## RESEARCH



# Effects of a school-based physical activity intervention on mental health indicators in a sample of Brazilian adolescents: a cluster randomized controlled trial

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## Abstract

**Purpose** To test the effects of a physical activity intervention program on symptoms of mental disorders among adolescents.

**Methods** This study is a 12-week cluster randomized controlled trial. The sample consisted of 306 adolescents (45,8% male, age: 13,6 [0,72] years; 54.2% female, age: 13.5 [0.69] years), randomized into an intervention group (N=165) and a control group (N=141). The physical activity program involved sessions including muscle strengthening and cardiorespiratory exercises and lifestyle guidance. The mental health indicators analyzed were: anxiety, depression, sleep, and psychological well-being. Intervention effects were analyzed by generalized estimating equations.

**Results** After 12 weeks, no significant improvements were observed in the intervention group for sleep; anxiety; depression, and psychological well-being. In the subgroup analysis, significant group×time interactions were observed for adolescents who were classified with moderate symptoms of depression (mean difference: -0.97, p=0.002) and anxiety (mean difference: -3.03, p=0.01) with favorable effects for intervention group.

**Conclusion** After the 12-week intervention period, it can be concluded that 12 weeks of school-based physical activity intervention significantly reduced symptoms of anxiety and depression in adolescents with moderate/severe symptoms. Furthermore, the intervention contributed to the maintenance of psychological well-being, since the control group showed a significant reduction in this mental health indicator.

Keywords Physical exercise, Lifestyle, Anxiety, Depression, Adolescence

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## Background

Mental health is defined as a state of well-being and effective functioning in which an individual realizes their abilities, is resilient to life's stresses, and can make a beneficial contribution to his or her community, such as social action, cultural and social development [1]. Presenting good mental health is relevant to overall health and it is associated with decreased morbidity and mortality [2, 3, 4]. Adolescence represents a period of rapid growth and development, characterized by neuronal plasticity [5], self-concept formulation [6], and the establishment of behavioral patterns [7]. Hence, mental disorders developed in childhood and adolescence may result in short- and long-term consequences, including reduced quality of life, psychiatric and somatic comorbidity, disability, loss of work, and reduced life expectancy [8],

Some behaviors may have positive impacts on young people's mental health. Findings from observational studies suggest that participation in physical activity (PA) and decreasing sedentary behavior can improve adolescents' mental health [9, 10]. Scientific literature describes that the positive effects of PA on mental health can occur through three mechanisms: neurobiological, psychosocial and behavioral [11]. The neurobiological mechanism hypothesis proposes that participation in physical activity improves cognition and mental health through changes in the structure and functional composition of the brain, such as: neurotrophin gene, and protein expression; grey matter volume and activation and release of endogenous opioids, as well as the synthesis and bioavailability of neurotransmitters, such as dopamine, noradrenaline and serotonin. The psychosocial mechanism hypothesis recognizes that physical activity provides an opportunity for social interaction (relatedness), mastery in the physical domain (selfefficacy and perceived competence), improvements in appearance self-perceptions (body image), and independence (autonomy). Finally, the behavioral mechanism hypothesis proposes that changes in mental health outcomes resulting from physical activity are mediated by changes in relevant behaviors and associated with improved sleep duration, sleep efficiency, sleep onset latency and reduced sleepiness [11].

School- based PA inteventions has potentially beneficial effects for reducing symptoms of mental disorders on adolescents. A 8-week randomized controlled trial [12] found improvements in psychological well-being. Similarly, a 12-week intervention during physical education classes [13] resulted in a 41% reduction in depressive symptoms in the intervention group (IG). However, Åvitsland et al. [14] in a 29-week PA program and Smith et al. [15] in a 10-week resistance program, did not find changes on adolescents' mental health indicators. A possible explanation for the inconsistency between the results may be the type of intervention used, as well as the weekly frequency of the interventions. Since there is no current consensus if PA in the school context might improve adolescents 'mental health, additional intervention studies are needed to confirm these findings.

Given the increase in the prevalence of adolescents with mental disorders (mainly anxiety and depression) and the reduction in PA practice, in part due to the COVID-19 pandemic [16, 17], PA interventions are needed. The promotion of PA to maintain and/or improve adolescents' mental health indicators is vital, especially in South American countries with low economic development such as Brazil, where research addressing physical activity interventions in the school environment on mental health indicators is scarce [18]. In Brazil, it is estimated that 26.7% of adolescents aged between 12 and 14 years have some kind of mental disorder [19]. Furthermore, COVID-19 has negatively impacted adolescents mental health, with an increased number of young people with anxiety, depression and sleep disorders [17, 20].

Thus, the main objective of the current study was to determine the effects of a 12-week school-based PA program on mental health indicators (anxiety, depression, psychological well-being and sleep) in school-aged adolescents. Since the practice of PA might be effective for adolescents with higher symptoms of mental disorders [21], the secondary objective was to evaluate the effects of the PA program among subgroups of adolescents with different levels of anxiety and depressive symptoms (normal, light, or moderate/severe) at baseline. The current study hypothesizes that adolescents in the intervention group will show significant improvement on mental health indicators after 12 weeks of a PA program.

## Methods

## Study design

This study adopted a 12-week randomized controlled trial design, following Consolidated Standards of Reporting Trials (CONSORT) recommendations [22]. The trial was approved by the human research ethics committee of the States University of Northern of Parana, Brazil (n° 4.452.513) and registered in the protocol of Clinical Trials (NCT05070377, 7/10/2021).

The secondary public schools in City, Brazil, including students from 12 to 15 years old (i.e., Grades 8th and 9th) were eligible to participate of the study. The schools were recruited through a list provided by the Regional Education Center. Then, emails were sent directly to eligible schools. Since the schools had expressed interest in the study, a member of the research team met with the school agent and explained the study requirements.

The inclusion criteria for schools were: being a public secondary school and having at least one class in the 8th and 9th grades, and Physical Education classes twice a week. Of the 6 eligible public secondary schools, 4 agreed to participate in the program and were randomized allocated to either a control or an intervention condition by an independent researcher using a computer-based random number generator. Eligible participants were grade 8 or 9 adolescents of both sexes aged between 12 and 15 years.

For this trial, sample size calculation was based effect size of 0.10, power of 90%, a 5% level of significance and correlation was assumed as 0.03. Considering an assumed attrition of 20%, a minimum of 300 students was required. Considering that each school class has approximately 25 students, 6 classes were randomized from each group, totaling 150 students in each condition (intervention and control).

A total of 306 students were included in the data analysis. The adolescent participants, as well as their parents/ guardians, were provided with information about the aims of the investigation and gave informed written consent. The data were collected at 2-time points (baseline [March 2022] and post-intervention [July 2022]). Flow of participants throughout the study is shown in Fig. 1.

#### Physical activity intervention

The PA program (*ActTeens Program*) was based on the Resistance Training for Teens program [23]. The PA intervention included two components: (a) structured PA sessions delivered within Physical Education (PE); and (b) healthy lifestyle guidance via mobile health (m-Health). During the implementation process, the PA program workshop (ActTeens Program) was held for PE teachers and staff, which covered all aspects of the intervention (see supplementary Table 1).

The structured PA sessions were implemented over 12 weeks and delivered within PE lessons, twice a week, for 20 min per lesson. The structured PA session was designed for satisfying participants' basic psychological needs which include autonomy, competence, and relatedness of the students, and to promote autonomous



Fig. 1 Flow of participants throughout the study

motivation and self-efficacy for PA [24]. They consisted of a combination of muscle-strengthening and aerobic exercise, following standardized sections: (i) warm-up including movement-based games (3 min); (ii) structured PA (15 min); and (iii) cool-down, including static stretching (2 min). In each session, participants were free to choose their own groups (i.e., groups of 4-5 people) and were free to choose the sequence of exercises they would like to perform (i.e., 4–5 exercises), using a variety of cards, incorporating aerobic and resistance exercises. At the end of the structured PA session, the adolescents were asked to report the intensity immediately after the last exercise of the session using Borg's rating of perceived exertion scale [25]. The structured PA sessions were led by the Actteens Program Staff together with the Physical Education teacher. Details about the structured PA sessions have been previously described [26].

Guidance on healthy behavior was provided through weekly messages, comprising video or infographic, utilizing the WhatsApp<sup>\*</sup> app. These messages were disseminated to both adolescents (twice a week) and their parents (twice a month), emphasizing social support. The content of the messages was tailored to promote and encourage active behavior while offering guidance on healthy eating habits.

## **Control group**

Adolescents and their parents in the control group (CG) received the same messages about healthy behavior by WhatsApp<sup>®</sup> as the intervention group and were guided to maintain their usual PA practice.

## Measures and data collection

All assessments were conducted in the school by trained research assistants, who were blinded to group allocation at all time points (baseline and post-intervention). Self-report information was assessed using specific questionnaires. Measurements of weight (kg) and height (cm) followed a standardized process and were performed by qualified staff. The weight was measured to the nearest 0.1 kg using a standardized scale, and height was measured to the nearest 0.1 kg using a standardized scale, and height was measured to the nearest 0.1 cm using a stadiometer (Welmy<sup>\*</sup>, São Paulo, Brazil). BMI was calculated by equation [BMI = weight (kg)/height (m<sup>2</sup>)].

The data collection procedure was organized in the following order: (1) anthropometric assessments; (2) sociodemographic information (i.e., sex, age, level of education), and (3) survey about anxiety, depression, wellbeing, and sleep.

#### Implementation and reach

A process evaluation was conducted, which included: (1) implementation of the intervention (number of structured AP sessions that were conducted); (2) reach (number of students who agreed to participate in the program).

## Primary outcome: Mental health Anxiety and depression

The anxiety and depression symptoms were assessed using the *Depression, Anxiety, and Stress Scale - Short Form* (DASS-21) [27] which is validated for Brazilian adolescents [28]. The DASS-21 is a self-report assessment that comprises 21 questions and contains three subscales scored on a four-point scale each, ranging from 0 (not at all) to 3 (almost always), where lower score is better. For this study, only the depression and anxiety subscales were used. The DASS-21 questionnaire presents values that indicate reliability of the factorial structure of r = 0.83 for anxiety and r = 0.90 for depression [28].

## Psychological well-being

The psychological well-being was measured using a a 7-item subscale of the KIDSCREEN-27 questionnaire, which is validated for Brazilian adolescents [29]. For each item, participants responded using a scale with scores ranging from one to five, where higher score is better.

#### Sleep

The sleep score was calculated using the items in the Pittsburgh Sleep Quality Index (PSQI) [30], validated for Brazilian adolescents [31]. The PSQI includes 19 questions, categorized into seven groups (i.e., sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications, and day-time dysfunction). Each constituent question produces a score on a 4-point Likert-type scale (from 0 to 3), where lower score is better.

#### **Control variables**

We used sex, age, somatic maturation, and PA as control variables. Somatic maturation was estimated through the evaluation of somatic maturation by determining the distance in years of the individual from the baseline peak height velocity (PHV) using sex-specific mathematical models [32].

PA practice was assessed using the *Physical Activity Questionnaire for Adolescents – PAQ-A*, which consists of eight questions structured to discern low (score 1) to high (score 5) PA during the last seven days. The total score of this questionnaire was calculated by adding all questions' average scores. This instrument was adapted and validated for Brazilian adolescents [33].

## Statistical analyses

The general characteristics of the participants were presented using mean and standard deviation for continuous variables and absolute and relative frequency for

 Table 1
 General characteristics of the sample at the time of baseline

Variables	Intervention	Control group	Total	
	group ( <i>n</i> = 165)	( <i>n</i> =141)	( <i>n</i> =306)	
Age (years)	$13.5 \pm 0.71$	13.6±0.66	13.5±0.69	
Male n, (%)	79 (47.9)	61 (43.3)	140 (45.8)	
Female n, (%)	86 (52.1)	80 (56,7)	166 (54.2)	
Weight (kg)	$55.7 \pm 14.1$	$54.2 \pm 14.3$	$55.0 \pm 14.2$	
Height (cm)	$162.5 \pm 0.07$	161.9±0.07	161.9±0.07	
BMI (kg/m²)	$20.8 \pm 4.6$	$20.8 \pm 4.6$	$20.8 \pm 4.6$	
PHV (years)	$0.61 \pm 0.81$	$0.64 \pm 0.79$	$0.63 \pm 0.80$	
PA (score)	$2.3 \pm 0.66$	2.2±0.71	$2.3 \pm 0.69$	

BMI: Body mass index; PA: Physical activity; PHV: Peak height velocity.

categorical variables. The Kolmogorov-Smirnov test was used to verify data normality. Groups were compared using Student's t-tests at baseline, a bias corrected and accelerated (BCa) bootstrap method with 1000 samples was used. To analyze the effect of the intervention program on the mental health indicators, generalized estimating equations (GEE) models were used. The GEE models were constructed for each outcome, and the guasi-likelihood corrected by the model independence criterion (QICc) was used to evaluate the fit of the model to the data, with lower QICc indicating a better model fit. The analyzes were adjusted for class cluster and for the following variables: sex, age, PHV as well PA (difference score between post- and pre-intervention). Likewise, according to the methods described above, GEE models were constructed for each subgroup of anxiety and depression symptoms according to the cutoff points: normal (percentile: 0-78th); mild (percentile: 78-87th) or moderate/severe (percentile: > 87th) proposed by Lovibond and Lovibond (2004) [34]. Statistical analyzes were performed with intention to treat. Cohen's d was also calculated (adjusted difference between the intervention and control groups over time divided by the pooled SD of change) and interpreted as follows: d = 0.2, d = 0.5, and d = 0.8, considered as small, medium, and large effect sizes, respectively [35]. The data obtained were entederd in an Excel program and the analyses were performed using the statistical software package *Statistical Package for the Social Sciences* Version 20 (IBM, New York, NY, USA), with significance set at p < 0.05.

## Results

In total, 306 adolescents (166 females, age = 13.5[0.69] years) completed the baseline assessments. Overall, the structured sessions were delivered in 83.3% of PE lessons and the reach of the ActTeens intervention was 85.2% (306/359). The baseline characteristics of the study sample are presented in Table 1, no statistically significant difference was found between the groups.

The comparisons of mental health indicators in IG and CG at baseline and post 12 weeks are shown in Table 2. We did not observe a significant difference for sleep, anxiety, depression, and psychological well-being in the IG in comparison to baseline values. In the CG, we found a significant reduction in psychological well-being score (mean difference: -1.65, p=0.003) after 12 weeks. Furthermore, a significant group×time interaction was observed in the psychological well-being score (mean difference: 1.65, p=0.02).

Sub-group analyses for the anxiety and depression symptoms were conducted (Table 3). After 12 weeks of intervention, there was a significant reduction in depression symptoms (mean difference: -0.83, p=0.001) for adolescents of IG who were classified with higher symptoms. There was a significant increase in anxiety symptoms (mean difference: 2.10, p=0.004) for adolescents

 Table 2
 Mental health indicators in intervention and control group at baseline and 12 weeks

	Group	Baseline mean (Cl95%)	12 weeks mean (Cl95%)	Changed over time		Group x time interaction <sup>a</sup>		Cohen´s d
				Mean <sup>†</sup>	р	β (SE)	р	-
Sleep	IG	4.1 (3.6; 4.6)	4.5 (4; 5)	0.40	0.130	0.71	0.060	0.22
	CG	5 (4.3; 5.6)	4.7 (4.1; 5.2)	-0.31	0.260	(0.38)		
Anxiety	IG	4.4 (3.5; 5.2)	4.8 (3.9; 5.7)	0.48	0.230	0.11	0.850	0.02
	CG	4.9 (3.9; 5.9)	5.3 (4.3; 6.3)	0.37	0.410	(0.61)		
Depression	IG	4 (3.3; 4.7)	4.5 (3.7; 5.2)	0.44	0.170	0.009	0.980	0.01
	CG	4.4 (3.5; 5.4)	4.9 (4; 5)	0.44	0.340	(0.57)		
Psychological	IG	24 (22.8; 25.2)	24 (22.9; 25.1)	0.00	0.990	1.65	0.020#	0.26
well-being	CG	24.6 (23.2; 26.1)	23 (21.8; 24.2)*	-1.65	0.003*	(0.75)		

IG; Interventiom group; CG: Control group; CI95%: Confidence interval; β: Beta values standardized; SE: Standard error;

values adjusted for physical activity, PHV and sex;

<sup>a</sup>: the values of intervention group is a reference

<sup>†</sup>difference of means: Follow-up - baseline

\*p<0.05 intragroup significant difference compared to baseline value

 $p^* < 0.05$  significative interaction group x time

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		Baseline mean (Cl95%)	12 weeks mean (CI95%)	Changed over time		Group x time interaction <sup>a</sup>		Cohen's
				Mean <sup>†</sup>	p	β (SE)	p	<sup>–</sup> d
Anxiety								
Normal	IG (82)	2.3 (1.9; 2.8)	2.2 (1.7; 2.7)	-0.17	0.500	-0.33 (0.38)	0.390	0.14
	CG (66)	1.9 (1.4; 2.5)	2.1 (1.6; 2.6)	0.15	0.570			
Light	IG (10)	8.3 (7.9; 8.7)	8.1 (7.7; 8.5)	-0.19	0.360	-0.24 (0.32)	0.440	0.39
	CG (6)	8.5 (8;8.9)	8.5 (8.2; 8.8)	0.05	0.810			
Moderate	IG (54)	14.5 (13; 15.9)	13.6 (12.3; 14.9)	-0.87	0.360	-3.03 (1.21)	0.010#	0.50
/severe	CG (47)	12.3 (11.3; 13.3)	14.4 (13.3; 15.6)	2.1	0.004*			
Depression								
Normal	IG (92)	2.7 (2; 3.3)	2.9 (2.2; 3.6)	0.22	0.390	0.33	0.450	0.11
	CG (75)	2.7 (1.9; 3.5)	2.6 (1.9; 3.4)	-0.10	0.770	(0.44)		
Light	IG (17)	11.3 (10.7; 12)	10.9 (10.2; 11.6)	-0.44	0.100	-0.83 (0.46)	0.070	0.22
	CG (10)	11.2 (10.5; 12)	11.7 (11; 12.3)	0.38	0.300			
Moderate	IG (41)	15 (15; 15)	14.1 (13.7; 14.5)	-0.83	0.001*	-0.97 (0.31)	0.010#	1.11
/severe	CG (41)	14.7 (13.9; 15.5)	14.8 (14.6; 15.1)	0.13	0.600			

IG; Interventiom group; CG: Control group; Cl95%: Confidence interval; β: Beta values standardized; SE: Standard error;

values adjusted for physical activity, PHV and sex;

<sup>a</sup>: the values of intervention group is a reference

<sup>†</sup>difference of means: Follow-up - baseline

\*p<0.05 intragroup significant difference compared to baseline value

<sup>#</sup>p < 0.05 significative interaction group x time

of CG who were classified with higher symptoms. Significant group×time interaction were observed for adolescents who were classified with higher symptoms of depression (mean difference: -0.97, p = 0.002) and anxiety (mean difference: -3.03, p = 0.01). with favorable effects for the IG.

## Discussion

The current study aimed to assess the effects of 12 weeks of a school-based PA program on adolescents' mental health indicators. In adolescents with moderate depressive symptoms at baseline, a significant decrease in depressive symptoms was found post-intervention. This result demonstrates the importance of PA for adolescents with higher symptoms of depression and anxiety, adding support to the use of PA as an effective treatment for adolescents with mental health disorders. Regarding the group x time effect, a significant reduction in the psychological well-being of the CG was observed after 12 weeks, while the IG showed no significant changes, demonstrating that the intervention could help in maintaining psychological well-being.

Scientific evidence have shown that physical activity interventions might have beneficial effects on adolescents mental health [36], however, these effects seem to be more pronounced in adolescents who present a clinical diagnosis of depression at the beginning of the interventions [37]. In this perspective, PA may be particularly helpful in children and adolescents with elevated depressive symptons [21]. Regular physical exercise promotes physiological changes (release of neurotransmitters and hormones) that provide beneficial effects on anxiety and depressive symptoms [38]. Besides physiological changes, the psychological mechanisms (distraction hypothesis and social interaction) can be taken into consideration [39]. Thus, the social interaction promoted during groupbased PA can lead to beneficial results in mental health indicators [38], however, in the present study, social interaction between adolescents was not evaluated, making it impossible to associate the results of the intervention with psychological mechanisms. Additionally, in the present study, the activities proposed during PE classes were carried out in groups, enabling greater interaction between students. Furthermore, the possibility of choosing the exercises performed and the order in which they were performed made the sessions more enjoyable. At the end of the program, 74.1% of the intervention group thought their overall satisfaction with the program was good or excellent, and 58.2% thought the sessions were fun and enjoyable (data not shown).

Although regular PA practices are effective in providing beneficial effects on the psychological well-being of children and adolescents [40] no significant changes were observed in this mental health indicator of adolescents of IG in the current study. However, a significant decrease (worsening) in the values of psychological wellbeing of adolescents between the moments (p < 0.05) was observed on CG. Psychological well-being refers to an individual's perception of their success in relationships, self-esteem, life purpose and optimism [41]. Therefore, activities that aim to improve individual's basic psychological needs (autonomy, competence, and relationships make them more likely to feel that they are achieving their goals (that is, to experience greater psychological well-being). Thus, the improvement or maintenance of psychological well-being can be mediated through the enhancement of basic psychological needs [42].

Sleep plays an important role in health promotion [43]. However, in the present study, no significant differences were found in sleep scores after the 12-week intervention period in both groups. Scientific evidence reports that PA interventions improve this indicator in adolescents, in whom increasing the number of daily steps can have a great effect on improving sleep quality [44], just as resistance exercise interventions can promote significant improvements in sleep quality, total sleep duration, and a significant reduction in daytime sleepiness [45]. The mechanism that explains the effect of regular PA on sleep is based on the hypothesis of energy conservation and body restoration theories, which postulate that changes in sleep may be due to the depletion of body energy and tissue damage that occurs during exercise, which recovers with sleep [46]. In addition, regular PA effects on sleep are associated with circadian rhythm, metabolic, immunological, and thermoregulatory effects [47, 48], and vascular and endocrine effects [49].

The inclusion of muscle-strengthening exercises combined with aerobic exercise is easily applicable, since these activities have a duration of approximately 20 min, with great potential for insertion in schools [50]. Thus, the strategy used within the school environment in the current study presents a relevant applicability, since it does not change the curricular structure of the subject.

Even knowing the importance of PA in promoting adolescent health, the control absence of the intensity of structured PA performed during PE classes should be pointed out as a limitation of this study. In addition, no objective method was used and mental health indicators were assessed by self-reported methods, which may be subject to recall bias. Furthermore, this study was carried out with a sample from one city, so caution is needed when generalizing the findings. On the other hand, the strengths of this research should be highlighted, such as the low sample loss (3,5%), which is very common in school-based trials, as well as its applicability, as it indicates the importance of implementing interventions with strategies that encourage active behavior, creating new opportunities for this population without radically modify the curriculum content of PE classes.

## Conclusion

After the 12-week of a school-based physical activity intervention we found a significant reduction on anxiety and depression symptoms in adolescents with moderate/ severe symptoms. Furthermore, the physical activity intervention was important for maintaining psychological well-being for the IG, since the CG showed a significant reduction in psychological well-being. Further studies should be conducted using strategies proposed in the ActTeens with objective control of the intensity of the structured activities delivered within PE lessons, as well the influence of contextual factors on mental health indicators in adolescents.

## **Supplementary Information**

The online version contains supplementary material available at https://doi.or g/10.1186/s12889-025-21620-y.

Supplementary Material 1

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#### Author contributions

Jadson M. Silva: Conceptualization, Investigation, Writing – Original Draft, Writing – Review & Editing, Supervision. Géssika C. Santos: Conceptualization, Methodology, Formal analysis, Investigation, Writing – Original Draft, Writing – Review & Editing, Supervision. Rodrigo O. Barbosa: Conceptualization, Investigation, Writing – Review & Editing. Thais M. S. Silva: Conceptualization, Investigation, Writing – Review & Editing. Renan C. Correa: Conceptualization, Investigation, Writing – Review & Editing Bruno G. G. Costa: Conceptualization, Writing – Review & Editing. Sarah G. Kennedy: Conceptualization, Writing – Review & Editing. Antonio Stabelini Neto: Conceptualization, Methodology, Formal analysis, Writing – Original Draft, Writing – Review & Editing, Supervision.

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#### Data availability

Data will be available from the corresponding author on reasonable request.

#### Declarations

#### Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Human Research Ethics Committee of the State University of Northern of Parana, Brazil (n°: 4.452.513). All procedures applied in the research study were in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants and their literate legal guardian.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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