



Effects of hypoxic training interventions on cardiometabolic health of adults with overweight and obesity: A systematic review and meta-analysis

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Abstract

Obesity rates have surpassed underweight globally, increasing the burden of cardiometabolic complications on healthcare systems. Hypoxic training has emerged as a potential intervention to improve cardiometabolic health in adults with obesity, but evidence remains inconclusive. This systematic review and meta-analysis evaluated whether hypoxic training is more effective than normoxic training in this context. A systematic search of PubMed, Web of Science, and Cochrane Library (up to June 2025) identified randomised controlled trials comparing hypoxic and normoxic training in adults with overweight or obesity. Outcomes included glucose homeostasis, lipid profile, and blood pressure. Subgroup, moderation, and sensitivity analyses were also conducted to explore sources of heterogeneity and assess the robustness of findings. Of 1815 studies screened, 9 (278 participants) met the criteria. Meta-

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analysis results demonstrated no significant differences between hypoxic and normoxic training for fasting glucose ($p = 0.118$) or fasting insulin ($p = 0.415$), with substantial heterogeneity observed across studies ($I^2 = 60\%–77\%$). Similarly, lipid profile markers and blood pressure showed no significant between-group differences (all $p > 0.05$), also with moderate to high heterogeneity. Subgroup and moderation analyses partially explained this variability, suggesting greater fasting glucose reductions with shorter and lower-intensity hypoxic interventions. Hypoxic training did not outperform normoxic training in improving cardiometabolic outcomes. However, the considerable variability in intervention duration, hypoxic dose, and exercise intensity across studies limits the certainty of these findings. Well-designed, adequately powered trials are needed to determine whether specific hypoxic training protocols or participant characteristics may modulate efficacy in adults with overweight or obesity.

KEYWORDS

cardiovascular disease, meta-analysis, systematic review, weight management

1 | INTRODUCTION

The prevalence of obesity has risen significantly in recent decades (from 6.7% in 1990 to 11.2% in 2021), globally exceeding underweight and reaching a pandemic burden.¹ In Italy, 22% of women and 20% of men are obese, with a substantial impact on the healthcare system.^{1,2} Indeed, obesity is associated with a wide range of health issues.³ However, cardiometabolic conditions are the leading cause of obesity-related diseases.^{4,5} Cardiometabolic health, encompassing factors such as cardiovascular function and metabolic processes like glucose homeostasis and lipid metabolism, is crucial for overall health and longevity, especially for adults with obesity.^{6,7} Fasting glucose is strongly associated with both metabolic and cardiovascular diseases.^{8–10} A fasting glucose level between 5.6 and 6.9 mmol/L is classified as pre-diabetes¹¹ and according to Huang et al.,⁹ levels above 5.6 mmol/L are associated with an increased risk of cardiovascular diseases.

Given these alarming trends, many exercise interventions have been developed to counter the obesity pandemic.^{12,13} Hypoxic training, which involves exercise in a normobaric (breathing air with a reduced oxygen concentration at constant atmospheric pressure) or hypobaric (breathing air at reduced atmospheric pressure, leading to lower oxygen availability) environment with reduced oxygen levels, appears to be a feasible approach for improving body composition and cardiometabolic health in adults with obesity.^{14–18} Several studies have shown promising results for hypoxic training at improving metabolic profiles and reducing fat mass percentages.^{19–21} Moreover, hypoxic training allows participants to train with a reduced mechanical load and stress, specifically in the case of relative hypoxic training, which maintains the same physiological load with reduced mechanical strain.^{22,23} Beyond these biomechanical advantages, hypoxia may further enhance cardiometabolic adaptations through specific molecular

pathways. Specifically, low-frequency intermittent hypoxia, or hypoxic conditioning, directly increases reactive oxygen species, activating pathways that upregulate hypoxia-inducible factors HIF-1 α and HIF-1 β .²⁴ This, in turn, stimulates the production of vascular endothelial growth factor (VEGF), which promotes vascular endothelial genesis and has been associated with improved insulin sensitivity in hypoxic training for adults with obesity.²⁵ Concomitantly, HIF-1-related signaling influences lipid metabolism by promoting fatty acid oxidation and reducing lipogenesis,²⁶ while improved endothelial function and vascular remodelling may contribute to reductions in blood pressure.²⁷ These adaptations can potentially translate into improved cardiovascular health and metabolic efficiency.^{25,27} Despite these potential benefits, few reviews have rigorously examined the effects of hypoxic training on body composition,^{28,29} with most lacking selective inclusion criteria and a systematic search strategy. Moreover, the effects on cardiometabolic health have received limited attention. Therefore, the primary aim of this systematic review and meta-analysis was to compare the effects of exercise training performed under normobaric hypoxia versus normoxia on cardiometabolic health in adults with overweight or obesity. Therefore, we hypothesised that exercise training performed under normobaric hypoxia would lead to greater improvements in fasting glucose compared to equivalent training under normoxia. In line with previous evidence suggesting enhanced endothelial and metabolic adaptations to hypoxia, we further expected potential favourable effects on lipid profile and blood pressure, although these were considered secondary outcomes.

2 | MATERIALS AND METHODS

The protocol for the systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews

TABLE 2 Characteristics of included studies.

Study	Participants characteristics				Intervention design				Hypoxic load	Altitude (m)		
	Group	Sample size	Age (years)	Weight (kg)	BMI (kg/m ²)	Type of exposure	Type of training	Protocol			Volume	Intensity
Ghait et al. ¹⁹	Normoxia	13 (M)	52 ± 7.5	99.9 ± 15.5	32.4 ± 4.8	None	Aerobic	HIT: cycling at 80% or 100% at maximal workload	3 session per week of 40 min; 8 weeks	High	-	Sea level
	Hypoxia	10 (M)	51 ± 8.3	95.4 ± 19.4	31.5 ± 4.0	Active, normobaric	Aerobic	HIT: cycling at 80% or 100% at maximal workload	3 session per week of 40 min; 8 weeks	High	Relative	4200
Jung et al. ³⁵	Normoxia	10 (W)	43.8 ± 8.6	66.3 ± 11	25.1 ± 3.3	None	Pilates	Pilates training using a tubing band	3 session per week of 50 min; 12 weeks	Low	-	Sea level
	Hypoxia	12 (W)	47.2 ± 6.4	68.0 ± 10.1	27.1 ± 4.3	Active, normobaric	Pilates	Pilates training using a tubing band	3 session per week of 50 min; 12 weeks	Low	Not specified	3000
Gatterer et al. ³⁶	Normoxia	6 (M)	52.4 ± 7.9	103.2 ± 15.11	36.3 ± 4.0	None	Aerobic	65%–70% of the maximal heart rate using a treadmill, cycle ergometer or a cross trainer	2 session per week of 90 min; 32 weeks	Moderate	-	Sea level
	Hypoxia	12 (W)	50.3 ± 10.3	105.5 ± 20.0	37.9 ± 8.1	Active + passive, normobaric	Aerobic	65%–70% of the maximal heart rate using a treadmill, cycle ergometer or a cross trainer	2 session per week of 90 min; 32 weeks	Moderate	Relative	3500
Fernandez-Mendez et al. ³⁷	Normoxia	2 (M)	32.2 ± 8.4	96.6 ± 9.6	32.9 ± 2.7	None	Aerobic	Walking on a treadmill at each individual's preferred walking speed	3 session per week of 60 min; 3 weeks	Low	-	Sea level
	Hypoxia	2 (M)	34.8 ± 4.7	96.8 ± 9.5	34.1 ± 2.6	Active, normobaric	Aerobic	Walking on a treadmill at each individual's preferred walking speed	3 session per week of 60 min; 3 weeks	Low	Not specified	3000
Wiesner et al., 2009 ²¹	Normoxia	8 (M)	42.1 ± 1.7	87.5 ± 3.6	32.5 ± 0.8	None	Aerobic	Walking on a treadmill at 65% of maximum oxygen consumption	3 session per week of 60 min; 4 weeks	Moderate	-	Sea level
	Hypoxia	10 (M)	42.2 ± 1.2	93.4 ± 2.6	33.1 ± 0.3	Active, normobaric	Aerobic	Walking on a treadmill at 65% of maximum oxygen consumption	3 session per week of 60 min; 4 weeks	Moderate	Relative	2740
Chacaroun et al. ³⁸	Normoxia	8 (M)	56 ± 11	Not reported	31.8 ± 3.2	None	Aerobic	Cycling at 75 ± 3% of the maximal heart rate	3 session per week of 45 min; 8 weeks	High	-	Sea level
	Hypoxia	11 (M)	52 ± 12	Not reported	31.2 ± 2.4	Active, normobaric	Aerobic	Cycling at 75% ± 3% of the maximal heart rate	3 session per week of 45 min; 8 weeks	High	Relative	3700
Morishima et al. ³⁹	Normoxia	11 (M)	30 ± 2	73.8 ± 4	25.4 ± 0.9	None	Aerobic	Cycling at 55% of the maximal oxygen uptake	3 session per week of 60 min; 4 weeks	Moderate	-	Sea level
	Hypoxia	9 (M)	32 ± 3	74.4 ± 4.2	25.6 ± 1.2	Active, normobaric	Aerobic	Cycling at 55% of the maximal oxygen uptake	3 session per week of 60 min; 4 weeks	Moderate	Relative	2500
Klug et al. ⁴⁰	Normoxia	11 (M)	57.6 ± 2.2	108.5 ± 3	34.1 ± 0.9	None	Aerobic	Walking on a treadmill at 50%–60% of their individual maximal heart rate	3 session per week of 60 min; 6 weeks	Moderate	-	Sea level
	Hypoxia	12 (M)	55.0 ± 2.1	109.1 ± 5.2	35.5 ± 1.4	Active, normobaric	Aerobic	Walking on a treadmill at 50%–60% of their individual maximal heart rate	3 session per week of 60 min; 6 weeks	Moderate	Relative	2500

TABLE 2 (Continued)

Study	Participants characteristics				Intervention design							
	Group	Sample size	Age (years)	Weight (kg)	BMI (kg/m ²)	Type of exposure	Type of training	Protocol	Volume	Intensity	Hypoxic load	Altitude (m)
Camacho-Cardenosa et al., 2018a ²⁰	Normoxia	13 (W)	43.14 ± 7.67	80.41 ± 16.27	29.59 ± 5.25	None	Aerobic	HIIT using a cycle ergometer at 90% Wmax	3 session per week of 60 min; 12 weeks	Moderate	-	Sea level
	Hypoxia	13 (W)	44.43 ± 7.18	80.1 ± 18.88	30.03 ± 6.37	Active, normobaric	Aerobic	HIIT using a cycle ergometer at 90% Wmax	3 session per week of 60 min; 12 weeks	Moderate	Absolute	2500
Camacho-Cardenosa et al., 2018b ²⁰	Normoxia	15 (W)	40.05 ± 8.66	77.94 ± 11.31	28.74 ± 4.77	None	Aerobic	HIIT using a cycle ergometer at 130% Wmax	3 session per week of 60 min; 12 weeks	High	-	Sea level
	Hypoxia	18 (W)	37.4 ± 10.25	73.73 ± 11.11	27.71 ± 4.55	Active, normobaric	Aerobic	HIIT using a cycle ergometer at 130% Wmax	3 session per week of 60 min; 12 weeks	High	Absolute	2500

Note: Camacho-Cardenosa et al., 2018a and Camacho-Cardenosa et al., 2018b are data from the same study but using four different groups. Abbreviations: BMI, body mass index; HIIT: high-intensity interval training; M, men; W, women; Wmax: maximal power.

Likewise, low-intensity protocols resulted in a larger decrease in fasting glucose under hypoxia (SMD = -0.93, 95% CI = -1.58 to -0.27, $p = 0.006$), while moderate- and high-intensity interventions showed no significant effects ($p > 0.05$). Altitude did not significantly moderate any outcome ($p > 0.05$), but baseline levels were significant moderators for fasting glucose ($p = 0.020$) and fasting insulin ($p < 0.001$), indicating that participants with higher initial values experienced greater hypoxia-induced improvements.

The effect of the hypoxic training on lipid profile biomarkers is shown in Figure 4. LDL, HDL, total cholesterol (TC) and triglycerides (TG) did not change significantly in the hypoxic compared to the normoxic interventions (LDL; SMD = -0.20, 95% CI = -0.44, 0.05, $p = 0.473$; HDL; SMD = 0.08, 95% CI = -0.13, 0.29, $p = 0.112$; TC; SMD = -0.02, 95% CI = -0.27, 0.24, $p = 0.892$; and TG; SMD = 0.02, 95% CI = -0.19, 0.23, $p = 0.874$) without having high heterogeneity (LDL; Q (df = 7) = 5.49, $p = 0.599$; $I^2 = 0.00\%$; HDL; Q (df = 6) = 5.87, $p = 0.438$; $I^2 = 0.00\%$; TC; Q (df = 6) = 7.08, $p = 0.313$; $I^2 = 15.29\%$; and TG; Q (df = 8) = 8.29, $p = 0.396$; $I^2 = 4.67\%$). When analysing the post-pre differences, both training methods reduced the LDL levels (hypoxia: SMD = -0.26, 95% CI = -0.48, 0.05, $p = 0.018$; normoxia: SMD = -0.31, 95% CI = -0.53, -0.09, $p = 0.007$). However, while hypoxia reduced the HDL levels (SMD = -0.27, 95% CI = -0.53, -0.01, $p = 0.043$), normoxic training reduced the TG levels (SMD = -0.41, 95% CI = -0.76, -0.05, $p = 0.026$) (Figures S3 and S4). Sensitivity, publication bias, and influence diagnostics for lipid profile outcomes (Figures S9-S12, S18-S20, and S27-S30) confirmed the robustness of the between-group post-pre differences. Leave-one-out sensitivity analyses showed that the exclusion of any single study did not substantially alter the pooled estimates for LDL-C, HDL-C, total cholesterol, or triglycerides. Funnel plots appeared symmetrical, and Egger's tests revealed no significant publication bias for LDL-C ($p = 0.460$), HDL-C ($p = 0.102$) and triglycerides ($p = 0.332$), though for total cholesterol Egger's value was significant ($p = 0.0497$). Influence diagnostics further supported model stability, as standardised residuals, Cook's distances, and leverage statistics showed no outliers or studies that disproportionately influenced heterogeneity or overall model fit. Subgroup and moderation analyses for lipid outcomes (Tables S7-S9) indicated that neither intervention duration, exercise intensity, nor altitude significantly influenced the between-group post-pre differences. Programs lasting less than 8 weeks and those exceeding 8 weeks showed no significant effects on LDL-C, HDL-C, total cholesterol, or triglycerides (all $p > 0.05$). Similarly, low-, moderate-, and high-intensity interventions showed no significant between-group differences (all $p > 0.05$). Moderation analysis revealed no significant effects of altitude ($p > 0.05$) or baseline lipid levels ($p > 0.05$).

The effect of the hypoxic training on blood pressure is shown in Figure 5. Post-pre changes in systolic (SBP) and diastolic blood pressure (DBP) did not differ significantly between the two interventions (SBP; SMD = 0.00, 95% CI = -0.35, 0.35, $p = 0.995$; and DBP SMD = -0.01, 95% CI = -0.45, 0.44, $p = 0.976$) with significant heterogeneity for both outcomes (SBP; Q (df = 7) = 19.25, $p = 0.007$; $I^2 = 63.64\%$; and DBP; Q (df = 7) = 30.32, $p < 0.001$; $I^2 = 76.92\%$).

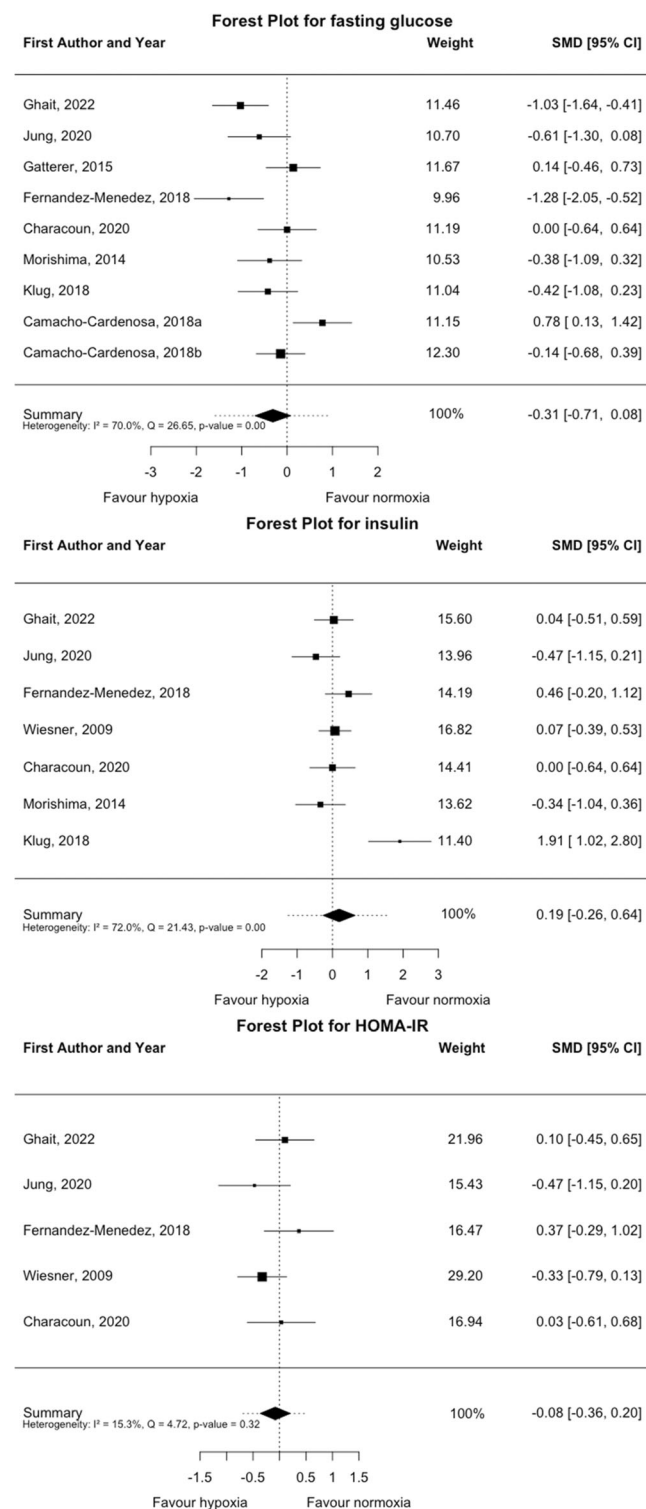


FIGURE 3 Forest plot of standardised mean differences (estimate) for fasting glucose, fasting insulin and homeostatic model assessment for insulin resistance (HOMA-IR). A negative value indicates a greater reduction in outcome after hypoxic interventions than after normoxic interventions, whereas a positive value indicates a smaller reduction in outcome after hypoxic interventions than after normoxic interventions. CI, confidence interval; SMD, standardised mean difference.

However, when analysing the single intervention effect, while normoxic intervention only reduced DBP (SMD = -0.29 , 95% CI = -0.51 , -0.07 , $p = 0.010$), hypoxia reduced both SBP and DBP (SBP; SMD = -0.44 , 95% CI = -0.68 , -0.20 , $p < 0.001$; and DBP SMD = -0.45 , 95% CI = -0.78 , -0.11 , $p = 0.009$) (Figure S5). Sensitivity, publication bias, and influence diagnostics (Figures S13, S14, S22, S23, and S31, S32) confirmed the robustness of the between-group post-pre differences in blood pressure outcomes. Leave-one-out and influence analyses showed that no individual study greatly affected the pooled estimates for SBP or DBP, while Egger's tests indicated no publication bias for SBP ($p = 0.723$) while it was significant for DBP ($p = 0.0131$). Subgroup and moderation analyses (Tables S7–S9) suggested limited influence of intervention characteristics. Shorter (<8 weeks) and moderate- to high-intensity interventions showed borderline effects on SBP, whereas DBP remained unchanged ($p > 0.05$). Altitude moderated SBP responses ($p = 0.024$), and higher baseline SBP predicted greater reductions ($p < 0.001$).

4 | DISCUSSION

The primary aim of this study was to review the effects of normobaric hypoxic training on cardiometabolic outcomes, with fasting glucose as the main outcome. Secondary outcomes, including insulin levels, HOMA-IR, BP, lipid profile, were also analysed. We also analysed within-group pre-post changes to assess the effect of each intervention.

Overall, our analyses did not reveal significant differences between normobaric hypoxic interventions when compared to those performed under normoxic conditions. Outcome-specific trends favoured one condition or the other, as explored in subgroup and moderation analyses. Hypoxic training therefore appears to provide comparable cardiometabolic benefits to normoxic training in adults with overweight or obesity.

4.1 | The effects of normobaric hypoxic training on glucose homeostasis

On fasting glucose, we did not find any differences between the effects of training interventions performed under hypoxic and normoxic conditions. Subgroup analyses suggested that shorter and lower-intensity hypoxic protocols may be more effective for fasting glucose. This may be due to heterogeneity in baseline glucose and training characteristics. This aligns with our moderation analysis, which identified baseline fasting glucose as a significant predictor of the response to hypoxic training, suggesting greater improvements in participants with higher baseline values. While some studies found a higher reduction in fasting glucose for hypoxic interventions, most of the studies found no differences.^{19,37} Conversely, Camacho-Cardenosa et al.²⁰ found a greater reduction for the

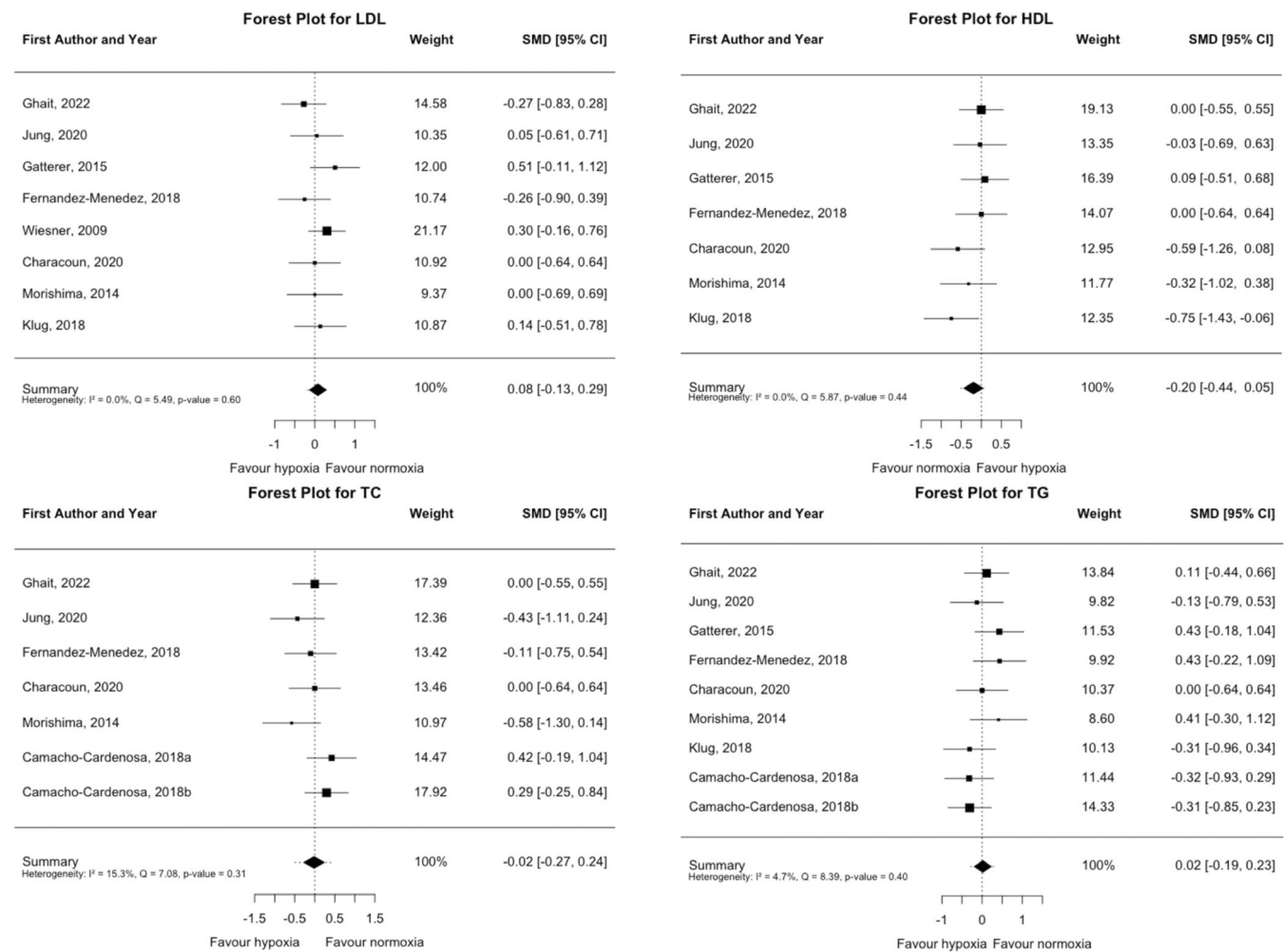


FIGURE 4 Forest plot of standardised mean differences (estimate) for low-density and high-density lipoprotein (HDL and LDL), total cholesterol (TC) and triglycerides (TG). A negative value indicates a greater reduction in outcome after hypoxic interventions than after normoxic interventions, whereas a positive value indicates a smaller reduction in outcome after hypoxic interventions than after normoxic interventions. CI, confidence interval; SMD, standardised mean difference.

normoxic interventions. Even if there were no differences between hypoxia and normoxia, when considering within-group changes, only the hypoxic training led to a reduced fasting glucose after the intervention. This should be considered a crucial marker for the training interventions, since it has been related to several cardiometabolic diseases as mentioned in the introduction.^{42,43}

Our findings regarding insulin levels did not reveal significant differences between normobaric hypoxic and normoxic conditions. Similarly, insulin levels did not differ between conditions. Nonetheless, when comparing pre- and post-interventions results, normoxic training led to a slight significant improvement in insulin levels. Moreover, our moderation results, showed that baseline insulin values significantly moderated the changes, revealing larger improvements among participants with higher initial insulin levels.

No clear differences were observed for HOMA-IR. Overall, most studies reported that all the training interventions led to improvements in the general health of the targeted population. The greater fasting glucose response under hypoxia may relate to HIF-1-mediated

metabolic effects, as previously mentioned in the introduction.²⁵ However, the findings do not clearly indicate which condition was more effective in enhancing these outcomes, especially regarding the HOMA-IR marker. However, the limited number of HOMA-IR studies restricts interpretation. In addition, differences in participants' baseline glucose and insulin levels may have influenced the magnitude of the observed effects. Future studies should focus specifically on adults with impaired glucose homeostasis to understand whether hypoxic training could be a valid alternative to normoxic training.

4.2 | The effects of normobaric hypoxic training on lipid profile

Most studies reported lipid profile improvements, with no significant differences between conditions. Subgroup and moderation analyses did not identify moderators of the between-group effects. Within-group analyses showed that both conditions reduced LDL. These

4.4 | Practical implications

Our systematic review and meta-analysis found that hypoxic training produced similar benefits to normoxic training in adults with overweight or obesity. However, the current literature lacks standardisation in hypoxic training protocols. Specifically, studies differed in intervention duration, training type, and simulated altitude. Most employed relative-intensity hypoxic protocols that matched physiological effort to normoxic training conditions.¹⁹⁻²¹ Additionally, some studies included in this systematic review and meta-analysis exhibited minor methodological limitations, likely due to the novelty of the topic, which may have influenced our findings. However, sensitivity and influence diagnostics indicated that no single study disproportionately affected the overall estimates, suggesting that these methodological differences did not substantially bias the pooled results.

We acknowledge that our study has some limitations. Firstly, the lack of stratification based on overweight and obesity status might have provided additional information on hypoxic training. However, a subgroup meta-analysis could not be performed because the included studies reported combined data for participants with overweight and obesity, without providing separate values for each group. In addition, although we have performed publication bias analyses, we should also consider the bias due to the small number of studies available for some outcomes (e.g., HOMA-IR). Moreover, since we have considered only studies written in English this could have led to language bias. Finally, the limited literature on this topic prevented us from isolating the effects of relative or absolute hypoxic training.

Our study presents also several strengths. One of the strengths of this systematic review and meta-analysis is the inclusion of a substantial number of studies, despite the stringent inclusion and exclusion criteria and the novelty of the topic. Moreover, this is the first systematic review and meta-analysis analysing the impact of hypoxic training on cardiometabolic health in adults with overweight and obesity. In addition, we performed within-groups comparisons to understand whether the training protocols performed were effective on cardiometabolic health.

5 | CONCLUSIONS

This meta-analysis found no significant difference between the effectiveness of hypoxic and normoxic training on cardiometabolic markers in adults with overweight and obesity. However, significant heterogeneity in the results makes a definitive interpretation difficult. Future studies with standardised protocols focusing on specific subgroups are needed to clarify the potential benefits of hypoxic training.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

The peer review history for this article is available at <https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.70303>.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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