



QUALITY IN SPORT

eISSN 2450-3118 · Open Access · Peer-reviewed

apcz.umk.pl/QS Nicolaus Copernicus
University in Toruń



NOWAK, Julia, GRANDOS, Julia, ŁASZCZYCH, Mateusz, BRALEWSKA, Barbara, WYKROTA, Julia, POLAK, Mateusz, JONAKOWSKI, Jakub, KUCZYŃSKI, Kacper, and NICPOŃ, Tomasz. Objective Exercise Outcomes During GLP-1 Based Therapy: Distinguishing Cardiorespiratory Fitness from Walking Capacity. A Narrative Review. *Quality in Sport*. 2026;76:75671. <https://doi.org/10.12775/QS.2026.76.75671>

ARTICLE TIMELINE

Received: 25.08.2026. Revised: 06.09.2026. Accepted: 15.09.2026. Published: 27.09.2026.

The journal has been awarded 20 points in the parametric evaluation by the Polish Ministry of Higher Education and Science (Annex to the announcement of 05.01.2024, No. 32553). Unique Journal Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).

Punkty Ministerialne z 2019 – aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych). © The Authors 2026.

OPEN ACCESS · CC BY-NC-SA 4.0 This article is published with open access under the License Open Journal Systems of Nicolaus Copernicus University in Toruń, Poland, and is distributed under the terms of the Creative Commons Attribution Non-commercial Share Alike License (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the work is properly cited. The authors declare no conflict of interest regarding the publication of this paper.

Objective Exercise Outcomes During GLP-1 Based Therapy: Distinguishing Cardiorespiratory Fitness from Walking Capacity. A Narrative Review

Julia Nowak*

ORCID <https://orcid.org/0009-0009-8295-7204>

Email: Julia.k.nowak@gmail.com

Nikolay Pirogov Specialized District Hospital in Łódź

Jakub Grandos

ORCID <https://orcid.org/0009-0002-5859-6532>

Email: kuba.grandos@gmail.com

St. John of God Brothers Hospitaller Hospital in Lodz, Poland

Mateusz Łaszczych

ORCID <https://orcid.org/0009-0009-2999-759X>

Email: matlaszczych@gmail.com

Central Teaching Hospital of the Medical University of Łódź

Barbara Bralewska

ORCID <https://orcid.org/0000-0002-1587-4064>

Email: bbralewska99@gmail.com

Central Teaching Hospital of the Medical University of Łódź

Julia Wykrota

ORCID <https://orcid.org/0000-0002-7695-5474>

Email: wykrotajulia@gmail.com

Nikolay Pirogov Specialized District Hospital in Łódź

Mateusz Polak

ORCID <https://orcid.org/0009-0003-1904-7044>

Email: mat.polak@icloud.com

Provincial Hospital in Poznan – Greater Poland Specialist Center Poland

Jakub Jonakowski

ORCID <https://orcid.org/0009-0006-7027-4375>

Email: kuba.jonakowski@gmail.com

Nikolay Pirogov Specialized District Hospital in Łódź

Kacper Kuczyński

ORCID <https://orcid.org/0009-0006-5969-9313>

Email: kacper.mailme@gmail.com

Municipal Medical Center Dr. Karol Jonscher, Łódź, Poland

Tomasz Nicpoń

ORCID <https://orcid.org/0009-0006-8153-9981>

Email: tomasz.nicpon.00@gmail.com

Central Teaching Hospital of the Medical University of Łódź

* Corresponding author: Julia Nowak, Julia.k.nowak@gmail.com

Abstract

Background: Glucagon-like peptide-1 (GLP-1) receptor agonists and related incretin-based therapies can produce substantial weight loss and metabolic benefits. Their effects on objective exercise outcomes are less clear because studies use non-interchangeable endpoints ranging from directly measured oxygen uptake (VO_2) to walking distance.

Objective: To summarize objective exercise outcomes during GLP-1-based therapy and separate directly measured cardiorespiratory fitness from changes observed with exercise training and from disease-specific walking capacity.

Methods: We searched PubMed and tracked relevant citations up to July 2026. Adult clinical studies reporting at least one objective exercise outcome were grouped by outcome domain.

Results: Ten clinical studies were included. In the 193-participant secondary analysis, liraglutide alone did not improve VO_2 -derived fitness or physical-performance outcomes. Two smaller trials of exenatide or liraglutide without structured exercise were also neutral. VO_2 improved when structured exercise was included, but comparisons with matched exercise did not establish a clear additive drug effect. Walking outcomes improved most clearly in peripheral artery disease, whereas coronary artery disease and ischemia-focused endpoints were neutral. During substantial weight loss, body-mass-normalized VO_2 may rise partly because body mass in the denominator falls; absolute VO_2 , VO_2 normalized to fat-free mass, workload, strength, and body composition therefore require separate interpretation.

Conclusions: The meaning of an objective exercise outcome depends on what was measured. Current evidence does not consistently show an independent improvement in directly measured cardiorespiratory fitness with pharmacotherapy alone. Structured exercise remains the best-supported context for improving aerobic fitness. Disease-specific gains in walking capacity should not be interpreted as generalized cardiorespiratory-fitness gains.

Keywords: glucagon-like peptide-1 receptor agonists, cardiorespiratory fitness, oxygen uptake, walking capacity, exercise training

1. Introduction

Glucagon-like peptide-1 (GLP-1) receptor agonists and related incretin-based therapies are used in the treatment of type 2 diabetes (T2D) and obesity [1]. Randomized trials have shown substantial weight loss with liraglutide, semaglutide, and tirzepatide in adults with overweight or obesity [2-4]. This has raised the question of whether objective exercise outcomes also improve during treatment. Lower body mass can reduce the mechanical cost of weight-bearing activities such as walking or stair climbing, but better performance in these tasks does not by itself establish an improvement in cardiorespiratory fitness (CRF).

CRF reflects the integrated capacity of the respiratory, cardiovascular, and skeletal-muscle systems to transport and use oxygen during exercise. It is most directly assessed by measuring oxygen uptake (VO_2), typically reported as maximal oxygen uptake ($\text{VO}_{2\text{max}}$) or peak oxygen uptake ($\text{VO}_{2\text{peak}}$), during cardiopulmonary exercise testing (CPET) [5-6]. The broader literature, however, uses the term “exercise capacity” for a heterogeneous set of outcomes, including 6-minute walk distance (6MWD) [7-10], maximum treadmill walking distance [11], estimated metabolic equivalents (METs) and exercise duration [12], ischemic thresholds [13], and stair-climb performance and muscular strength [14]. These outcomes are clinically relevant, but they measure different physiological or disease-specific limitations and should not be treated as interchangeable markers of CRF [5-7,15-16].

Previous reviews considered glucose- or weight-lowering therapies in relation to physical function, activity, fitness, body composition, or recreational sport, but did not use the specific analytic separation applied here between VO_2 -derived CRF, exercise-training response, and disease-specific walking or ischemia-focused outcomes [17-20]. This review therefore mapped which objective exercise outcomes had been assessed, in which populations, and with which tests, and then interpreted the findings according to what each outcome measures. The synthesis distinguished VO_2 -derived CRF outcomes from disease-specific functional and ischemia-focused outcomes. Within the CRF evidence, pharmacotherapy-only studies were considered separately from studies that included structured exercise.

Substantial weight loss adds a separate interpretive problem. VO_2 may be reported as an absolute value or normalized to body mass or fat-free mass (FFM), while external workload provides a complementary measure of exercise performance [14,21-24]. Body-mass-normalized VO_2 may increase as the denominator decreases, even if absolute oxygen uptake changes little [22-24]. Outcome scaling was therefore treated as an additional interpretive layer rather than a separate outcome domain. This distinction is also relevant to exercise science, because improvements in weight-bearing performance or body-mass-normalized VO_2 during

substantial weight loss may be misinterpreted as improved aerobic fitness when the underlying outcome is not considered. The review focused on adults enrolled in studies in which heart failure was not the primary target condition.

2. Methods

We searched PubMed and tracked citations. The last search was performed on 24 July 2026. Search concepts combined GLP-1-based therapies with objective exercise outcomes, including cardiorespiratory fitness, oxygen uptake, walking capacity, exercise tolerance, and physical performance. Because of clinical and methodological heterogeneity, findings were synthesized narratively by outcome domain and were not quantitatively pooled.

Eligible publications were adult clinical studies of GLP-1 receptor agonists or related incretin therapies that reported at least one objective exercise outcome. We excluded studies focused primarily on heart failure, pediatric or preclinical populations, self-reported activity alone, body composition without exercise testing, and protocols. The PubMed search identified 242 records. After title and abstract screening, 170 were excluded and 60 were retained only for contextual or background use. Twelve reports were retrieved and assessed in full. One retrospective cardiac-rehabilitation report was excluded because its design did not isolate a treatment effect attributable to a GLP-1 receptor agonist. The primary synthesis included 10 clinical studies represented by 11 reports; the parent report by Lundgren et al. [25] was retained for contextual interpretation. Figure 1 summarizes study selection.

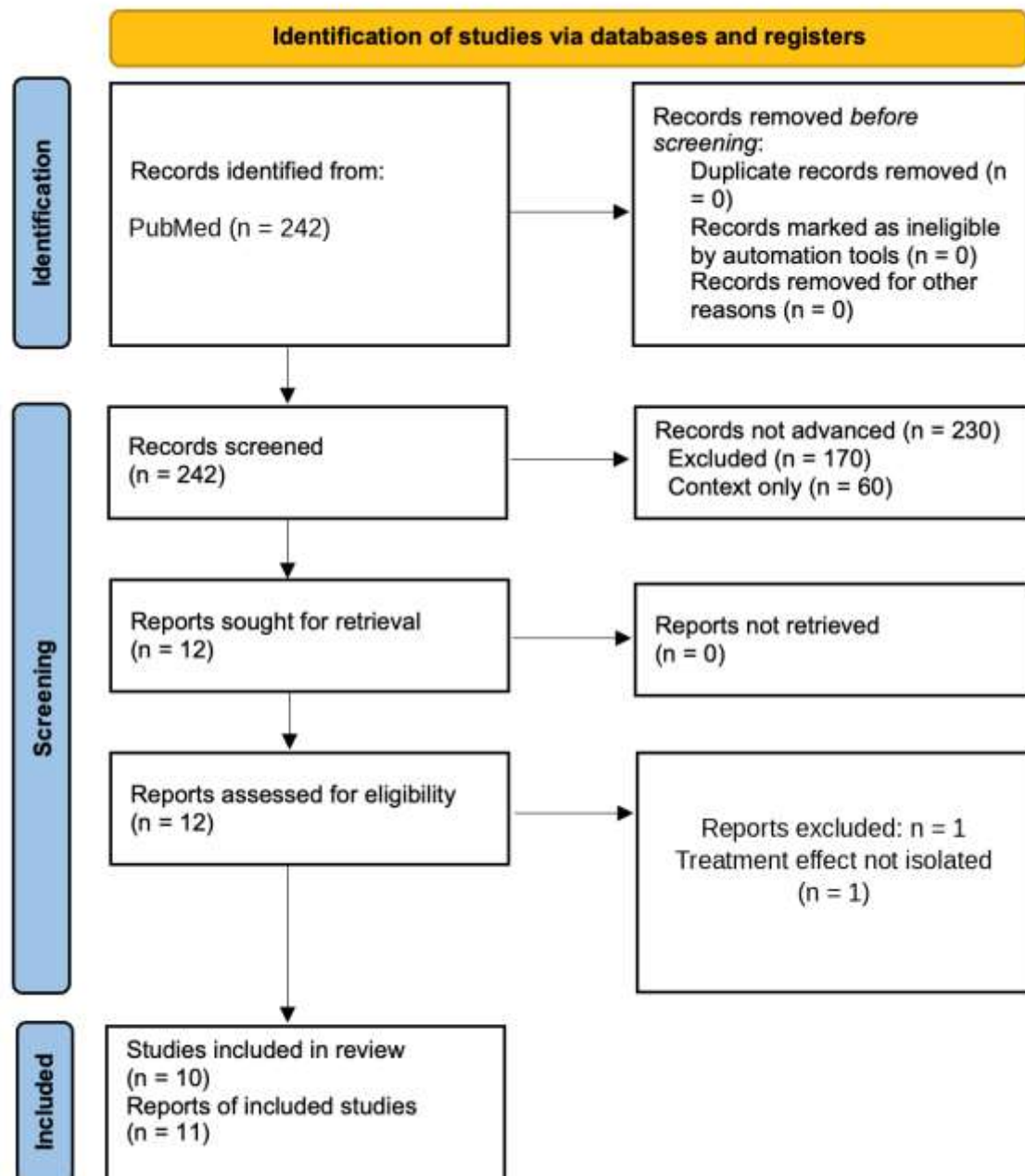


Figure 1. Study-selection flow diagram

3. Direct cardiorespiratory fitness during glucagon-like peptide-1-based therapy

The studies reporting VO_2 -derived cardiorespiratory fitness fell into two groups: GLP-1 receptor agonist therapy without structured exercise and GLP-1 receptor agonist therapy given alongside an exercise intervention. These settings answer different questions. Pharmacotherapy-only studies test whether CRF changes in the absence of a training stimulus. Exercise co-intervention studies show whether participants remain responsive to training

during treatment and whether the drug adds a benefit beyond the same exercise exposure. A change in a combined-treatment arm cannot be attributed to the drug unless training exposure and the comparator permit that inference. Measurement method also matters. VO_2max or VO_2peak measured from respiratory gas exchange during maximal testing provides a more direct assessment of integrated CRF than a value estimated from a submaximal protocol [5-6,26]. Directly measured and estimated values were therefore interpreted within their study designs rather than treated as equivalent outcomes.

3.1. Pharmacotherapy without structured exercise

The four-arm trial reported by Lundgren et al. [25], with fitness outcomes analyzed by Jensen et al. [14], provided the largest dataset for pharmacotherapy without structured exercise. In the 193-participant secondary analysis, liraglutide alone did not significantly improve $\text{VO}_2\text{peak}/\text{FFM}$, absolute or body-mass-normalized VO_2peak , peak workload, stair-climb performance, or knee-extensor torque relative to placebo/usual activity [14]. Two smaller drug-only trials showed the same pattern: exenatide did not increase VO_2peak or improve submaximal VO_2 kinetics [27], and the trial by Wagner et al. [10] found no significant change in VO_2max or 6MWD. These studies do not rule out an effect, but they do not show an independent CRF benefit from pharmacotherapy alone.

Metabolic improvement and CRF are not equivalent. Maximal oxygen uptake depends on cardiac output and the arteriovenous oxygen difference. Improvements in maximal oxygen uptake can arise from central and/or peripheral adaptations, including changes in stroke volume, vascular conductance, muscle perfusion, capillary density, and mitochondrial oxidative capacity [5-6,26]. Weight loss, improved glycemic control, or favorable resting cardiovascular measures may make activity easier, but they do not establish higher maximal oxygen-transport capacity.

3.2. Exercise co-interventions

VO_2 improved most clearly when structured exercise was included. In the secondary analysis by Jensen et al. [14], the exercise-containing arms improved VO_2peak normalized to FFM, body-mass-normalized VO_2peak , absolute VO_2peak , peak workload, and stair-climb performance. Exercise plus liraglutide increased $\text{VO}_2\text{peak}/\text{FFM}$ by 3.0 mL/min/kg FFM compared with liraglutide alone; exercise alone produced similar benefits.

When exercise exposure was matched, no clear additive drug effect emerged. Mensberg et al. [28] reported similar increases in estimated VO_2max with exercise plus liraglutide and exercise

plus placebo (+0.5 versus +0.4 L/min). Ingersen et al. [29] also found that aerobic training improved VO₂max during semaglutide treatment and with training alone. The design was consistent with preserved training responsiveness but did not isolate an independent semaglutide effect. The available data therefore link the clearest VO₂ gains to structured exercise, not to a demonstrated training-like effect of GLP-1 receptor agonist therapy.

The full evidence base included adults with obesity, T2D, peripheral artery disease (PAD), or coronary artery disease (CAD) and evaluated exenatide, liraglutide, or semaglutide. Table 1 groups the studies by the objective exercise outcome assessed.

Table 1. Included clinical studies and objective exercise outcomes

Study and population	Intervention / comparator	Objective exercise outcome	Principal finding
Scalzo et al. [27]; N=23 adults with uncomplicated T2D	Exenatide 10 µg twice daily versus placebo for 12 weeks; no structured exercise	Maximal cycle test with gas exchange; VO ₂ peak and submaximal VO ₂ kinetics	VO ₂ peak and submaximal VO ₂ kinetics did not improve [27].
Wagner et al. [10]; N=24 adults with T2D	Liraglutide 1.8 mg/day versus placebo for 6 months; no structured exercise	Cycle ergometry with respiratory gas analysis; VO ₂ max primary endpoint; 6MWD secondary	VO ₂ max and 6MWD did not differ significantly from placebo [10].
Jensen et al. [14]; N=193 adults with obesity without diabetes	Liraglutide 3.0 mg/day, exercise, combined treatment, or placebo/usual activity for 52 weeks	Maximal cycle CPET; VO ₂ peak/FFM, VO ₂ peak/body mass, absolute VO ₂ peak, workload, stair-climb, knee-extensor torque	Liraglutide alone did not improve fitness; exercise plus liraglutide increased VO ₂ peak/FFM by 3.0 mL/min/kg FFM versus liraglutide alone, and exercise alone produced similar benefits [14].

Study and population	Intervention / comparator	Objective exercise outcome	Principal finding
Mensberg et al. [28]; N=33 sedentary adults with overweight/obesity and T2D	Liraglutide plus supervised exercise versus placebo plus the same exercise program for 16 weeks	Estimated VO ₂ max from a submaximal bicycle test	Estimated VO ₂ max increased similarly in both groups (+0.5 versus +0.4 L/min) [28].
Ingersen et al. [29]; N=31 inactive adults with T2D and body mass index >28 kg/m ²	Semaglutide before and during 12 weeks of supervised cycle training versus training alone	Maximal oxygen-uptake testing	VO ₂ max improved with training in both groups [29].
Bonaca et al. [11]; N=792 adults with T2D and symptomatic PAD	Semaglutide 1.0 mg/week versus placebo for 52 weeks; no structured exercise	Constant-load treadmill maximum and pain-free walking distance	The primary endpoint favored semaglutide (estimated treatment ratio 1.13, 95% confidence interval 1.06–1.21) [11].
Caruso et al. [8]; 55 analyzed adults with T2D and PAD	Liraglutide 1.8 mg/day versus conventional risk-factor treatment for 6 months	6MWD and peripheral tissue oxygenation	6MWD +25.1 m versus control; peripheral tissue oxygenation improved [8].
Chowdhary et al. [9]; N=41 adults with T2D without established cardiovascular disease	Liraglutide versus pioglitazone for 16 weeks each	6MWD; myocardial perfusion and energetics	6MWD increased from 488 to 521 m after liraglutide [9].

Study and population	Intervention / comparator	Objective exercise outcome	Principal finding
Kumarathurai et al. [12]; adults with T2D and stable CAD	Liraglutide plus metformin versus placebo plus metformin in a crossover trial	Cycle exercise to exhaustion; estimated METs and exercise duration	Estimated METs and exercise duration did not improve [12].
Myat et al. [13]; N=22 with obstructive CAD and inducible ischemia	Liraglutide versus saline placebo in a randomized crossover trial	Treadmill ischemic threshold, ST-segment depression, rate-pressure product, and exercise duration	Ischemic threshold, ST-segment depression, rate-pressure product, exercise duration, and exercise hemodynamics did not improve [13].

6MWD, 6-minute walk distance; CAD, coronary artery disease; CPET, cardiopulmonary exercise testing; FFM, fat-free mass; METs, metabolic equivalents; N, number of participants; PAD, peripheral artery disease; T2D, type 2 diabetes; VO₂max, maximal oxygen uptake; VO₂peak, peak oxygen uptake.

4. Functional walking capacity and disease-specific exercise tolerance

4.1. Walking capacity in peripheral artery disease and other clinical populations

Walking outcomes were most clearly positive in PAD. In the trial by Bonaca et al. [11], semaglutide improved the primary endpoint—the ratio to baseline in maximum walking distance during a standardized constant-load treadmill test—in adults with symptomatic PAD and T2D (estimated treatment ratio 1.13, 95% confidence interval 1.06–1.21; P=0.0004). In a supportive comparison on the absolute scale, the trial authors also reported a 39.9 m greater improvement in maximum walking distance versus placebo. In the trial by Caruso et al. [8], liraglutide improved 6MWD by 25.1 m versus control and increased peripheral tissue oxygenation. Outside PAD, Chowdhary et al. [9] reported an increase in 6MWD from 488 to 521 m after liraglutide, together with improved myocardial perfusion and energetics. The active-comparator crossover design, however, did not permit a direct inference about CRF. These findings concern function, not direct CRF. Walking performance is influenced by limb perfusion, claudication pain, gait, body mass, motivation, and musculoskeletal or pulmonary

limitations [7,15-16]. It therefore answers a different question from maximal oxygen uptake. The positive evidence is strongest for disease-specific walking capacity; it does not establish a generalized gain in aerobic fitness.

4.2. Coronary artery disease and ischemia-focused testing

Studies focused on CAD or myocardial ischemia were neutral. Kumarathurai et al. [12] found no improvement in estimated METs or exercise duration with liraglutide in adults with T2D and stable CAD. In the trial by Myat et al. [13], liraglutide did not improve ischemic threshold, ST-segment depression, rate-pressure product, exercise duration, or exercise hemodynamics in obstructive CAD. These endpoints address narrower questions than directly measured maximal oxygen uptake. Estimated METs and exercise duration reflect performance within a specific test protocol, whereas ischemic thresholds and ST-segment changes are intended to detect myocardial ischemia. The neutral results therefore show that liraglutide did not improve the measured CAD-related endpoints in these studies; they do not establish the absence of other metabolic or cardiovascular effects, and they do not provide a direct test of CRF. PAD walking distance is also limited by a different clinical problem, particularly claudication and lower-limb perfusion. Positive PAD findings should therefore not be generalized to CAD-related exercise tolerance, and the CAD findings should not be used to infer an effect on generalized aerobic fitness.

5. Interpreting exercise outcomes during weight loss

How VO_2 is expressed matters during substantial weight loss. Absolute VO_2 describes the total amount of oxygen used at peak exercise and is not changed by a mathematical denominator. VO_2 normalized to body mass is useful for activities in which body weight must be moved, but it may rise when body mass falls even if absolute oxygen uptake changes little. Simple ratio scaling also assumes a proportional relationship between body size and VO_2 that may not hold across populations [22-24]. Normalization to FFM narrows the denominator to non-fat tissue, but it does not produce a muscle-specific measure. FFM includes organs, body water, bone mineral, connective tissue, and skeletal muscle, and its value also depends on the method used to estimate body composition [21,30]. $\text{VO}_{2\text{peak}}/\text{FFM}$ should therefore be interpreted as a complementary expression of oxygen uptake rather than as a direct measure of skeletal-muscle oxidative capacity.

External workload adds information that none of these ratios provides. A rise in $\text{VO}_{2\text{peak}}/\text{body mass}$ accompanied by stable absolute $\text{VO}_{2\text{peak}}$ and unchanged peak workload would have a

different interpretation from concordant increases in absolute VO_2peak , scaled VO_2peak , and workload. The study by Jensen et al. [14] was especially informative because it reported absolute VO_2peak , $\text{VO}_2\text{peak/body mass}$, $\text{VO}_2\text{peak/FFM}$, and peak workload in the same trial. This made it possible to examine whether apparent improvement was confined to a relative value or was also present in oxygen uptake and external work. No single metric should be treated as definitive during major weight loss.

Body composition and task-based performance provide further context but do not replace exercise testing. A change in FFM does not specify how much skeletal muscle was gained or lost and does not show whether strength changed [14,21,30]. Stair-climb performance may improve because less body mass is moved, whereas knee-extensor torque tests a more specific component of muscular function. Reporting these outcomes side by side allows the reader to distinguish changes in body composition, force production, task performance, and CRF. Table 2 summarizes the main evidence pattern.

Table 2. Direction and interpretation of evidence across objective exercise-outcome domains

Outcome domain	Main evidence	Direction of findings	Interpretation
Direct CRF with GLP-1 receptor agonist therapy alone	Jensen (liraglutide-alone arm); Scalzo; Wagner	Neutral	The largest trial and two smaller drug-only trials did not demonstrate significant VO_2 -derived fitness improvement with pharmacotherapy alone [10,14,27].
CRF with structured exercise	Jensen; Mensberg; Ingersen	Improvement with exercise; no clear additive drug effect when exercise was matched	Training exposure is the most plausible driver of the observed VO_2 improvement [14,28-29].

Outcome domain	Main evidence	Direction of findings	Interpretation
Functional walking capacity	Bonaca; Caruso; Chowdhary	Positive, strongest in PAD	Walking benefits are clinically meaningful but reflect submaximal or disease-specific function rather than direct CRF [8-9,11].
CAD and ischemia-focused tolerance	Kumarathurai; Myat	Neutral	No improvement in estimated METs, exercise duration, or ischemia-focused endpoints; PAD findings should not be generalized to CAD [12-13].

CAD, coronary artery disease; CRF, cardiorespiratory fitness; METs, metabolic equivalents; PAD, peripheral artery disease; VO₂, oxygen uptake.

6. Practical implications and research gaps

Outcome selection should follow the clinical question. When aerobic fitness is the goal, body-weight reduction and improved walking performance cannot substitute for direct CRF assessment. CPET or maximal oxygen-uptake testing is appropriate when the question concerns integrated aerobic capacity. Standardized walking tests are more appropriate when the clinical problem is functional limitation, claudication, or walking endurance, and direct strength or performance testing is needed when muscular function is the outcome of interest. During substantial weight loss, follow-up testing should use the same exercise protocol as baseline and report body mass at each time point. Absolute VO₂, scaled VO₂, and peak workload should be considered together. An improvement in one measure should not automatically be extended to the other domains.

From a sport-science perspective, the available evidence does not establish that GLP-1-based therapy improves athletic or sport-specific performance. Most included studies involved clinical populations, and the clearest positive findings concerned disease-specific walking capacity or VO₂ improvements observed alongside structured exercise. Changes in body mass, VO₂ normalized to body mass, walking distance, or task performance should therefore not be interpreted as evidence of improved sport performance without an outcome that directly

addresses that question. In physically active individuals, the choice of test should match the performance domain of interest and distinguish changes related to weight loss from changes in aerobic capacity, strength, or training response.

Structured exercise remains the best-supported intervention for improving VO_2 -derived outcomes, while pharmacotherapy and exercise have different primary effects and should be viewed as complementary [14,28-29,31]. Across the included evidence, weight loss, walking performance, and maximal oxygen uptake did not always change in parallel. This is not contradictory; each outcome describes a different component of physical capacity.

Future trials should prespecify exercise outcomes and distinguish pharmacotherapy alone, exercise alone, combined treatment, and an appropriate control whenever the design permits. Matched exercise exposure is especially important. Without comparable training dose and adherence, improvement in a combined-treatment group cannot be separated from differences in the exercise intervention. Studies should report the frequency, intensity, duration, and mode of training, together with attendance or adherence and treatment tolerability. They should also distinguish primary endpoints from secondary or exploratory exercise outcomes.

Absolute and scaled VO_2 , peak workload, and ventilatory thresholds should be reported together when CRF is assessed [22-23,26]. Body composition measures [21,30,32] and direct strength or task-based performance outcomes [14] should remain separate rather than being combined under a broad label of exercise capacity. The included studies did not evaluate tirzepatide, dedicated resistance-training co-interventions, or dietary adequacy. Evidence in physically active or athletic populations and for recovery and sport-specific performance also remains limited [19]. Studies in physically active and athletic populations should report training status and training exposure alongside absolute and scaled VO_2 , strength, body composition, and sport-specific performance outcomes.

7. Strengths and limitations

One strength of this review is that it does not treat all exercise outcomes as equivalent. Direct VO_2 -derived CRF, training response, walking capacity, ischemia-focused testing, physical performance, and body composition were interpreted separately. Grouping reports from the same parent trial also reduced double-counting of the evidence reported by Lundgren et al. [25] and Jensen et al. [14].

The evidence base is small and heterogeneous in population, agent, comparator, treatment duration, exercise exposure, endpoint status, and outcome scaling. Several exercise outcomes were secondary or exploratory.

Most participants came from clinical rather than athletic populations, and direct CRF data for newer incretin therapies are sparse. Excluding studies in which heart failure was the primary condition reduced syndrome-specific confounding but also narrowed the clinical scope. The conclusions should therefore be read as a construct-specific narrative synthesis, not as definitive evidence of treatment efficacy or absence of efficacy.

8. Conclusions

Objective exercise outcomes during GLP-1-based therapy are not interchangeable. Current studies do not consistently show an independent improvement in directly measured CRF with pharmacotherapy alone. VO₂ improvements are most evident when structured exercise is included. Gains in walking capacity, particularly in PAD, are clinically relevant but should not be interpreted as generalized CRF gains. Future studies should separate drug and training effects and report absolute and scaled VO₂ alongside workload, walking, strength, and body-composition outcomes.

Author Contributions

Conceptualization, J.N. and M.L.; methodology, M.L. and J.N.; literature screening and evidence mapping, K.K., J.W., B.B. and J.N.; writing - original draft preparation, M.P., J.G., J.J., J.N., and M.L.; writing - review and editing, M.P., J.G., J.J., J.N., and M.L.; visualization, M.P. and T.N.; All authors have read and agreed to the submitted version of the manuscript.

Funding Statement

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

No new data were created or analyzed in this study. All data discussed are available in the cited primary studies listed in the references.

Acknowledgments

Not applicable.

Conflict of Interest Statement

The authors declare no conflict of interest.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

In preparing this work, the authors used Claude (Anthropic) for the purpose of supporting language editing, manuscript organization, formatting assistance, linguistic flow, and bibliographic consistency checks. After using this tool/service, the author(s) have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

References

1. American Diabetes Association Professional Practice Committee for Diabetes. 8. Obesity and weight management for the prevention and treatment of diabetes: Standards of Care in Diabetes-2026. *Diabetes Care* 2026; 49(Suppl 1): S166–S182. <https://doi.org/10.2337/dc26-S008>.
2. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al.; SURMOUNT-1 Investigators. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med* 2022; 387: 205–216. <https://doi.org/10.1056/NEJMoa2206038>.
3. Pi-Sunyer X, Astrup A, Fujioka K, Greenway F, Halpern A, Krempf M, et al.; SCALE Obesity and Prediabetes NN8022-1839 Study Group. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med* 2015; 373: 11–22. <https://doi.org/10.1056/NEJMoa1411892>.
4. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al.; STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med* 2021; 384: 989–1002. <https://doi.org/10.1056/NEJMoa2032183>.
5. American Thoracic Society; American College of Chest Physicians. ATS/ACCP statement on cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2003; 167: 211–277. <https://doi.org/10.1164/rccm.167.2.211>.
6. Ross R, Blair SN, Arena R, Church TS, Despres JP, Franklin BA, et al. Importance of assessing cardiorespiratory fitness in clinical practice: A case for fitness as a clinical vital sign. *Circulation* 2016; 134: e653–e699. <https://doi.org/10.1161/CIR.0000000000000461>.
7. American Thoracic Society. ATS statement: Guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002; 166: 111–117. <https://doi.org/10.1164/ajrccm.166.1.at1102>.
8. Caruso P, Maiorino MI, Longo M, Porcellini C, Matrone R, Digitale Selvaggio L, et al. Liraglutide for lower limb perfusion in people with type 2 diabetes and peripheral artery

- disease: The STARDUST randomized clinical trial. *JAMA Netw Open* 2024; 7: e241545. <https://doi.org/10.1001/jamanetworkopen.2024.1545>.
9. Chowdhary A, Thirunavukarasu S, Joseph T, Jex N, Kotha S, Giannoudi M, et al. Liraglutide improves myocardial perfusion and energetics and exercise tolerance in patients with type 2 diabetes. *J Am Coll Cardiol* 2024; 84: 540–557. <https://doi.org/10.1016/j.jacc.2024.04.064>.
 10. Wagner AM, Miranda-Calderın G, Ugarte-Lopetegui MA, Marrero-Santiago H, Suarez-Castellano L, Lopez-Madrado MJ, et al. Effect of liraglutide on physical performance in type 2 diabetes: Results of a randomized, double-blind, controlled trial (LIPER2). *Diabetes Metab* 2019; 45: 268–275. <https://doi.org/10.1016/j.diabet.2018.08.010>.
 11. Bonaca MP, Catarig AM, Houliand K, Ludvik B, Nordanstig J, Ramesh CK, et al.; STRIDE Trial Investigators. Semaglutide and walking capacity in people with symptomatic peripheral artery disease and type 2 diabetes (STRIDE): A phase 3b, double-blind, randomised, placebo-controlled trial. *Lancet* 2025; 405: 1580–1593. [https://doi.org/10.1016/S0140-6736\(25\)00509-4](https://doi.org/10.1016/S0140-6736(25)00509-4).
 12. Kumarathurai P, Anholm C, Nielsen OW, Kristiansen OP, Mølvig J, Madsbad S, et al. Effects of the glucagon-like peptide-1 receptor agonist liraglutide on systolic function in patients with coronary artery disease and type 2 diabetes: A randomized double-blind placebo-controlled crossover study. *Cardiovasc Diabetol* 2016; 15: 105. <https://doi.org/10.1186/s12933-016-0425-2>.
 13. Myat A, Redwood SR, Arri S, Gersh BJ, Bhatt DL, Marber MS. Liraglutide to improve coronary haemodynamics during exercise stress (LIONESS): A double-blind randomised placebo-controlled crossover trial. *Diabetol Metab Syndr* 2021; 13: 17. <https://doi.org/10.1186/s13098-021-00635-6>.
 14. Jensen SBK, Fiorenza M, Juhl CR, Sandsdal RM, Jensen E, Seier SS, et al. Physical fitness with exercise and GLP-1 receptor agonist treatment alone or combined after diet-induced weight loss: A secondary analysis of a randomized controlled trial in adults with obesity. *Sports Med* 2026; 56: 1785–1800. <https://doi.org/10.1007/s40279-025-02386-0>.
 15. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease. *Circulation* 2017; 135: e726–e779. <https://doi.org/10.1161/CIR.0000000000000471>.
 16. Gornik HL, Aronow HD, Goodney PP, Arya S, Packard Brewster L, Byrd L, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS guideline for the

- management of lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024; 149: e1313–e1410. <https://doi.org/10.1161/CIR.0000000000001251>.
17. Ahmad E, Arsenyadis F, Almaqhawi A, Barker M, Jobanputra R, Sargeant JA, et al. Impact of novel glucose-lowering therapies on physical function in people with type 2 diabetes: A systematic review and meta-analysis of randomised placebo-controlled trials. *Diabet Med* 2023; 40: e15083. <https://doi.org/10.1111/dme.15083>.
 18. Jobanputra R, Sargeant JA, Almaqhawi A, Ahmad E, Arsenyadis F, Webb DR, et al. The effects of weight-lowering pharmacotherapies on physical activity, function and fitness: A systematic review and meta-analysis of randomized controlled trials. *Obes Rev* 2023; 24: e13553. <https://doi.org/10.1111/obr.13553>.
 19. Topolski K, Tłoczek W, Śliwa W, Twardowska D, Jelonek B, Tomczak B, et al. GLP-1 receptor agonists in recreational athletes: emerging weight-reduction strategy or potential health risk? A review of current evidence. *Quality in Sport* 2026; 55: 71600. <https://doi.org/10.12775/QS.2026.55.71600>.
 20. Turczynowski K, Lichoń J, Kuna P, Turczynowski K, Kuna W, Pietrucha J, et al. Impact of GLP-1 receptor agonists on body composition and physical performance in patients with obesity: a comprehensive review of current research. *Quality in Sport* 2026; 51: 68929. <https://doi.org/10.12775/QS.2026.51.68929>.
 21. Heymsfield SB, Brown J, Ramirez S, Prado CM, Tinsley GM, Gonzalez MC. Are lean body mass and fat-free mass the same or different body components? A critical perspective. *Adv Nutr* 2024; 15: 100335. <https://doi.org/10.1016/j.advnut.2024.100335>.
 22. Lee J, Zhang X. Is there really a proportional relationship between VO₂max and body weight? A review article. *PLoS One* 2021; 16: e0261519. <https://doi.org/10.1371/journal.pone.0261519>.
 23. Lolli L, Batterham AM, Weston KL, Atkinson G. Size exponents for scaling maximal oxygen uptake in over 6500 humans: a systematic review and meta-analysis. *Sports Med* 2017; 47: 1405–1419. <https://doi.org/10.1007/s40279-016-0655-1>.
 24. Zhou N. Assessment of aerobic exercise capacity in obesity, which expression of oxygen uptake is the best? *Sports Med Health Sci* 2021; 3: 138–147. <https://doi.org/10.1016/j.smhs.2021.01.001>.

25. Lundgren JR, Janus C, Jensen SBK, Juhl CR, Olsen LM, Christensen RM, et al. Healthy weight loss maintenance with exercise, liraglutide, or both combined. *N Engl J Med* 2021; 384: 1719–1730. <https://doi.org/10.1056/NEJMoa2028198>.
26. Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF, et al.; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee. Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. *Circulation* 2010; 122: 191–225. <https://doi.org/10.1161/CIR.0b013e3181e52e69>.
27. Scalzo RL, Moreau KL, Ozemek C, Herlache L, McMillin S, Gilligan S, et al. Exenatide improves diastolic function and attenuates arterial stiffness but does not alter exercise capacity in individuals with type 2 diabetes. *J Diabetes Complications* 2017; 31: 449–455. <https://doi.org/10.1016/j.jdiacomp.2016.10.003>.
28. Mensberg P, Nyby S, Jørgensen PG, Storgaard H, Jensen MT, Sivertsen J, et al. Near-normalization of glycaemic control with glucagon-like peptide-1 receptor agonist treatment combined with exercise in patients with type 2 diabetes. *Diabetes Obes Metab* 2017; 19: 172–180. <https://doi.org/10.1111/dom.12797>.
29. Ingersen A, Schmücker M, Alexandersen C, Graungaard B, Thorngreen T, Borch J, et al. Effects of aerobic training and semaglutide treatment on pancreatic beta-cell secretory function in patients with type 2 diabetes. *J Clin Endocrinol Metab* 2023; 108: 2798–2811. <https://doi.org/10.1210/clinem/dgad326>.
30. Oliver CJ, Climstein M, Rosic N, Bosy-Westphal A, Tinsley G, Myers S. Fat-free mass: Friend or foe to metabolic health? *J Cachexia Sarcopenia Muscle* 2025; 16: e13714. <https://doi.org/10.1002/jcsm.13714>.
31. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016; 39: 2065–2079. <https://doi.org/10.2337/dc16-1728>.
32. Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, et al. Effect of semaglutide on body composition in adults with overweight or obesity: exploratory analyses of the STEP 1 study. *Diabetes Obes Metab* 2022; 24: 93–106. <https://doi.org/10.1111/dom.14524>.