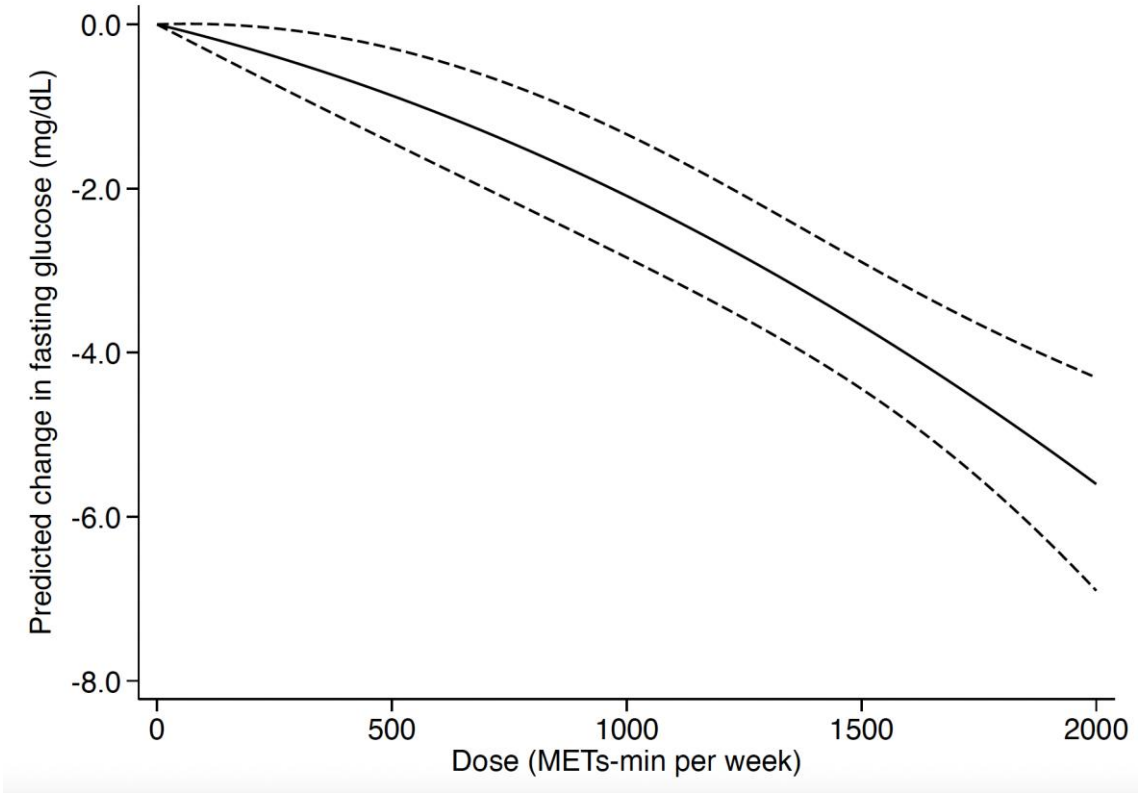
eFigure 9. Sensitivity Analyses Once Each Study Was Excluded for Fasting Glucose



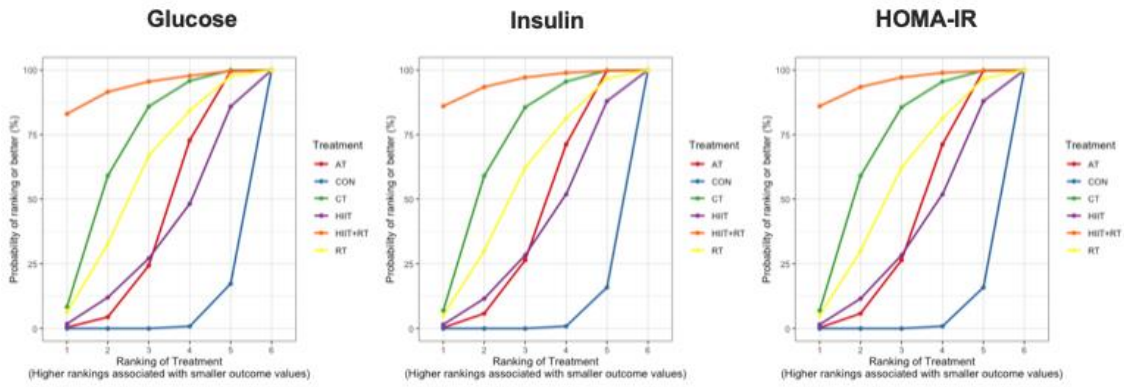
eFigure 10. Dose-Response Association Between Metabolic Equivalent of Task Minutes (MET-min) per Week and Differences in Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) in Children and Adolescents With Excess Weight and Insulin Resistance (ie, HOMA-IR ≥ 3.16)



eFigure 11. Dose-Response Association Between Metabolic Equivalent of Task Minutes (MET-min) per Week and Differences in Fasting Glucose in Children and Adolescents With Excess Weight



eFigure 12. Rankogram for Each Type of Physical Exercise



Glucose levels						
Rank	**AT**	**RT**	**CT**	**HIIT**	**HIIT+RT**	**CON**
1	0.4	5.4	9.6	1.1	83.6	0.0
2	5.0	28.8	63.4	10.8	91.9	0.0
3	27.6	63.0	86.5	26.9	96.0	0.0
4	73.3	83.1	95.0	49.3	98.5	0.8
5	99.8	96.9	99.8	88.3	99.5	15.8
6	100.0	100.0	100.0	100.0	100.0	100.0
SUCRA	41.2	55.5	70.9	35.3	93.9	3.3
Insulin levels						
Rank	**AT**	**RT**	**CT**	**HIIT**	**HIIT+RT**	**CON**
1	0.3	4.3	8.7	1.8	84.8	0.0
2	4.0	26.7	65.3	10.6	93.4	0.0
3	23.5	62.3	89.2	27.8	97.2	0.0
4	72.7	81.0	96.9	49.6	98.7	1.1
5	99.6	97.2	99.9	86.1	99.5	17.7
6	100.0	100.0	100.0	100.0	100.0	100.0
SUCRA	40.0	54.3	72.0	35.2	94.7	3.8
HOMA-IR						
Rank	**AT**	**RT**	**CT**	**HIIT**	**HIIT+RT**	**CON**
1	0.3	5.1	7.0	1.5	86.1	0.0
2	5.8	30.0	59.2	11.6	93.5	0.0
3	26.4	62.4	85.7	28.3	97.2	0.0
4	71.3	81.4	95.6	51.9	99.0	0.9
5	99.8	96.8	99.8	88.0	99.7	15.9
6	100.0	100.0	100.0	100.0	100.0	100.0
SUCRA	40.7	55.1	69.4	36.3	95.1	3.4

AT, aerobic training, CON, control group; CT, concurrent training, HIIT, high-intensity interval training; HIIT+resistance, high-intensity interval training plus resistance training; HOMA-IR, homeostasis model assessment of insulin resistance; RT, resistance training; SUCRA, Surface Under the Cumulative RAnking curve.

eFigure 13. Network Meta-analysis Confidence Rating for Glucose, Insulin, and Homeostatic Model Assessment for Insulin Resistance Outcomes

Glucose levels

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	**Confidence rating**
AT:CON	27	Some concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	**Low**
AT:CT	4	Some concerns	Some concerns	No concerns	Some concerns	Some concerns	No concerns	**High**
AT:HIIT	7	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
AT:RT	4	Major concerns	Some concerns	No concerns	Some concerns	Some concerns	No concerns	**Low**
CON:CT	11	Some concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
CON:HIIT	5	Major concerns	Some concerns	No concerns	Major concerns	No concerns	No concerns	**Low**
CON:HIIT+RT	3	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Major concerns	**Low**
CON:RT	6	Some concerns	Some concerns	No concerns	No concerns	Some concerns	Major concerns	**Low**
CT:HIIT+RT	3	Some concerns	Some concerns	Some concerns	No concerns	No concerns	Major concerns	**Low**
CT:RT	3	Major concerns	Some concerns	Some concerns	No concerns	Major concerns	Major concerns	**Low**
HIIT:HIIT+RT	1	Some concerns	Some concerns	Some concerns	No concerns	No concerns	No concerns	**High**
AT:HIIT+RT	0	Some concerns	Some concerns	Some concerns	No concerns	Some concerns	Major concerns	**Low**
CT:HIIT	0	Some concerns	Some concerns	Some concerns	Major concerns	No concerns	Major concerns	**Low**
HIIT:RT	0	Major concerns	Some concerns	Some concerns	Some concerns	Some concerns	Major concerns	**Low**
HIIT+RT:RT	0	Some concerns	Some concerns	Some concerns	Major concerns	No concerns	Major concerns	**Low**

Insulin levels

Comparison	**Number of studies**	**Within-study bias**	**Reporting bias**	**Indirectness**	**Imprecision**	**Heterogeneity**	**Incoherence**	**Confidence rating**
AT:CON	19	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**High**
AT:CT	3	Some concerns	Some concerns	Some concerns	No concerns	Major concerns	No concerns	**Low**
AT:HIIT	6	Some concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	**Low**
AT:HIIT+RT	1	Some concerns	Some concerns	Some concerns	No concerns	Major concerns	No concerns	**Low**
AT:RT	2	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
CON:CT	10	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**High**
CON:HIIT	4	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**High**

CON:HIIT+RT	3	Some concerns	Some concerns	Some concerns	No concerns	Some concerns	No concerns	**High**
CON:RT	4	Some concerns	Some concerns	No concerns	Some concerns	Some concerns	No concerns	**High**
CT:HIIT+RT	1	Some concerns	Some concerns	Some concerns	Major concerns	No concerns	No concerns	**Low**
CT:RT	2	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Major concerns	**Low**
HIIT:HIIT+RT	1	Some concerns	Some concerns	Some concerns	Major concerns	No concerns	No concerns	**Low**
CT:HIIT	0	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
HIIT:RT	0	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
HIIT+RT:RT	0	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**

HOMA-IR

Comparison	Number of studies	Within-study bias	Reporting bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
AT:CON	15	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**High**
AT:CT	2	Some concerns	Some concerns	Some concerns	No concerns	Major concerns	No concerns	**Low**
AT:HIIT	5	Some concerns	Some concerns	No concerns	No concerns	Major concerns	No concerns	**Low**
CON:CT	10	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**High**
CON:HIIT	5	Some concerns	Some concerns	No concerns	No concerns	Some concerns	No concerns	**High**
CON:HIIT+RT	3	Some concerns	Some concerns	Some concerns	No concerns	Some concerns	No concerns	**High**
CON:RT	2	Major concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Low**
CT:HIIT+RT	2	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
CT:RT	1	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
HIIT:HIIT+RT	1	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
AT:HIIT+RT	0	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**
AT:RT	0	Some concerns	Some concerns	Some concerns	Major concerns	No concerns	No concerns	**Low**
CT:HIIT	0	Some concerns	Some concerns	Some concerns	No concerns	Major concerns	No concerns	**Low**
HIIT:RT	0	Some concerns	Some concerns	Some concerns	Major concerns	No concerns	No concerns	**Low**
HIIT+RT:RT	0	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No concerns	**Moderate**

AT, aerobic training; CON, control group; CT, concurrent training; HIIT, High Intensity Interval Training; HIIT+RT, High Intensity Interval Training + resistance training; HOMA-IR; Homeostatic Model Assessment for Insulin Resistance; RT, resistance training.

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