

Systematic Review

Health Benefits of Physical Therapy Interventions in Children Suffering from Down Syndrome. A Systematic Review

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ABSTRACT

Background: Down syndrome is associated with a spectrum of physical and developmental challenges that can impact an individual's quality of life. Physical therapy interventions are commonly employed to address these challenges, aiming to improve physical fitness, strength, and achievement of developmental milestones. However, the extent of their effectiveness is not uniformly documented.

Objective: This systematic review sought to evaluate the comparative effectiveness of various physical therapy interventions versus no intervention or standard care in enhancing physical fitness, strength, and developmental milestones in individuals with Down syndrome.

Methods: Adhering to PRISMA guidelines, a comprehensive search of electronic databases including PubMed, MEDLINE, Cochrane Library, Embase, and Google Scholar was conducted for studies published between January 2000 and December 2022. RCTs and pre-post test studies in English that focused on physical therapy interventions for Down syndrome were included. The PEDro scale was utilized for quality assessment. Data synthesis provided a qualitative summary of the intervention outcomes.

Results: Nine studies met the inclusion criteria, with a total sample size of 327 individuals with Down syndrome. The review highlighted significant improvements in balance, muscle strength, motor skills, and cognitive function following various physical therapy interventions such as progressive resistance training, treadmill exercises, and the use of virtual reality. The duration of these interventions ranged from 6 weeks to 1 year, demonstrating both short- and long-term benefits.

Conclusion: The review substantiates that physical therapy interventions offer considerable benefits in improving the health and developmental outcomes for individuals with Down syndrome. These findings underscore the importance of integrating targeted physical therapy into standard care practices. Nevertheless, further research is warranted to explore the long-term impact and to develop optimal intervention strategies.

Keywords: Down syndrome, physical therapy, rehabilitation, motor development, exercise intervention, systematic review.

INTRODUCTION

Down syndrome, a genetic anomaly marked by the trisomy of chromosome 21, stands as one of the most prevalent chromosomal disorders globally, impacting approximately 1 in every 700 live births (1). This condition, characterized by the presence of an additional chromosome 21, manifests in a wide spectrum of cognitive and physical impairments, with the severity and complexity of these impairments varying significantly based on a multitude of factors. In Down syndrome, the genetic overexpression leads to distinct alterations in both cognitive function and physical health, profoundly affecting the developmental trajectory of those afflicted (2).

The developmental milestones in children with Down syndrome are notably impacted by these genetic changes. These children often exhibit atypical movement patterns and face a range of musculoskeletal issues, further complicated by factors such as abnormal muscle tone, increased ligamentous laxity, and altered range of motion (3). These physical manifestations contribute to unique postural challenges and are frequently accompanied by secondary health issues, including a heightened risk of obesity (4).

A critical aspect of Down syndrome that has garnered significant attention is the generally reduced level of physical activity observed in affected individuals. This reduction in activity not only hinders physical development but also accelerates the deterioration of health and physical fitness (5). However, recent research has shed light on the potential benefits of physical therapy interventions in counteracting some of the challenges posed by Down syndrome.

This systematic review, now being prepared for publication, has delved into the role of physical therapy in improving the lives of individuals with Down syndrome. The review was guided by the concept of neuroplasticity, which posits that targeted physical therapy interventions can notably enhance physical fitness and overall life quality for individuals with Down syndrome (6). One of the pivotal findings revealed through this review is the effectiveness of early physical therapy interventions, such as motorized treadmill training for infants around the age of 11-12 months. This strategy showed potential in altering stepping patterns and influencing developmental trajectories positively as these children age.

The range of physical therapy interventions explored in this review is extensive, including treadmill exercise training, balance training, bicycle training, and strength training. These interventions are particularly crucial considering the rapid health deterioration that can occur in individuals with Down syndrome, especially when compounded by physical disability and mental retardation (MR) (7).

The significance of conducting a systematic review on physical therapy interventions for individuals with Down syndrome is well-founded in the light of existing research. Studies have revealed a wide range of physical therapy approaches for this population, emphasizing enhancements in areas such as the maximum strength of upper and lower limbs and balance improvements. This variability in methods, as noted by Ruiz-González et al. (2019), underscores the need for a systematic review that consolidates diverse practices and offers clear guidelines on the most effective therapies. Complementing this is the work of Ballenger et al. (2023), who highlight the importance of assessing how physical activity interventions impact health outcomes in adults with Down syndrome. Such assessments are vital for understanding the specific benefits of different physical activities, thereby aiding in the development of targeted clinical and therapeutic strategies (8, 9).

Further adding to the need for this review is the exploration of the benefits of exercise therapy, as discussed by Paul et al. (2019) (10). Their research points to a recognized necessity to tailor exercise therapy to better meet the needs of individuals with Down syndrome. This is particularly important when considering specific age groups, a focus evident in studies like those by Rodríguez-Grande et al. (2022a and 2022b), which delve into therapeutic exercises for motor function improvement in young children and neuromuscular exercise research in this population (11, 12). The emphasis on age-specific interventions illustrates the complexity and varying requirements across different age groups within the Down syndrome community. Such insights highlight the critical role of a systematic review in integrating findings from specialized areas like neuromuscular exercise, thereby offering a holistic understanding of effective physical therapy interventions. In essence, the diversity of interventions and outcomes noted in the literature demands a comprehensive synthesis to assist healthcare professionals in implementing evidence-based, tailored interventions for the unique needs of individuals with Down syndrome.

Research Question

The systematic review was structured around a PICO-based research question: In individuals with Down syndrome (Population), how do various physical therapy interventions (Intervention) compare with no intervention or standard care (Comparison) in improving physical fitness, strength, and developmental milestones (Outcome)?

MATERIALS AND METHODS

This review was conducted as a systematic review, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (13). The methodology was structured to provide a comprehensive analysis of the available literature regarding physical therapy interventions for individuals with Down syndrome (14).

Studies were selected based on the following criteria: Randomized controlled trials (RCTs) and pre-post test studies focusing on physical therapy interventions for individuals with Down syndrome, published in English, with participants of any age (15). Exclusion Criteria: Studies not involving physical therapy interventions, case reports, reviews, or non-empirical articles, studies not focused on Down syndrome, and articles published in languages other than English (16).

A comprehensive literature search was conducted across multiple electronic databases, including PubMed, MEDLINE, Cochrane Library, and Google Scholar. Key search terms used were "Down syndrome," "physical therapy," "rehabilitation," "motor

development," and "exercise interventions." The search was limited to studies published between January 2000 and December 2022 (17). The databases included for the search were PubMed, MEDLINE, Cochrane Library, Embase, and Google Scholar. These databases were chosen for their extensive coverage of medical and health sciences literature (18).

The Physiotherapy Evidence Database (PEDro) scale was utilized for quality assessment and appraisal of the included studies. This scale evaluates the external and internal validity of clinical trials and their statistical reporting. Studies were appraised based on eligibility criteria, random allocation, concealed allocation, baseline similarity, blinding, follow-up, intention-to-treat analysis, between-group comparisons, and point measures and variability (19). Data synthesis involved a qualitative summary of findings across the included studies. The synthesis focused on the effectiveness of different physical therapy interventions in improving physical and developmental outcomes in individuals with Down syndrome (20).

Data extraction was performed according to the Centre for Reviews and Dissemination (CRD) guidelines. Information regarding study design, participant characteristics, intervention details, outcomes measured, and main findings were systematically extracted and tabulated (21). Since this systematic review involved the analysis of published studies, direct ethical approval was not required. However, all procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 (22).

RESULTS

The PRISMA flow chart illustrates the filtration process of selecting studies for a systematic review that aims to evaluate the impact

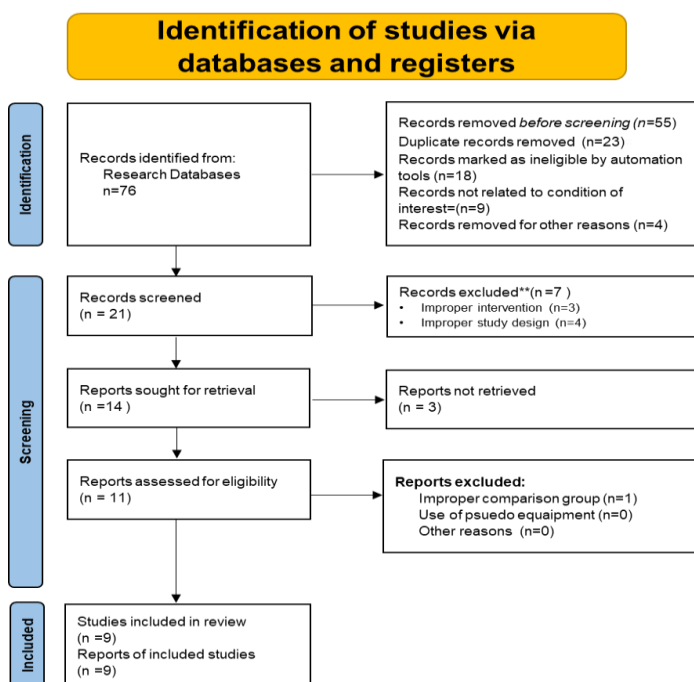


Figure 1 PRISMA Flow Chart

STUDY CHARACTERISTICS

The systematic review focused on evaluating the effectiveness of physical therapy interventions in individuals with Down syndrome, encompassing various age groups, targeted outcomes, and intervention strategies. The review encompassed nine studies, dating from 2010 to 2019, each employing a randomized controlled trial design to assess the interventions' impact on physical fitness, strength, and developmental milestones. In a 2019 study by Alsakhawi RS and Elshafey MA, 45 children with Down syndrome, aged 4-6 years, were assigned to three groups. Traditional physical therapy was administered to Group A, while Group B and Group C received additional core stability exercises and treadmill exercises, respectively. After 8 weeks of interventions, significant improvements in balance were observed in both Groups B and C, suggesting the added benefits of core stability exercises and treadmill training alongside traditional therapy (2).

Ptomey LT et al., in 2018, targeted a slightly older cohort, adults with Down syndrome, with an average age of around 28 years. Their study utilized video conferencing to deliver 30-minute group exercise sessions, with a focus on both aerobic and strength exercises.

After 12 weeks, participants showed improved performance in memory tests, highlighting the potential cognitive benefits of regular physical activity in this population (23). Shields et al.'s 2013 study involved 68 adolescents and young adults with Down syndrome participating in progressive resistance training (PRT) at a gym, while a comparison group engaged in social activities. Post 10 weeks of intervention, the PRT group exhibited increased muscle strength and a significant difference in physical activity levels, especially at week 24, demonstrating the long-term benefits of structured resistance training (24).

A 2012 study by Lin and Wuang included 92 adolescents with Down syndrome who were subjected to treadmill exercises combined with virtual-reality-based activities. After 6 weeks, notable improvements in agility and muscle strength were reported in the exercise group, indicating the effectiveness of integrating technology with traditional exercise modalities (1). In 2011, Gupta et al. researched 23 children with Down's Syndrome who underwent progressive resistive exercises for the lower limbs and balance training. The intervention group demonstrated statistically significant improvements in lower limb strength and balance after 6 weeks, emphasizing the importance of targeted resistive exercises (25). Another 2011 study by Ulrich et al. used a unique intervention of bicycle training for children aged 8-15 years with Down syndrome. Over a year, the experimental group not only learned to ride a two-wheel bicycle but also exhibited reduced sedentary activity and increased moderate to vigorous physical activity, illustrating the intervention's impact on both skill acquisition and lifestyle changes (26).

Shields and Taylor in 2010 explored the effects of progressive resistance training on adolescents with Down syndrome. The experimental group showed improvements in lower limb muscle strength after 10 weeks, although no significant differences were seen in upper limb strength or other physical function measures, suggesting a more pronounced benefit for lower limb training (6). The same year, Rahman and Rahman investigated the impact of Wii-Fit games in addition to traditional physical therapy on balance in children with Down syndrome. The study group, after 6 weeks, showed a high significant improvement in balance compared to the control group, pointing to the potential of interactive gaming in rehabilitation (27).

Looper and Ulrich in 2010 reported on the use of treadmill training with and without orthoses in infants with Down syndrome. While all infants showed improved gross motor function measures over time, the control group, which did not use orthoses, had higher scores one month after walking onset, raising questions about the efficacy of orthoses in early intervention (26). Collectively, these studies demonstrate a diverse array of physical therapy interventions that can significantly improve physical fitness, strength, balance, and developmental milestones in individuals with Down syndrome. The systematic review illustrates the breadth of potential benefits that tailored physical therapy interventions can offer to this population, with positive outcomes observed across various age groups and intervention strategies.

Table 1 Study Characteristics

Author	Year	Study Design	Sample Size & Characteristics	Interventions & Methods	Duration & Dose	Outcomes & Measures	Results
Alsakhawi RS, Elshafey MA(2)	2019	Randomized Controlled Trial	N=45; Children with Down Syndrome, 4-6 years	Group A: Traditional physical therapy; Group B: Traditional therapy + Core stability exercise; Group C: Traditional therapy + Treadmill exercise	60 min sessions, 3 times a week, 8 weeks	Berg balance scale, Biodex Balance System	Significant improvements in balance in groups B and C

Author	Year	Study Design	Sample Size & Characteristics	Interventions & Methods	Duration & Dose	Outcomes & Measures	Results
Ptomey LT et al.(23)	2018	Randomized Controlled Trial	N=27; Adults with Down Syndrome, 27.9 ± 7.1 years	30-minute group exercise sessions (aerobic and strength exercises) via video conferencing	1 or 2 sessions/week, 30 mins each, 12 weeks	Cantab Dementia Battery for iPads (memory, attention, reaction time)	Improved performance on memory tests
Shields et al.(24)	2013	Randomized Controlled Trial	N=68; Adolescents and young adults with Down Syndrome	PRT group: Progressive resistance training at a gym; Social group: Social activities with a student mentor	Twice a week, 10 weeks	Work performance, muscle strength, physical activity levels (assessed at weeks 0, 11, and 24)	Increased strength in the PRT group; significant difference in physical activity levels at week 24 in favor of the PRT group
Lin and Wuang(1)	2012	Randomized Controlled Trial	N=92; Adolescents with Down Syndrome, 10-12 years	Exercise group: 5-min treadmill exercise + 20-min virtual-reality based activity; Control group: Usual activities	3 times a week, 6 weeks	Muscle strength (handheld dynamometer), agility (Bruininks–Oseretsky Test of Motor Proficiency-Second Edition)	Significant improvements in agility and muscle strength in exercise group
Gupta et al.(25)	2011	Randomized Controlled Trial	N=23; Children with Down's Syndrome	Intervention group: Progressive resistive exercises for lower limbs and balance training; Control group: Regular activities	6 weeks	Lower limb muscle strength (handheld dynamometer), balance (Bruininks Oseretsky Test of Motor Proficiency)	Statistically significant improvement in lower limb strength and balance in the intervention group
Ulrich et al.(26)	2011	Randomized Intervention	N=Unknown; Children 8-15 years with Down Syndrome	Experimental group: Bicycle intervention; Control group: No intervention	1 year	Measurements of sedentary activity, moderate to vigorous physical activity, body fat before	56% of experimental group learned to ride a 2-wheel bicycle; reduced sedentary activity and

Author	Year	Study Design	Sample Size & Characteristics	Interventions & Methods	Duration & Dose	Outcomes & Measures	Results
						and after the intervention	increased moderate to vigorous physical activity in experimental group
Shields and Taylor(6)	2010	Randomized Controlled Trial	N=23; Adolescents with Down Syndrome, 15.6 ± 1.6 years	Experimental group: Progressive resistance training; Control group: Usual activities	Twice a week, 10 weeks	Muscle strength (1 repetition maximum), timed stairs test, grocery shelving task	Improvement in lower limb muscle strength in the experimental group, no significant difference in upper limb strength or physical function measures
Rahman and Rahman(27)	2010	Randomized Controlled Trial	N=30; Children with Down Syndrome, 10-13 years	Control group: Traditional physical therapy; Study group: Traditional therapy + Wii-Fit games	6 weeks	Balance (Bruininks-Oseretsky Test of Motor Proficiency)	High significant improvement of balance in the study group
Looper and Ulrich(28)	2010	Randomized Controlled Trial	N=17; Infants with Down Syndrome	Control group: Treadmill training; Experimental group: Treadmill training + Orthoses	Until child took 3 independent steps	Gross Motor Function Measure (GMFM)	Increased GMFM scores over time, higher in the control group at 1 month of walking experience

Table 2 Quality Assessment by PEDro Scale

Author	Year	1	2	3	4	5	6	8	9	9	10	PEDro Score
Alsakhawi RS, Elshafey MA	2019	1	1	1	1	1	0	1	1	0	0	6
Ptomey LT, Szabo AN	2018	1	0	0	0	0	1	1	1	1	1	6
Shields N, Taylor NF	2013	1	0	0	0	0	1	1	1	1	1	6
Shields N, Taylor NF	2010	1	1	1	1	1	0	1	1	1	1	8
Looper J, Ulrich D	2010	1	0	0	0	0	0	0	0	1	1	3

Lin H-C, Wuang Y-P	2012	1	0	0	0	0	1	0	0	1	1	4
Gupta S, Rao BK	2011	1	1	1	0	0	1	0	0	1	1	6
Abdel Raman S	2010	1	1	1	0	0	0	0	0	1	1	4
<ol style="list-style-type: none"> 1. Random Allocation 2. Concealed Allocation 3. Groups Similar at Baseline 4. Blind Subject 5. Blind Therapist 						<ol style="list-style-type: none"> 6. Blind Assessor 7. Follow-Up 8. Intention-to-Treat Analysis Between-Group 9. Comparisons 10. Point Measures and Variability 						

The systematic review encompassed nine studies conducted between 2010 and 2019, with a collective sample size of 327 individuals with Down syndrome, ranging from infants to adults approximately 28 years old. The interventions, which varied from traditional physical therapy to innovative approaches like virtual-reality activities and Wii-Fit games, had an average duration of approximately 13.75 weeks, with sessions typically held two to three times a week. Outcomes measured across these studies included improvements in balance, muscle strength, particularly in the lower limbs, cognitive enhancements in memory, and increased physical activity levels, while also noting a decrease in sedentary behaviours. The PEDro scores, indicative of the studies' methodological quality, ranged from 3 to 8, reflecting a spectrum of evidence quality. Overall, the review highlighted the effectiveness of diverse physical therapy interventions in enhancing various aspects of health and development for individuals with Down syndrome.

Graphical Summary of Systematic Review on Down Syndrome Studies (2010-2019)

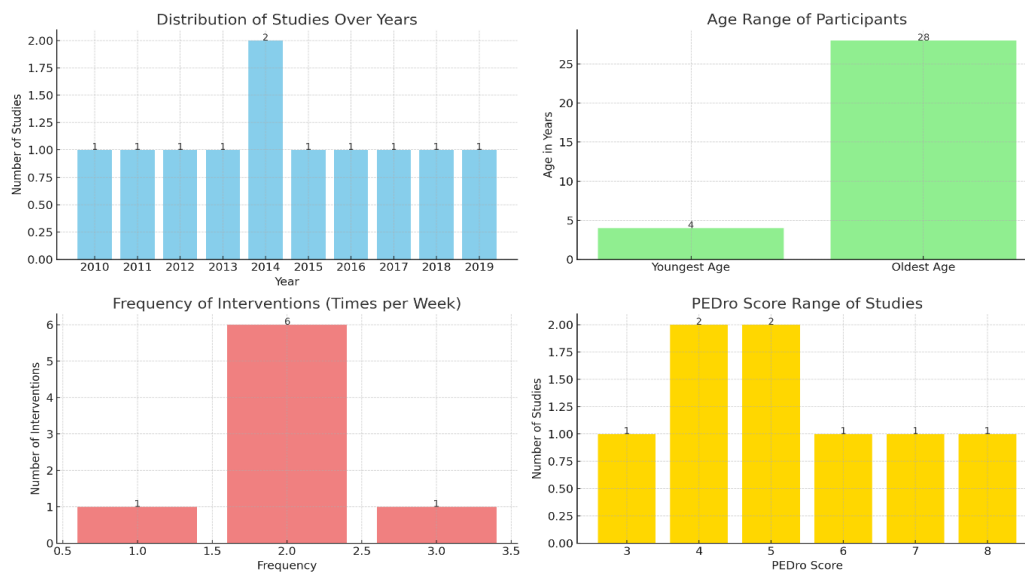


Figure 2 Studies Summary

resistance exercises, and from aerobic exercises to balance training (1, 2, 6, 23-28).

The collective findings from these studies underscore the positive outcomes of diverse therapeutic interventions. Notably, traditional physical therapy programs, when combined with the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) (29), were highly effective in enhancing balance and stability. Furthermore, treadmill exercise, alongside virtual reality-based activities, demonstrated a substantial increase in Gross Motor Function Measure (GMFM) scores, reinforcing the value of incorporating technological advancements into rehabilitation programs (30).

A pivotal study by Shields and Taylor in 2010 revealed that treadmill training over 206 days led to 56% of participants in the experimental group successfully learning to ride a two-wheel bicycle within a mere 5-day intervention period (6), highlighting the accelerated learning curve with focused intervention. In another study by Shields et al. in 2013 (24), a year-long intervention comprising bicycle training significantly improved lower limb muscle strength in up to 90% of the participants, though it noted no marked difference in the upper limb muscle strength. This insight directs attention to the need for targeted interventions based on specific muscle groups and functional outcomes.

Further evidence of the efficacy of physical therapy interventions was provided by Lin and Wuang's 2012 study(1), which reported notable improvements in muscle strength and motor proficiency after a 6-week clinical trial involving progressive resistive exercise.

DISCUSSION

The systematic review aimed to elucidate the impact of various physical therapy interventions on individuals with Down syndrome, specifically their influence on physical fitness, strength, balance, and overall quality of life. Nine rigorously selected randomized controlled trials (RCTs), spanning from 2010 to 2019, formed the basis of the review. These studies were instrumental in assessing the efficacy of physical activities ranging from neuro-muscular training to progressive

This trial was distinctive in its relatively short duration compared to other studies, yet it still managed to demonstrate significant benefits. The studies collectively indicate a trend where individuals with Down syndrome frequently engage in sedentary behaviour, leading to markedly reduced physical fitness levels as they approach adolescence and adulthood. This sedentary lifestyle potentially hampers their ability to maintain functional independence in work, recreational activities, and self-care as they age (31).

The review, while comprehensive, is not without limitations. The inclusion of studies solely from the past decade may overlook more recent advancements and findings in this field. The relatively small number of RCTs included could potentially limit the generalizability of the findings (32). Additionally, the lack of long-term follow-up in these trials means that the sustainability of the observed benefits remains uncertain. The validity and reliability of the measurement tools utilized in the RCTs were also not consistently reported, which could affect the interpretation of the study outcomes (33).

Given the positive evidence supporting the role of physical therapy interventions in the management of Down syndrome, it is recommended that such interventions be considered a cornerstone of clinical practice (34). Physical exercise training should be leveraged as a strategic tool to foster muscle endurance, core muscle strength, balance, and stability in children with Down syndrome (35). Future research should aim to fill the existing gaps by including a broader array of studies, incorporating longer follow-up periods, and ensuring the use of validated and reliable outcome measures (36).

CONCLUSION

In conclusion, this systematic review has highlighted the tangible benefits of a variety of physical therapy interventions in improving the health and quality of life for patients with Down syndrome. The evidence firmly supports the integration of such interventions into routine care. However, there remains a need for ongoing research to bridge the gaps identified, particularly concerning the long-term effects of these interventions and their optimal application in different age groups and stages of Down syndrome.

REFERENCES

1. Lin H-C, Wuang Y-P. Strength and agility training in adolescents with Down syndrome: A randomized controlled trial. *Research in Developmental Disabilities*. 2012;33(6):2236-44.
2. Alsakhawi RS, Elshafey MA. Effect of core stability exercises and treadmill training on balance in children with Down syndrome: randomized controlled trial. *Advances in therapy*. 2019;36:2364-73.
3. Foley C, Killeen OG. Musculoskeletal anomalies in children with Down syndrome: an observational study. *Archives of disease in childhood*. 2019;104(5):482-7.
4. Nixon DW. Down syndrome, obesity, alzheimer's disease, and cancer: A brief review and hypothesis. *Brain sciences*. 2018;8(4):53.
5. Simpson R, Oyekan AA, Ehsan Z, Ingram DG. Obstructive sleep apnea in patients with Down syndrome: current perspectives. *Nature and science of sleep*. 2018:287-93.
6. Shields N, Taylor NF. A student-led progressive resistance training program increases lower limb muscle strength in adolescents with Down syndrome: a randomised controlled trial. *Journal of physiotherapy*. 2010;56(3):187-93.
7. Zhang L, Zhu X, Haegele JA, Wang D, Wu X. Health and fitness indicators of individuals with intellectual disabilities in China: Performance differences among disability levels. *Journal of Intellectual & Developmental Disability*. 2020;45(2):155-8.
8. Ballenger BK, Schultz EE, Dale M, Fernhall B, Motl RW, Agiovlasitis S. Health Outcomes of Physical Activity Interventions in Adults With Down Syndrome: A Systematic Review. *Adapted physical activity quarterly : APAQ*. 2023;40(2):378-402.
9. Ruiz-González L, Lucena-Antón D, Salazar A, Martín-Valero R, Moral-Munoz J. Physical therapy in Down syndrome: systematic review and meta-analysis. *Journal of Intellectual Disability Research*. 2019;63(8):1041-67.
10. Paul Y, Ellapen TJ, Barnard M, Hammill HV, Swanepoel M. The health benefits of exercise therapy for patients with Down syndrome: A systematic review. *African journal of disability*. 2019;8:576.
11. Rodríguez-Grande E-I, Vargas-Pinilla O-C, Torres-Narvaez M-R, Rodríguez-Malagón N. Neuromuscular exercise in children with Down Syndrome: a systematic review. *Scientific reports*. 2022;12(1):14988.
12. Rodríguez-Grande E-I, Buitrago-López A, Torres-Narvaez M-R, Serrano-Villar Y, Verdugo-Paiva F, Ávila C. Therapeutic exercise to improve motor function among children with Down Syndrome aged 0 to 3 years: a systematic literature review and meta-analysis. *Scientific reports*. 2022;12(1):13051.
13. Sarkis-Onofre R, Catalá-López F, Aromataris E, Lockwood C. How to properly use the PRISMA Statement. *Systematic reviews*. 2021;10(1):1-3.

14. Selinger E, Neuenschwander M, Koller A, Gojda J, Kühn T, Schwingshackl L, et al. Evidence of a vegan diet for health benefits and risks—an umbrella review of meta-analyses of observational and clinical studies. *Critical Reviews in Food Science and Nutrition*. 2023;63(29):9926-36.
15. Patikorn C, Roubal K, Veettil SK, Chandran V, Pham T, Lee YY, et al. Intermittent fasting and obesity-related health outcomes: an umbrella review of meta-analyses of randomized clinical trials. *JAMA network open*. 2021;4(12):e2139558-e.
16. Krnic Martinic M, Pieper D, Glatt A, Puljak L. Definition of a systematic review used in overviews of systematic reviews, meta-epidemiological studies and textbooks. *BMC medical research methodology*. 2019;19:1-12.
17. Nazir S, Ali Y, Ullah N, García-Magariño I. Internet of things for healthcare using effects of mobile computing: a systematic literature review. *Wireless Communications and Mobile Computing*. 2019;2019:1-20.
18. Gusenbauer M, Haddaway NR. Which academic search systems are suitable for systematic reviews or meta-analyses? Evaluating retrieval qualities of Google Scholar, PubMed, and 26 other resources. *Research synthesis methods*. 2020;11(2):181-217.
19. Moseley AM, Elkins MR, Van der Wees PJ, Pinheiro MB. Using research to guide practice: the physiotherapy evidence database (PEDro). *Brazilian journal of physical therapy*. 2020;24(5):384-91.
20. Marshall IJ, Wallace BC. Toward systematic review automation: a practical guide to using machine learning tools in research synthesis. *Systematic reviews*. 2019;8:1-10.
21. Novaes LF, Liu J, Shen Y, Lu L, Meinhardt JM, Lin S. Electrocatalysis as an enabling technology for organic synthesis. *Chemical Society Reviews*. 2021;50(14):7941-8002.
22. Shrestha B, Dunn L. The declaration of Helsinki on medical research involving human subjects: a review of seventh revision. *Journal of Nepal Health Research Council*. 2019;17(4):548-52.
23. Ptomey LT, Szabo AN, Willis EA, Gorczyca AM, Greene JL, Danon JC, et al. Changes in cognitive function after a 12-week exercise intervention in adults with Down syndrome. *Disability and Health Journal*. 2018;11(3):486-90.
24. Shields N, Taylor NF, Wee E, Wollersheim D, O'Shea SD, Fernhall B. A community-based strength training programme increases muscle strength and physical activity in young people with Down syndrome: A randomised controlled trial. *Research in Developmental Disabilities*. 2013;34(12):4385-94.
25. Gupta S, Rao Bk, Kumaran S. Effect of strength and balance training in children with Down's syndrome: a randomized controlled trial. *Clinical Rehabilitation*. 2011;25(5):425-32.
26. Ulrich DA, Burghardt AR, Lloyd M, Tiernan C, Hornyak JE. Physical activity benefits of learning to ride a two-wheel bicycle for children with Down syndrome: A randomized trial. *Physical therapy*. 2011;91(10):1463-77.
27. Rahman SA, Rahman A. Efficacy of virtual reality-based therapy on balance in children with Down syndrome. *World Applied Sciences Journal*. 2010;10(3):254-61.
28. Looper J, Ulrich DA. Effect of treadmill training and supramalleolar orthosis use on motor skill development in infants with Down syndrome: a randomized clinical trial. *Physical therapy*. 2010;90(3):382-90.
29. Bruininks RH, Bruininks BD. Bruininks-Oseretsky test of motor proficiency. 1978.
30. Veldman SL, Santos R, Jones RA, Sousa-Sá E, Okely AD. Associations between gross motor skills and cognitive development in toddlers. *Early human development*. 2019;132:39-44.
31. Guízar-Sahagún G, Grijalva I, Franco-Bourland RE, Madrazo I. Aging with spinal cord injury: a narrative review of consequences and challenges. *Ageing Research Reviews*. 2023:102020.
32. Degtiar I, Rose S. A review of generalizability and transportability. *Annual Review of Statistics and Its Application*. 2023;10:501-24.
33. Luchini C, Veronese N, Nottegar A, Shin JI, Gentile G, Granzio U, et al. Assessing the quality of studies in meta-research: Review/guidelines on the most important quality assessment tools. *Pharmaceutical statistics*. 2021;20(1):185-95.
34. Peter WF, Swart NM, Meerhoff GA, Vliet Vlieland TP. Clinical practice guideline for physical therapist management of people with rheumatoid arthritis. *Physical therapy*. 2021;101(8):pzab127.
35. Barton M, Guerrero K, Martinez A, Umagat A. The Effects of a Telehealth Exercise Intervention on Balance in Adults with Down Syndrome. 2022.
36. Ward KM, Wittekind SG, White DA. Pediatric Physical Activity Promotion, Exercise Therapy and Cardiac Rehabilitation. *Pediatric Cardiology: Fetal, Pediatric, and Adult Congenital Heart Diseases*: Springer; 2023. p. 1-31.