

Physical education lessons improve physical fitness and functional mobility in rural children with limited participation in regular physical activities: comparison of integrated neuromuscular training and core stabilization training

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Abstract

Study aim: It is crucial for children to thrive and grow up healthy, but without adequate physical fitness and mobility, this can be difficult to attain. Unfortunately, those living in rural areas are at a particular disadvantage when it comes to access to regular physical activity. However, by including exercise programs in the physical education lessons curriculum, these children can be provided with the opportunity to develop these crucial attributes. This study aims to investigate and compare the effects of core stabilization training (CST) and integrated neuromuscular training (INT) applied in physical education lessons on children's physical condition and functional mobility.

Material and methods: The study included 30 rural children (CST group: $n = 15$; INT group: $n = 15$) who did not regularly engage in physical activity. They underwent one hour of training twice a week for eight weeks in physical education lessons.

Results: At the end of 8 weeks, increases were observed in core stability, right hamstring flexibility, and functional mobility values in both groups ($p < 0.05$).

Conclusions: As a result, CST or INT programs applied in physical education lessons may be preferred for the development of physical fitness and physical mobility in children who do not regularly participate in physical activities, and they can provide equal opportunities.

Key words: Physical Education – Physical Activity – Training – Children's Health – Children

Introduction

Childhood is a critical period for the development of both healthy and unhealthy behaviors, as well as physical growth [17]. The amount of physical activity that children engage in during this period plays an important role in promoting the development of healthy behaviors and habits in children [47]. Research suggests that physical activity supports motor skill development and competencies in children [51]. Thus, childhood is acknowledged as a crucial period for motor skill development [46]. Children who lack an environment to develop motor skills through physical activity may remain less active during adolescence and may tend to adopt a sedentary lifestyle in adulthood [7, 52]. In other words, the inability to acquire motor competence during childhood creates a “competence barrier”, preventing participation in various sports activities in later stages of life [49].

Sports activities have direct and positive impacts on both physical and mental well-being [28]. Insufficient physical activity and impaired development of motor skills may lead to various health issues, especially childhood obesity [21]. The World Health Organization recommends that children and adolescents aged 5–17 years should engage in at least one hour of moderate to vigorous physical activity daily for optimal health [11]. The risk of inactivity and obesity in rural communities is higher than among those living in urban areas [56]. Children residing in rural areas face challenges in regular participation in physical activities due to financial constraints, transportation issues, and physical limitations [37], which places them in a disadvantaged position. For these children, there is a high possibility of health problems as well as incomplete motor development in later stages of life. The physical education course provides an opportunity for those children to engage in physical activity [18], and thus eliminate this disadvantage. The type of physical activity is also important

for the acquisition of motor skills and functional mobility. In this regard, physical education teachers bear a great responsibility, and core stability training and integrated neuromuscular training are recommended physical activities for children to do in their physical education classes.

Core stability plays an important role in the stabilization of the proximal parts of the body in sports. Insufficient strength and coordination in the core muscles can lead to decreased movement efficiency and overuse injuries [3]. Therefore, research has shown that core stability training (CST) has a positive impact on functional mobility and balance [24, 30]. Integrated neuromuscular training (INT) is a multidimensional activity that aims to improve motor skill development and physical fitness and address neuromuscular deficiencies. It encompasses strength and conditioning exercises that focus on resistance, dynamic stability, core strength, plyometric, and agility activities [42]. INT is an innovative approach that enhances basic movement skills in children as well as increasing muscle strength and improving movement mechanics [19, 20]. Research suggests that it is more beneficial to apply it before adolescence [42, 44]. Although studies on the effects of CST and INT separately in children exist in the literature [45, 50], there is no comparative study to determine which approach is more beneficial for children. Hence, this study aimed to determine and compare the effects of CST and INT on functional mobility, balance, hamstring muscle flexibility, and core stability in children aged 8-10 years who live in rural areas, do not engage in regular physical activity, and have no prior experience in any sports branch. The goal was to reveal whether CST or INT has a positive short-term effect, and which should be preferred for children's development. This study is unique as it presents new findings on the physical development of underprivileged children living in rural areas who face challenges in participating in regular physical activities due to socioeconomic and transportation barriers. The findings are intended to guide health policymakers and governments to ensure the short-term physical development of this disadvantaged group of children within the scope of physical education courses.

Material and methods

Study participants

The study sample comprised a total of 40 children enrolled in the 2nd, 3rd, and 4th grades at a village school in the Samanlı district of Yalova province. The G-power analysis revealed that 26 participants were required for the study, with a 95% confidence interval and 5% margin of error. Ultimately, 30 children voluntarily participated in the study. Table 1 presents the demographic information about the participants. Participants and their parents were

asked to complete an informed consent form for their consent for participation. To be eligible for the study, the participants had to reside in Samanlı village in Yalova province, be within the age range of 8-10 years, not regularly engage in physical activity, not have previous experience in any sports branches, have no injury or musculoskeletal disorder, and not have any developmental disabilities. The exclusion criteria included discontinuing participation, failure to meet inclusion criteria, and non-compliance with the procedures of the study. Ethical approval for the study was granted by the Yalova University Human Research Ethics Committee on May 8, 2023, with reference number 2023/79.

Study design

The participants were invited to the study area where the details were explained to both parents and children. Informed consent forms were signed, and participants' personal information, including age, gender, height, and weight was recorded. Following this, a series of tests, including the Functional Movement Screen test (FMS), static balance test using the TOGU balance machine, hamstring flexibility test (HF), 30-second sit-up test (SUT), and plank test (PT) for core stability were administered. Details about these tests are provided below. Then, 30 child participants were randomly assigned to either the core stability training group (CST) or the integrated neuromuscular training group (INT), as described below. The CST group underwent core training while the INT group received integrated neuromuscular training for 8 weeks in physical education lessons. Details about the training can be found in Table 2. At the end of the 8-week training period, the measurements were repeated, and the second set of measurements for all participants was recorded.

Measures

Hamstring flexibility measures. The gold standard for measuring hamstring flexibility, the goniometric technique, was employed in this study. The participants were instructed to lie on their back with the knee and hip of the leg positioned in a 90-degree flexion. Then, they were asked to extend the knee of the measured leg as far as possible while keeping the other leg on the floor in the knee extension position. The degree of knee flexion on the measured side was measured [9]. Two measurements were taken from the same leg, and the highest score was recorded. The measurement process was repeated for both legs.

30-second sit-up test. It was used as a core stabilization test. Augustsson et al. [6] defined the 30-second sit-up test as a measure of core strength and power. The participants were asked to perform as many sit-ups as possible within 30 seconds while lying on their backs with their knees

bent, hands behind their backs, and soles of their feet in contact with the ground. During the sit-ups, the feet were held to prevent them from losing contact with the ground. Each participant underwent one trial before the actual test. The participants were required to lie down with their shoulders touching the ground and their elbows reaching their knees in the upright position. The number of sit-ups repeated within 30-second intervals was recorded [6].

Plank test. It was used as a core stabilization test. The goal of the plank test is to evaluate participants' ability to maintain a neutral spine and pelvis position in the plank position, also known as the wooden board. Before the test, the participants received verbal, visual, and practical instructions about the implementation. During the test, the participants were asked to lift onto their toes and elbows, with their elbows positioned under their shoulders and their feet in dorsiflexion, while in the prone position on the mat. A stopwatch was used to measure the duration of the plank position. The test was concluded if participants were unable to maintain lumbopelvic-hip complex stability if there was spinal bending or pain. To save time, the test was limited to a maximum duration of 3 minutes, and participants were stopped when they reached this time limit [33]. Although some tests extend up to 7.5 minutes, it has been reported that 95% of plank duration in children aged 3–15 years falls within 2–3 minutes [10, 34]. The plank test is a valid and reliable assessment tool for children aged 8–12 years [10]. The test was conducted twice, and the highest score was recorded.

Functional Movement Screen test (FMS). FMS is a movement scoring method designed to identify movement deficiencies and asymmetries in individuals. The test comprises seven separate tests that assess functional mobility, including deep squats, hurdle steps, in-line lunges, shoulder mobility, straight-leg raises, trunk stability, and rotary stability tests. Participants receive a score between 0 and 3 for each test, which increases as the movement improves. The maximum possible score is 21 points [14]. The FMS test has been shown to be valid and reliable [54].

Static balance test. Balance is the ability to maintain the body's center of gravity with maximum stability and minimum sway [16]. In this study, balance was measured using a computerized balance test with a balance device called TOGU. The participants underwent a 20-second static balance test in a static posture while standing upright on the balance pad, which in turn yielded the static balance score (SBS). An increase in the balance score indicates a decrease in balance.

Exercise intervention

The participants were randomly assigned to one of two groups. One group received core stability training for 8 weeks, while the other group underwent integrated

neuromuscular training. The exercise duration and repetition numbers are provided in Table 1. Prior to the training sessions, the participants completed a warm-up program, followed by a cool-down. Educational games were incorporated into the cool-down program to prevent boredom among the children.

The core stability training (CST) and integrated neuromuscular training (INT) programs were developed based on previous exercise studies on children [19, 20, 41, 43]. The training sessions were conducted twice a week for 8 weeks, each lasting 40 minutes, as a part of a physical education course. A standard warm-up protocol was applied before each training session. During the warm-up, the participants performed forward, backward, and side-to-side light jogging, as well as stretching the triceps and biceps, quadriceps, knee, heel, hip adductors, and trapezius muscles. Each stretch was held for 10 seconds, and knee pulls and heel touches were performed for 5 repetitions each. The warm-up lasted for a total of 5 minutes.

Statistical analysis

The normal distribution of the data was demonstrated by the results of the Shapiro-Wilk test and the values for skewness and kurtosis. Mean, standard deviation and percentage changes were determined as descriptive statistics. The paired-samples T-test was used to determine the difference between pre – and post-test scores within groups, and the independent-samples T-test was used to determine the difference between pre – and post-test scores between groups. The statistical significance level was set at $p \leq 0.05$. The effect size (Cohen's d) was analyzed in the study. The effect size was calculated using the formula $d = [(\text{mean } 1 - \text{mean } 2)/\text{common standard deviation}]$ and defined as small (0.20–0.49), medium (0.50–0.79) and large (>0.80) [13].

The normal distribution of the participants' equilibrium data was examined using the values for skewness and kurtosis and it was found that the values were in the range of (-2) – $(+2)$ and thus the data conformed to the normal distribution [22]. Therefore, parametric tests were preferred in the statistics.

Results

The participants of the study consisted of a total of 30 children, 17 girls and 13 boys. In the study, participants were divided into two groups: CST ($n = 15$; girls = 8; boys = 7) and INT ($n = 15$; girls = 9; boys = 6) groups. Demographic information about the participants is included in Table 2.

When the pre-test scores of the core and INT training groups were analyzed for each parameter, no significant difference was found between the two groups (Table 3)

Table 1. CST and INT programs

Weeks	CST Program	Set/Rep/ Duration	INT Program	Set/Rep/ Duration
1–2 Week	Abdominal Press	2 set/5 rep/10 s	Broad jump stick landing	2 set/4 rep
	Glute bridge	2 set/10 rep	Crossover hop stick	2 set/8 rep
	Plank	2 set/30 s	80 jump stick landing – ball catch	2 set/6 rep
	Side plank on knee (right-left)	2 set/20 s	BOSU double leg perturbations	2 set/20 s
3–4 Week	Abdominal Press	2 set/5 rep/10 s	BOSU both knees deep hold-ball catch and release	2 set/6 rep
	Single leg glute bridge (right-left)	2 set/8 rep	Broad jump stick landing	2 set/6 rep
	Side plank (right-left)	2 set/8 rep	Crossover hop stick	2 set/12 rep
	Plank	2 set/30 s	180 jump stick landing – ball catch	2 set/6 rep
			BOSU double leg pick	2 set/10 rep
5–6 Week			BOSU crunches	2 set/30 s
	Hip extension in plank position (right-left)	2 set/10 rep	BOSU single leg deep hold	2 set/30 s
	Brid dog (right-left)	2 set/10 rep	BOSU V sit toe touches	2 set/10 rep
	Side plank (right-left)	2 set/10 rep	BOSU superman	2 set/20 rep
	Crunch	2 set/10 rep	Get up and ball catch	2 set/6 rep
7–8 Week			Balloon drop and catch open-closed eyes	2 set/6 rep
	Glute bridge with foot on ball	2 set/15 rep	Crossover hop stick	2 set/8 rep
	Plank with foot on BOSU	2 set/45 s	180 jump stick landing – ball catch	2 set/6 rep
	Side Plank with foot on BOSU (right-left)	2 set/30 s	BOSU crunches	2 set/40 s
	Brid dog on BOSU (right-left)	2 set/30 s	BOSU V sit toe touches	2 set/10 rep
		BOSU superman	2 set/20 rep	

Table 2. Demographic information of the participants

Variables	All (n = 30)		CST Group (n = 15)		INT Group (n = 15)	
	Mean ± SD	Min-Max	Mean ± SD	Min-Max	Mean ± SD	Min-Max
Age [years]	8.87 ± 0.90	8.00–10.00	8.87 ± 0.92	8.00–10.00	8.87 ± 0.92	8.00–10.00
Weight [kg]	28.27 ± 6.97	19.20–46.70	29.16 ± 8.06	20.20–46.70	27.39 ± 5.83	19.20–38.5
Height [cm]	129.59 ± 8.89	118.00–157.00	131.12 ± 9.83	119.00–157.00	128.07 ± 7.88	118.00–141.00

Note: Values are expressed as mean ± standard deviation (SD).

($p > 0.05$). This showed that the two groups included in the study were not statistically significantly different from each other in terms of all measured parameters and suggested that the two groups were similar to each other.

When the difference between the pre- and post-test values of the CST group was examined, a significant difference was found in right hamstring flexibility ($t(14) = -4.325, p < 0.01, d = 0.97$), 30-s sit up test ($t(14) = -4.092, p < 0.01, d = 1.22$), plank test ($t(14) = -5.667, p < 0.001, d = 1.48$), FMS ($t(14) = -10.132, p < 0.001, d = 2.17$), and static balance scores ($t(186) = 2.845, p = 0.013, d = 0.94$). No significant difference was found in left hamstring flexibility values ($p > 0.05$) (Table 4).

Similarly, a significant difference was found between the pre- and post-test values of right hamstring flexibility ($t(14) = -3.299, p < 0.01, d = 0.73$), 30-s sit up test ($t(14) = -3.374, p < 0.01, d = 0.49$), plank test ($t(14) = -2.436, p = 0.029, d = 0.54$), and FMS ($t(14) = -6.658, p < 0.001, d = 1.51$) of the INT group. The post-test values were higher in these parameters (Table 4). However, no significant difference was found in the left hamstring flexibility values or static balance scores of the INT group ($p > 0.05$) (Table 4).

When the pre- and post-test differences of the variables were compared between the two exercise groups, no significant difference was found ($p > 0.05$) (Table 5).

Table 3. Differences between groups of pre-test measurements

Variables	CST Groups (n = 15)		INT Groups (n = 15)		P Value*
	Pre-test		Pre-test		
Right HF	150.05 ± 9.35		152.07 ± 11.98		0.61
Left HF	147.03 ± 8.92		150.16 ± 14.28		0.48
SUT	11.00 ± 6.14		13.33 ± 6.37		0.32
PT	52.73 ± 35.23		82.73 ± 52.81		0.08
FMS	12.20 ± 1.61		12.33 ± 2.35		0.86
SBS	3.07 ± 0.67		3.05 ± 0.72		0.96

Note: Values are expressed as mean ± standard deviation (SD). HF was measured in degrees, SUT and PT were measured in seconds, FMS and SBS are given as scores. *p* < 0.05 was considered as statistically significant. *p* values were calculated using the independent sample t test. Abbreviations: HF, hamstring flexibility; SUT, 30-s sit up test score; PT, plank test; FMS, Functional Movement Screen; SBS, static balance score.

Table 4. Comparison of mean scores of pre-post test measurements in the two groups

Variables	CST Groups (n = 15)				INT Groups (n = 15)			
	Pre-test	Post-test	*P Inter CST Group	Cohen's <i>d</i>	Pre-test	Post-test	*P Inter INT Group	Cohen's <i>d</i>
Right HF	150.05 ± 9.35	158.17 ± 7.34	0.00	0.97	152.07 ± 11.98	160.00 ± 9.66	0.01	0.73
Left HF	147.03 ± 8.92	151.21 ± 7.54	0.11	0.51	150.16 ± 14.28	154.76 ± 10.96	0.10	0.36
SUT	11.00 ± 6.14	16.87 ± 3.00	0.00	1.22	13.33 ± 6.37	16.80 ± 7.78	0.01	0.49
PT	52.73 ± 35.23	132.27 ± 67.49	0.00	1.57	82.73 ± 52.81	119.93 ± 82.56	0.03	0.54
FMS	12.20 ± 1.61	16.60 ± 2.38	0.00	2.17	12.33 ± 2.35	16.13 ± 2.67	0.00	1.51
SBS	3.07 ± 0.67	2.27 ± 1.00	0.01	0.94	3.05 ± 0.72	2.59 ± 0.96	0.09	0.54

Note: Values are expressed as mean ± standard deviation (SD). HF was measured in degrees, SUT and PT were measured in seconds, FMS and SBS are given as scores. *p* < 0.05 was considered as statistically significant. **p* values were calculated using the paired sample t test. Abbreviations: HF, hamstring flexibility; SUT, 30-s sit up test score; PT, plank test; FMS, Functional Movement Screen; SBS, static balance score.

Table 5. Comparison of mean differences in scores of pre-post test measurements in the two groups

Variables	CST Groups (n = 15)		INT Groups (n = 15)		*P Intra Groups
	Intertest difference Post-test – Pre-test		Intertest difference Post-test – Pre-test		
Right HF	8.13 ± 7.28		7.93 ± 9.31		0.95
Left HF	4.18 ± 9.53		4.60 ± 10.26		0.91
SUT	5.87 ± 5.55		3.47 ± 3.98		0.19
PT	79.53 ± 54.35		37.20 ± 59.13		0.051
FMS	4.40 ± 1.68		3.80 ± 2.21		0.41
SBS	-0.80 ± 1.09		-0.47 ± 1.01		0.39

Note: Values are expressed as mean ± standard deviation (SD). HF was measured in degrees, SUT and PT were measured in seconds, FMS and SBS are given as scores. *p* < 0.05 was considered as statistically significant. **p* values were calculated using the independent sample t test. Abbreviations: HF, hamstring flexibility; SUT, 30-s sit up test score; PT, planks test; FMS, Functional Movement Screen; SBS, static balance score.

Discussion

Physical inactivity in children is a prevailing public health concern and one of the major obstacles to the acquisition of fundamental movement skills [38, 40]. The physical education course and curriculum implemented in schools play a critical role in elevating physical activity levels and promoting the development of fundamental movement skills in children [15]. The course content holds particular importance for the active engagement of disadvantaged children in regular physical activity. At this point, designing effective training programs that enhance physical fitness in children and incorporating them into physical education course curricula is essential. Consequently, this study aimed to evaluate the effects of CST and INT programs added to the physical education curriculum on children living in rural areas. The absence of existing literature examining the effects of CST and INT highlights the uniqueness of our study. The study revealed the 8-week effects of CST and INT programs on physical fitness parameters, including functional mobility, balance, hamstring muscle flexibility, and core stability, in children aged 8-10 years residing in rural areas. The findings indicated that both CST and INT programs improved functional mobility, right hamstring flexibility, and core stability among the children. Effect sizes showed that the INT program had a small effect on sit-up strength, a medium effect on right hamstring flexibility, a medium effect on time in plank, and a large effect on functional mobility. The CST program exhibited a large effect on these parameters. Moreover, CST resulted in a significant improvement in static balance levels, while INT showed no effect on static balance.

The core serves as the responsible region for transferring force to the extremities, essential for cultivating correct functional movements in both the upper and lower extremities. It is important to stabilize the core in children to perform proper movement patterns [30, 35]. INT has been proven to improve curl-up results in children [19, 20]. Several studies have shown that integrated neuromuscular training (INT) programs improve abdominal and upper body strength [8, 15, 18, 39, 50]. This study confirmed that INT had a positive impact on core stability, which overlaps with existing literature. However, when the effect size of INT on core stability was examined in the study, it was found to have a small effect on improving 30-s sit-up results and a moderate effect on improving plank time. Again, in the current study, the effect of CST on these two parameters was high compared to INT. CST is widely recognized as a primary training type for core stability development [2]. Studies have shown that core stabilization exercises increase abdominal muscle strength and endurance in children [4, 27, 29] and provide improvement in plank

time [53]. This study established that both training types improved core stabilization in children, although the CST had a greater effect. However, it is recommended that CST programs be preferred first for core stability development.

Balance is considered a fundamental motor characteristic for the growth and development of children [55]. Improving balance enhances movement efficiency and reduces the risk of injury [26]. Nevertheless, Faigenbaum et al. [20] found that INT did not affect balance development in children while core stability training has been shown to improve both static and dynamic balance [1, 48]. Studies have shown that CST improves balance in children [25, 27, 32]. Consistent with existing literature, this study found that INT did not affect static balance in children, while CST improved it. CST exercises can be given priority in children for the development of static balance.

Functional mobility is essential for movement development in children and is closely linked to flexibility, which is a parameter that facilitates mobility formation in children. Alonso-Aubin et al. [5] reported that INT application increases the level of functional mobility in children, potentially attributed to neural plasticity. CST has been similarly found to increase functional mobility in children [12]. Both integrated neuromuscular and core stability training have been associated with positive effects on flexibility [19, 31]. The current study demonstrated that INT and CST applied within the scope of physical education lessons have a high level of effect on functional mobility in children. In addition, it was concluded that CST contributes to the improvement of flexibility at a high level and INT at a moderate level. In conclusion, CST and INT can be preferred in the development of flexibility and functional mobility in children, but if further development of flexibility is desired, CST may be more effective. In this study, only right hamstring flexibility was examined as flexibility. We recommend that the effects of CST and INT programs on flexibility be examined more comprehensively in future studies.

The adaptation and implementation of INT programs in physical education classes is recommended for the development of basic movement skills and physical fitness in children [36]. Within the scope of this study, the effects of INT and CST programs on children in physical education classes were comparatively analyzed. Previous studies on the effect of INT on children have primarily focused on INT programs lasting 15 to 20 minutes [5, 19, 20, 23]. However, this study investigated the effects of prolonged INT and CST with a training duration of 40 minutes. This situation suggests that use of prolonged training duration by physical education teachers may cause problems in practice. In this context, it is recommended that the short-term effects of INT and CST should be examined in future studies and short-term protocols should be created. Thus, the implementation of these programs in physical

education classes may become easier and their placement in curricula may be facilitated.

Limitation and recommendation

As seen in the study, both INT and CST added to the physical education curriculum had positive effects on physical fitness and functional mobility in children, which is consistent with the existing literature. However, the study has certain limitations. One session of INT and CST programs used in the study was planned as 40 minutes. However, it may not be possible in practice to apply these programs for the whole duration of a physical education lesson. The short attention span of children and the large number of children in a class make this situation difficult. To transfer these programs to physical education curricula, it is suggested that shorter programs should be planned with further studies. In addition, long-term effects need to be observed to add the exercises to the curriculum for the whole term. It is also recommended to implement these programs in the long term and determine their effects in similar studies. In addition, the fact that the sample of the study is limited to the Samanlı district of Yalova province can be considered as a limitation. It may have resulted in a low or medium effect size of the INT program on the measured parameters. Therefore, it is recommended to conduct similar studies with a larger sample size to enhance the generalizability of the results. Another limitation of the study is that the effect of flexibility was analyzed only for right hamstring flexibility. It is recommended that future studies should examine the effect of INT and CST programs on flexibility more comprehensively.

Conclusion

The study findings suggest that both CST and INT programs implemented in physical education lessons can improve functional mobility, flexibility, and core stabilization in children. Notably, CST has a greater effect on the development of these parameters compared to INT. Additionally, CST can also contribute to the development of static balance in children. Based on these results, it is recommended that both CST and INT be incorporated into the curriculum of physical education lessons. Both training models can provide physical fitness and functional mobility development for disadvantaged children residing in rural areas in terms of physical activity participation. This approach can create equal opportunities for them. The choice between the two training models may depend on the physical fitness component to be developed in children: The results show that the effects of CST on other parameters except functional mobility were larger than those of INT, and only CST had a positive effect on static balance. For example, if the goal is to improve balance,

the CST program is recommended. Future studies should explore the separate and combined effects of CST and INT in a more extensive sample group. To facilitate the integration of these programs into the curriculum for physical education lessons, it is suggested to shorten their duration to only 15–20-minute sessions in each physical education class and that one-term training programs be prepared. Certified athletic trainers, primary school physical education teachers, and physiotherapists should collaborate to design, implement, and evaluate training interventions specifically developed to improve physical fitness and prevent injuries during physical activity in children.

Conflict of interest: Authors state no conflict of interest.

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