

Downhill: a new rehabilitation frontier. A systematic review of the literature

Matteo Tamburlani,¹ Rossana Cuscito,² Alessio D'Angelo,² Giovanni Galeoto,³ Leonardo Papi,² Ilaria Ruotolo,³
Francesca Santini,² Annamaria Servadio,¹ Edoardo Tirelli,² Giovanni Sellitto³

¹Local Health Board Rome 2, Rome; ²Tor Vergata University, Rome; ³Department of Human Neurosciences, Sapienza University, Rome, Italy

Abstract

In the last few years, we have seen the gradual spread of a new treadmill training modality, which involves walking not on the flat but downhill, also known as “downhill”. This review aims to qualitatively assess the efficacy of downhill treatment on different patient populations and outline treatment routes for future efficacy studies. We searched five different databases: MEDLINE, SCOPUS, Web of Science, PEDro, and LILACS for studies to include. Only randomized controlled trials (RCTs) published in English were considered. PEDro scales and Risk of Bias 2 (RoB 2) assessment were used to evaluate the risk of bias. Forty-one RCTs were included, and three articles remained to be analyzed; the included studies showed 110 participants for three RCTs; of these, two were performed on patients diagnosed with chronic obstructive pulmonary disease (COPD), while one was for treating people with multiple sclerosis (MS). The outcome measures used in the studies were the pulmonary function test, the cardiopulmonary exercise test, the 6-Minute Walking Test, and the St. George Respiratory Questionnaire. In patients diagnosed with COPD, downhill training appears effective on functional capacity and symptoms of dyspnea and fatigue, while in people with MS, it increases strength and activity performance when compared to other walking training modalities. RoB 2 tool shows good methodological quality for all studies included in the review; when evaluated with the PEDro scale, all presented a score of 8. Downhill could be such an effective, safe, and feasible eccentric training modality that it can be considered a new rehabilitation strategy that could be implemented for patients with low exercise tolerance.

Key words: downhill walk, treadmill, rehabilitation, physiotherapy, aerobic training.

Correspondence to: Matteo Tamburlani, Local Health Board Rome 2, 00145 Rome, Italy.
Tel.: 3382243173. E-mail: matteo.tamburlani@aslroma2.it

Introduction

Regular physical activity has numerous benefits for overall health and can significantly contribute to preventing and managing various medical conditions, including cardiovascular disease, type 2 diabetes, and obesity [1].

Performing at least 150 minutes of moderate aerobic activity or 75 minutes of intense activity each week leads to improvements in cardiovascular health, mental health, strengthens the immune system, improves bone density and increases muscle strength [2,3]; many patients, however, encounter obstacles in adhering to exercise due to obesity, congestive heart failure, atherosclerosis, respiratory problems, or advanced age [4,5].

In 2018, the American guidelines recommended multimodal physical activity, including muscle strengthening, aerobic exercise, and balance exercises. Regular physical activity produces substantial benefits for people over 65 years of age, both in performing activities of daily living and in maintaining motor skills [3].

Based on the principle of specificity of training and strength, it has been hypothesized that eccentric and concentric actions provide a different stimulus to the muscle and, therefore, may produce dif-

ferent adaptations [6,7]; thus, concentric muscle actions, involving the shortening of muscle fibers, are typical of flat walking; eccentric actions, involving the active lengthening of muscle fibers, are typical of downhill walking [8].

During uphill or flat walking, the muscles of the lower limbs mainly perform concentric contractions, resulting in a high metabolic cost [9].

In downhill walking, on the other hand, significantly less oxygen consumption occurs, generating non-metabolic fatigue [10]. However, this exercise imposes a greater load on the muscle-tendon complex during braking to control the flexion speed of the knee, improving strength, muscular endurance, and joint stability [11,12]. The progressive ageing of the population worldwide inevitably results in more elderly people becoming frail [13-15].

Frailty is defined by the World Health Organization as “a clinically recognisable state in which the ability of older people to cope with everyday or acute stressors is compromised by increased vulnerability due to the decline in physiological reserve and function of multiple organ systems associated with age” [16].

Moreover, several studies have in turn shown that frailty exposes the elderly to an increased risk of falls, fractures, hospitalization, and even death [17,18].



Regular physical activity is safe for the healthy elderly, but also for the frail elderly, and reduces the risk of developing the main syndromes that lead to bedriddenness, as well as cognitive disorders and muscle weakness in these individuals.

The most frequently described activities include walking, low-intensity exercise, and even endurance exercises. Despite this established evidence, to date, participation in physical activities remains low among the elderly, particularly among those living in less affluent areas [19].

The efficacy of flat treadmill training is now widely recognized, as it promotes functional walking patterns and facilitates correct movement and timing of the lower limbs, thus eliminating the need for compensatory gait mechanisms [20] typical of subjects with progressive neurological disorders, such as stroke, multiple sclerosis (MS), and Parkinson's Disease [21,22]. In the last few years, we have seen the gradual spread of a new treadmill training modality, which involves walking not on the flat but downhill, also known as downhill walking.

This innovative therapeutic strategy is finding full application in the treatment of chronic neurological diseases [23], respiratory [24], and geriatric diseases [25]. In rehabilitation terms, the most obvious physiological effect concerns the decrease in cortical inhibition, which resulted in an improvement in muscle activation with a consequent improvement in gait and a clinically significant increase in exercise tolerance with a decrease in dyspnea [24].

The primary objective of this review is to qualitatively assess the efficacy of downhill treatment on different patient populations and outline treatment routes for future efficacy studies; the secondary objective is to assess the methodological quality of the studies included in the review.

Methods

This systematic review was conducted in accordance with the PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [26] and the Cochrane Handbook guidelines [27]. The protocol was registered in the Prospero database (PROSPERO ID: CRD42024534719).

Eligibility criteria: type of studies included and type of participants

This systematic review included all randomized controlled trials (RCTs) evaluating the efficacy of downhill treatment on different target populations. Limitations by language and year of publication were not applied. The eligibility criteria, as specified by the PICOS framework, were as follows: i) population – different patient populations with chronic diseases of neurological, orthopedic and cardiorespiratory interest; ii) interventions – downhill walking training; iii) comparisons – free walking training understood as flat or uphill walking; iv) outcomes – the primary outcomes considered in this study were all those related to the functional capacity of the patients, such as motor capacity, cardiopulmonary capacity. The secondary outcomes were all those referring to quality of life (QoL) and disability. All outcomes sought must be of rehabilitation interest; v) studies – only RCT studies were considered.

Exclusion criteria

Studies analyzing the efficacy of downhill on a pediatric population, studies of efficacy without a control group, and studies on healthy subjects were excluded.

Research strategy

The search strategy was conducted on MEDLINE (via PubMed), LILACS; PEDro, SCOPUS, and Web of Science on 31st March 2024. The combination of terms on PubMed and keywords on PubMed used was: (“downhill walk” [MeSH]) AND (“physiotherapy” [MeSH] OR (“rehabilitation” [MeSH] OR (“exercise” [MeSH])).

Adhering to the guidelines outlined in the PRISMA checklist, three independent physical therapists (MT, GS, and RC) performed the first screening for each database by title, keywords, and abstract. The second screening was instead performed on the full texts of the studies included in the review.

All articles included in the review were found from the start in the databases used and passed all screening stages; however, a process of “reference checking” and “citation tracking” was carried out to search for additional studies that met the review's eligibility criteria.

Data collection

Data extraction was performed following Cochrane methodology [28]. Reviewers extracted the clinical and demographic data of the study population, such as sex, age, and pathology of the subjects; information about the authors and year of publication was also extracted.

The reviewers focused on extracting information on the treatment programs and their frequency carried out in the study groups, the outcome measures used in the inclusion studies, and the results obtained in the different follow-ups.

Methodological quality and risk of bias

The methodological quality of each RCT included in this review was assessed using the Physiotherapy Evidence Database (PEDro) scoring scale. According to the PEDro criteria, the quality of the study can be classified into low quality (scores 0-3), medium quality (scores 4-7), and high quality (scores 8-10), with a score of 10 reflecting the highest quality [29].

Risk of bias (RoB) assessment was implemented through the Cochrane RoB 2 tool for RCTs, following the Cochrane Handbook for Systematic Reviews of Interventions. The tool has five domains used to generate the “overall RoB”. The RoB judgment for the second domain (RoB due to deviations from planned interventions) was carried out to quantify both the effect of the assignment and the effect of starting and adhering to the intervention. The third and fourth domains of the RoB tool (RoB due to missing outcome data and RoB in measurement of the outcome) were quantified instead of each of the measures of outcome present in the works included in the revision. Each domain was evaluated with one of the following options: “low RoB”, “some concerns” and “high RoB”. The criteria used for the evaluation of the RoB of the studies follow the Cochrane directives, for which they are judged “low RoB”. The studies that were presented for all domains have low RoB and are instead judged “some concerns”; the studies that have no more than a domain are also judged “some concerns”. The trials are judged to be at high RoB in at least one domain for this result, or the trial is judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result. Two authors evaluated RoB for each study, and disagreements were resolved by negotiation [30].



Results

The total number of articles identified through the media database search was 382 records; 24 duplicates were removed using EndNote® Basic, produced by Web of Science Group.

Of the remaining 358 records, the reviewers, by reading titles and abstracts, have selected 41 studies for full-text screening. The articles deemed eligible for inclusion according to the eligibility criteria were 3. The search process is depicted in Figure 1.

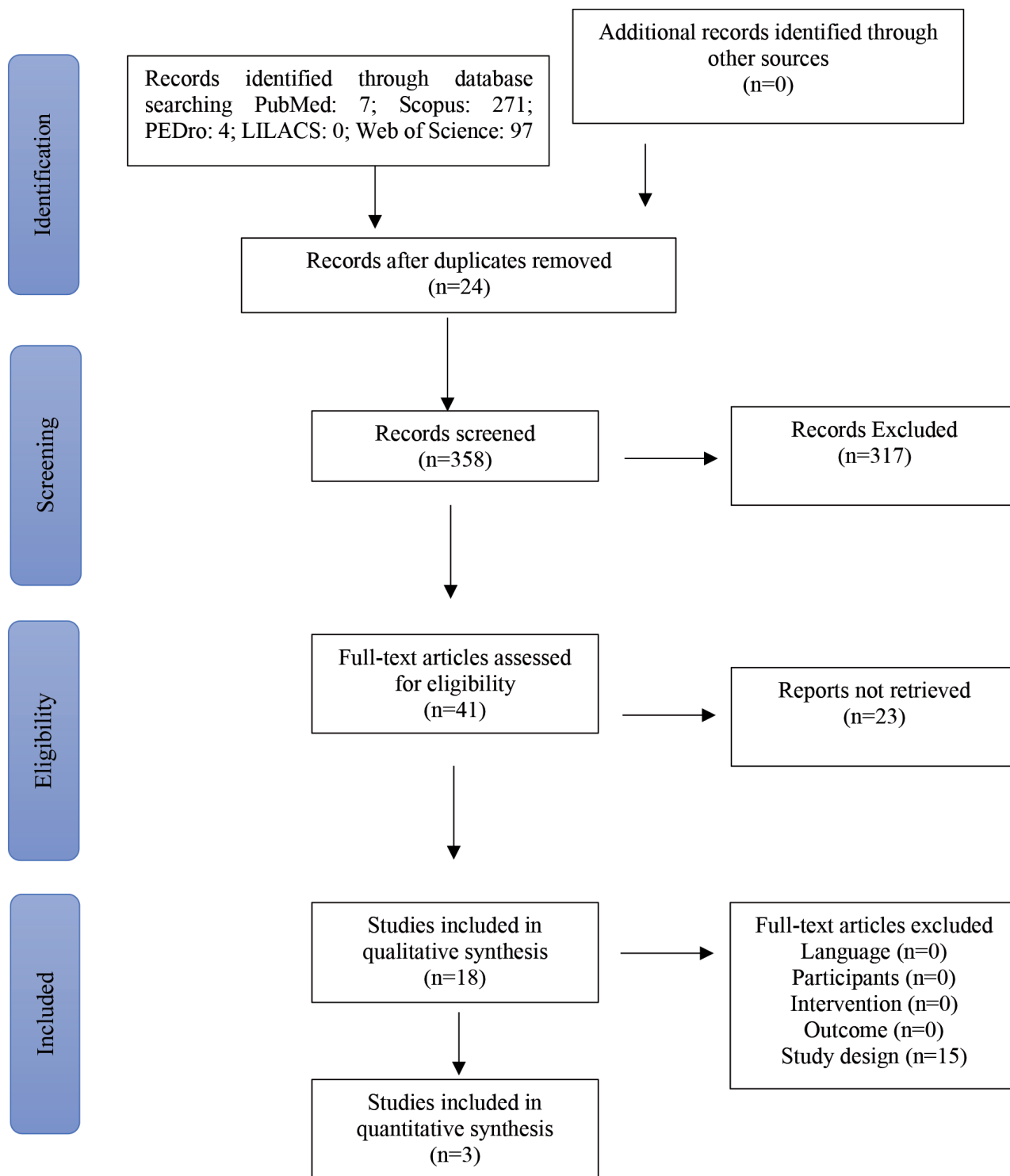


Figure 1. Flow chart.



Characteristics of the studies: type of participants and outcome measures

In this systematic review, only RCTs were included. The included studies represent a total of 110 participants for 3 RCTs; of these, 2 were performed on patients diagnosed with chronic obstructive pulmonary disease (COPD), in these, the average age of participants ranges from 62 to 64 years old [24,31], while 1 was for treating people with MS [23]. The average age of participants in this study was 34 years. This age difference is due to the characteristics of the disease. For the same reason, we note a difference in the gender distribution: in studies involving COPD patients, we note a predominance of the male gender [24,31]. In the study involving MS patients [23], on the contrary, the predominant gender is female (82% female vs. 18% male).

The primary outcome measures used in studies concerning the efficacy of downhill walking on patients with lung diseases were specific tests for the assessment of lung function, such as the pulmonary function test [32], the cardiopulmonary exercise test [24], and the 6-Minute Walking Test (6MWT) [24,31]. Work conducted on people with MS assessed muscle strength and balance [23]. In all the work, the secondary outcome measures evaluated the performance in daily activities, as health-related quality of life (St. George Respiratory Questionnaire (SGRQ)) [31], fatigue (cycle endurance test and cardiopulmonary exercise test) [23,24].

The study groups all carried out a rehabilitation program based on the use of downhill, with a treadmill inclination between -5 and -10%. The control groups, on the other hand, vary from patients who performed a free walk [31], a conventional walk on a treadmill with a neutral incline [24], and with a positive slope of 10%. [23]. All participants performed 3 weekly training sessions for 4-12 weeks [23,24,31].

All studies report outcome measures at baseline and at the end of treatment. The studies conducted in patients with COPD also present follow-ups at 3 and 12 weeks [24,31]. The study by Moezy *et al.* demonstrated statistically significant improvements in the experimental group at 6MWT, time up and go test, and SGRQ [31]. The work of Augusto *et al.* reported a faster weekly progression in treadmill speed in the study group and less dyspnea and perceived fatigue compared to conventional walking training [24].

Finally, Samei *et al.* report significant improvements in both experimental groups in terms of disability, fatigue, and mobility [23]. However, the downhill group shows a greater reduction in disability and fatigue intensity indices and a significant increase in the mobility index. It also shows better results in terms of functional activity and isometric torque of the quadriceps muscles than the uphill group, even after 4 weeks of follow-up.

The results obtained are detailed in *Supplementary Table 1*.

Methodological quality and risk of bias of included studies

When evaluated with the PEDro scale, the studies examined presented a score of 8. Therefore, all studies included in our review, in accordance with PEDro criteria, manifest high methodological quality (*Supplementary Table 2*).

Risk of bias

RoB 2 assessment shows a low RoB for all studies included in the review. In detail, although “overall” the work of Camillo *et al.* [24] is judged as “high RoB”, 4 domains out of 5 are also at

low RoB. The domain found to be exposed to a high RoB is the one referable to “bias due to deviations from intended interventions”, particularly on the effects, for all outcomes, of initiating and following interventions as specified in the trial protocol. Considering this, it is advisable to interpret the tool by investigating the individual domains and not the overall judgment. The other studies are judged positively, as all evaluated domains show a low RoB (Figure 2).

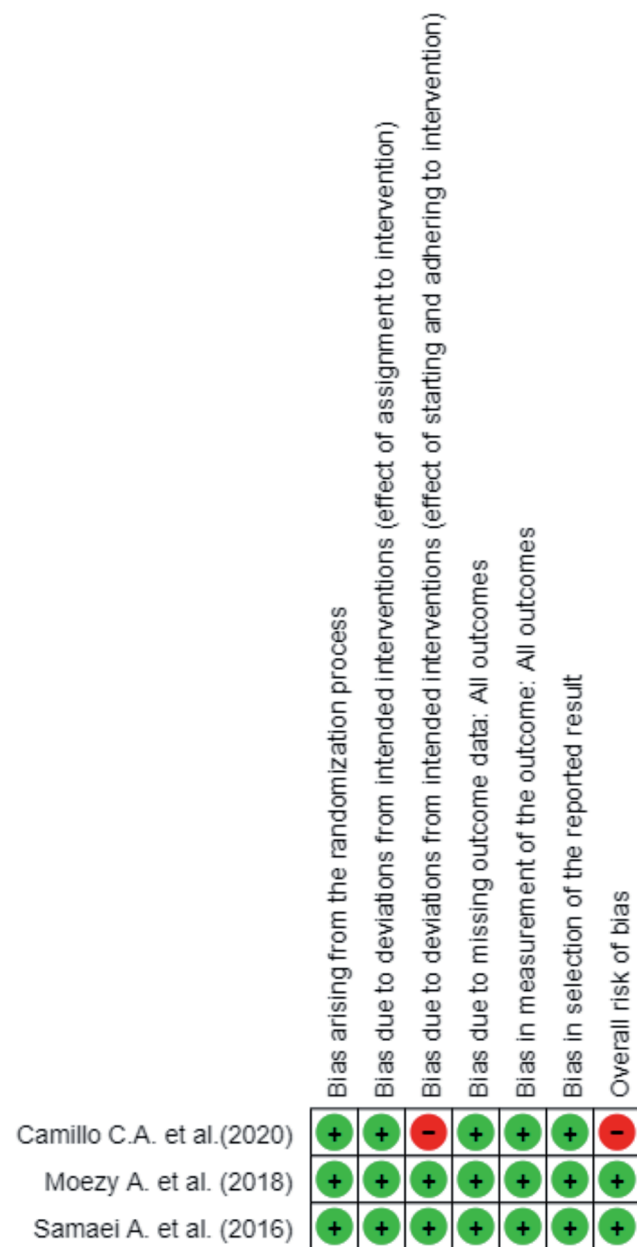


Figure 2. RoB 2 Cochrane tool. CAMILLO – a mean 77m improvement in 6MWD after 10 weeks of DT: PRE E POST CT 435±107, 491±111; PRE E POST DT 473±96, 550±90. MOEZY – 6-minute-walk test (m) et group 422.88±136.75 521.15±109.26, p 0.043 (significant); conventional group 438.87±110.47 406.12±137.54 , p 0.263.



Discussion

This systematic review primarily aimed to evaluate the efficacy of downhill exercise. The decision to include only studies that compare downhill treadmill training with other walking programs was made to ensure a consistent framework for evaluating the relative effects of different training modalities on functional outcomes. This comparative approach allows for a clearer assessment of the unique benefits or limitations of downhill training in contrast to conventional walking protocols, which vary in intensity and muscle engagement. By focusing on studies with direct comparisons, the review aims to enhance the applicability of findings to clinical practice, where choices between various walking programs are frequently considered for optimizing patient rehabilitation outcomes.

Downhill training represents an entirely innovative form of aerobic training of particular interest; it offers a unique opportunity to efficiently induce skeletal muscle stress while minimizing ventilatory demand during exercise [32,33]. In patients diagnosed with COPD and in people with MS, downhill training appears effective on functional capacity and symptoms of dyspnea and fatigue, and it increases strength and activity performance.

As regards the frequency of training in COPD patients, this remains in line with the average duration of training programs recommended by *Associazione Italiana Pneumologi Ospedalieri* (AIPO) and *Associazione Riabilitatori dell'Insufficienza Respiratoria* (ARIR) [34]. The results obtained from the studies included in this review are in line with the literature.

The training characteristics are similar in the 3 articles included in this systematic literature review. All articles use an intervention frequency of 3 sessions per week. In 2 articles, a fixed inclination of -10% is used, in one article, a progressive inclination from -5 to -7.5%. Exercise intensity was increased as tolerated by patients while monitoring heart rate.

In the experimental groups of the studies of COPD patients, statistically significant improvements over the control groups were found in terms of respiratory volumes and performance tests [31].

This improvement in the forced expiratory volume in 1 second is unexpected because it is known that aerobic training (cycling and walking) in subjects suffering from COPD does not affect resting lung function. Improvements in skeletal muscle function after physical training, in fact, translate into gains in exercise capacity despite the absence of changes in lung function. The improved oxidative capacity and efficiency of the skeletal muscles lead to less alveolar ventilation, which reduces dynamic hyper compression and improves effort expenditure [35].

The benefit of downstream training in COPD may be linked to the greater efficiency of the eccentric contraction, which allows a greater workload of the peripheral muscles with less ventilation [36]. This may have improved patients' ability to take inhaled pharmacological therapy.

Often, COPD patients, precisely because of the fatigue and, above all, the dyspnea they experience when walking, do not engage in regular physical activity and, in many cases, do not leave the home environment.

Downhill walking training was associated not only with significant and clinically relevant results in increasing the distance traveled in the 6MWT [24,31], but also with a faster weekly progression of treadmill speed compared to conventional treadmill training [31].

The two great properties of eccentric contraction, high force production, and low energy cost, make downhill a cost-effective task that could increase muscle mass and strength in patients and improve overall functional status [37].

In the study with MS patients, the results showed that downhill training also yielded significant data in the reduction of indices of disability, mobility, dynamic and static postural balance and, above all, fatigue recorded in most of the MS population; the recent study by Har-Nir *et al.* showed that for MS people, energy expenditure values are significantly lower during downhill walking and higher during uphill walking [38]. Walking on different types of inclines is considered essential for many activities of daily living for people with MS. Therefore, it is confirmed that this should be included as part of an exercise program [23].

Finally, it is worth noting the methodological reliability of the studies included in our review; in fact, at the PEDro scale, all studies scored "high", and at RoB 2, they showed a low RoB.

At present, downhill walking represents a very uncommon exercise modality within rehabilitation protocols and is very little investigated, as evidenced by the lack of clinical studies and the absence of reviews, which is why it is desirable that it be introduced into clinical practice and become an integral part of training protocols in patients with functional disabilities [36].

Limitations of the study

This review's limitations include the small sample size and the few available studies. A further limitation of this review is the non-inclusion of grey literature. This may not provide a complete overview of the topic. It is important to note that the use of downhill training has so far mainly been studied in relation to COPD and MS. Additionally, the certainty of evidence was not assessed.

Future research implications

It is crucial that future studies clarify the physiological benefits of downhill training in different diseases, defining more effective programs with relevant characteristics to definitively clarify its role and effectiveness as part of a rehabilitation program. However, in light of the results of this review, with 3 high-quality RCTs showing concordant positive results, it is possible to include downhill training as a training modality in rehabilitation programs.

Conclusions

Downhill could be such an effective, safe, and feasible eccentric training modality that it can be considered a new rehabilitation strategy that could be implemented for patients with low exercise tolerance. Its use is associated with an increased possibility of clinically significant improvements in functional status, muscle mass, and strength, thus representing a highly reliable type of training. The reduction in disability indices, improvement in mobility, postural balance, and, above all, fatigue make this type of training also valid for MS and capable of producing positive results on some of the cardinal symptoms that this pathology presents.



References

- Durstine JL, Gordon B, Wang Z, Luo X. Chronic disease and the link to physical activity. *J Sport Health Sci* 2013;2:3-11.
- Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment of chronic pain: why and when. *Best Pract Res Clin Rheumatol* 2015;29:120-30.
- Piercy KL, Troiano RP, Ballard RM, et al. The physical activity guidelines for Americans. *JAMA* 2018;320:2020-8.
- Kemps H, Kränkel N, Dörr M, et al. Exercise training for patients with type 2 diabetes and cardiovascular disease: what to pursue and how to do it. A position paper of the European Association of Preventive Cardiology (EAPC). *Eur J Prev Cardiol* 2019;26:709-27.
- Linder S, Abu-Omar K, Geidl W, et al. Physical inactivity in healthy, obese, and diabetic adults in Germany: an analysis of related socio-demographic variables. *PLoS One* 2021;16:e0246634.
- McCafferty WB, Horvath SM. Specificity of exercise and specificity of training: a subcellular review. *Res Q* 1977;48:358-71.
- Hortobagyi T, Hill JP, Houmard JA, et al. Adaptive responses to muscle lengthening and shortening in humans. *J Appl Physiol* 1996;80:765-72.
- Drexel H, Mader A, Saely CH, et al. Downhill hiking improves low-grade inflammation, triglycerides, body weight and glucose tolerance. *Sci Rep* 2021;11:14503.
- Malm C, Sjödin TLB, Sjöberg B, et al. Leukocytes, cytokines, growth factors and hormones in human skeletal muscle and blood after uphill or downhill running. *J Physiol* 2004;556:983-1000.
- Laursen B, Ekner R, Simonsen EB, et al. Kinetics and energetics during uphill and downhill carrying of different weights. *Appl Ergon* 2000;31:159-66.
- Howatson G, Hough P, Pattison J, et al. Trekking poles reduce exercise-induced muscle injury during mountain walking. *Med Sci Sports Exerc* 2011;43:140-5.
- Maeo S, Yamamoto M, Kanehisa H, Nosaka K. Prevention of downhill walking-induced muscle damage by non-damaging downhill walking. *PLoS One* 2017;12:e0173909.
- Ofori-Asenso R, Chin KL, Mazidi M, et al. Global incidence of frailty and prefrailty among community-dwelling older adults: a systematic review and meta-analysis. *JAMA Netw Open* 2019;2:e198398.
- To TL, Doan TN, Ho WC, Liao WC. Prevalence of frailty among community-dwelling older adults in Asian countries: a systematic review and meta-analysis. *Healthcare* 2022;10:895.
- Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc* 2012;60:1487-92.
- WHO. WHO clinical consortium on healthy ageing topic focus: frailty and intrinsic capacity. 2017. Available from: <https://www.who.int/publications/i/item/WHO-FWC-ALC-17.2>.
- Cheng M, Chang S. Frailty as a risk factor for falls among community dwelling people: evidence from a meta-analysis. *J Nurs Scholarsh* 2017;49:529-36.
- Kojima G. Frailty as a predictor of nursing home placement among community-dwelling older adults: a systematic review and meta-analysis. *J Geriatr Phys Ther* 2018;41:42-8.
- McPhee JS, French DP, Jackson D, et al. Physical activity in older age: perspectives for healthy ageing and frailty. *Biogerontology* 2016;17:567-80.
- Polese JC, Ada L, Dean CM, et al. Treadmill training is effective for ambulatory adults with stroke: a systematic review. *J Physiother* 2013;59:73-80.
- Robinson AG, Dennett AM, Snowdon DA. Treadmill training may be an effective form of task-specific training for improving mobility in people with Parkinson's disease and multiple sclerosis: a systematic review and meta-analysis. *Physiotherapy* 2019;105:174-86.
- Bishnoi A, Lee R, Hu Y, et al. Effect of treadmill training interventions on spatiotemporal gait parameters in older adults with neurological disorders: systematic review and meta-analysis of randomized controlled trials. *Int J Environ Res Public Health* 2022;19:2824.
- Samaei A, Bakhtiary AH, Hajjhasani A, et al. Uphill and downhill walking in multiple sclerosis. *Int J MS Care* 2016;18:34-41.
- Camillo CA, Osadnik CR, Burtin C, et al. Effects of downhill walking in pulmonary rehabilitation for patients with COPD: a randomised controlled trial. *Eur Respir J* 2020;56:2000639.
- Lindemann U, Schwenk M, Schmitt S, et al. Effect of uphill and downhill walking on walking performance in geriatric patients using a wheeled walker. *Z Gerontol Geriatr* 2017;50:483-7.
- Moher D, Liberati A, Tetzlaff J. Preferred reporting Items for Systemic reviews and Meta-Analyses (PRISMA) 2015 statement. *Syst Rev* 2015;4:1.
- Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev* 2019;10:ED000142.
- Noyes J, Booth A, Flemming K, et al. Cochrane qualitative and implementation methods group guidance series—paper 3: methods for assessing methodological limitations, data extraction and synthesis, and confidence in synthesized qualitative findings. *J Clin Epidemiol* 2018;97:49-58.
- Berardi A, Tofani M, Colalelli F, et al. The psychometric properties of the Italian version of the PEDro Scale. *Gazzetta Medica Ital Arch Sci Medice* 2022;181:357-65.
- Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:14898.
- Moezy A, Erfani A, Mazaherinezhad A, Javad Mousavi SA. Downhill walking influence on physical condition and quality of life in patients with COPD: a randomized controlled trial. *Med J Islam Repub Iran* 2018;32:49.
- Wanta DM, Nagle FJ, Webb P. Metabolic response to graded downhill walking. *Med Sci Sports Exerc* 1993;25:159-62.
- Liefeldt G, Noakes TD, Dennis SC. Oxygen delivery does not limit peak running speed during incremental downhill running to exhaustion. *Eur J Appl Physiol Occup Physiol* 1992;64:493-6.
- Crisafulli E, D'Abrosca F, Delicati O, et al. Raccomandazioni Italiane sulla pneumologia riabilitativa. Evidenze scientifiche e messaggi clinico-pratici. Available from: <https://www.aiporassegna.it/article/view/318>. [Article in Italian].
- Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society statement on pul-



- monary rehabilitation *Am J Respir Crit Care Med* 2006;173:1390-413.
36. Camillo CA, Burtin C, Hornikx M, et al. Physiological responses during downhill walking: a new exercise modality for subjects with chronic obstructive pulmonary disease? *Chron Respir Dis* 2015;12:155-64.
37. LaStayo P, Marcus R, Dibble L, et al. Eccentric exercise in rehabilitation: safety, feasibility, and application. *J Appl Physiol* 2014;116:1426-34.
38. Har-Nir I, Frid L, Kalron A. Energy expenditure and perceived effort during uphill and downhill walking in people with multiple sclerosis. *Eur J Phys Rehabil Med* 2023;59:25-31.

Online supplementary material:

Supplementary Table 1. Data extraction of included studies.

Supplementary Table 2. Methodological quality.

Received: 29 May 2024; Accepted: 11 November 2024; Early view: 16 January 2025.

Contributions: Matteo Tamburlani, Giovanni Sellitto, Annamaria Servadio: design of the work, acquisition, drafting of the work. Rossana Cuscito, Alessio D'Angelo, Francesca Santini, Edoardo Tirelli, Leonardo Papi, Ilaria Ruotolo: acquisition. Giovanni Galeoto, Annamaria Servadio: analysis, interpretation of data.

Conflict of interest: the authors declare that no conflict of interest.

Ethics approval and consent to participate: institutional review board approval was not needed for this systematic review. The protocol was registered in the Prospero database (PROSPERO ID: CRD42024534719).

Availability of data and materials: the datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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