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Effects of a recreational physical activity and healthy habits orientation program, using an illustrated diary, on the cardiovascular risk profile of overweight and obese schoolchildren: a pilot study in a public school in Brasilia, Federal District, Brazil

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Introduction: Educative strategies need to be adopted to encourage the consumption of healthy foods and to promote physical activity in childhood and adolescence. The effects of recreational physical activity and a health-habit orientation program using an illustrated diary on the cardiovascular risk profile of overweight and obese children was investigated.

Methods: The weight and height of 314 schoolchildren aged between 9 and 11 years old, in a public school in Brasilia, Federal District, Brazil, were recorded. According to the body mass index (BMI) classification proposed by the World Health Organization, 84 were overweight or obese for their age and sex. Of these children, 34 (40%) participated in the study. Students were divided into two groups matched for sex, age, BMI, percent body fat (%BF): the intervention group (IG, n = 17) and the control group (CG, n = 17). The IG underwent a program of 10 weeks of exercise with recreational activities and health-habit orientation using an illustrated diary of habits, while no such interventions were used with the CG during the study period. Before and after the intervention, the children's weight, height, BMI, %BF, waist circumference (WC), maximum oxygen intake (VO_{2max}), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, glucose, eating habits, and physical activity level (PAL) were assessed. In analyzing the data, we used descriptive statistics and paired and unpaired *t*-tests, using a significance level of 0.05. For assessment of dietary habits, a questionnaire, contingency tables, and the chi-squared test were used, with <0.05 set as the significance level.

Results: After 10 weeks of intervention, the IG showed a reduction in BMI (pre: 22.2 ± 2.1 kg/m^2 versus [vs] post: 21.6 ± 2.1 kg/m^2, $P < 0.01$); WC (pre: 70.1 ± 6.1 cm vs post: 69.1 ± 5.8 cm, $P < 0.01$); %BF (pre: 29.2% ± 4.6% vs post: 28.0% ± 4.8%, $P < 0.01$); systolic blood pressure ($P < 0.01$); VO_{2max} ($P = 0.014$); TC ($P < 0.01$); LDL ($P < 0.01$); triglycerides ($P < 0.01$); and intake of candy ($P < 0.01$) and soda drinks ($P < 0.01$), while an increase in the consumption of fruit ($P < 0.01$) and PAL ($P < 0.01$) were observed. The CG did not show any change in the health parameters assessed.

Conclusion: The program was effective in reducing risk factors for cardiovascular disease and the use of an illustrative diary may have been the key to this result, since students were motivated to change their poor eating habits and to increase their physical activity level.

Keywords: obesity, cardiovascular disease, physical activity level, body mass index, risk factor, motivation, children, change of habits

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Introduction

Worldwide, obesity is considered to be the epidemic of twenty-first century, and is related to the development of insulin resistance and diabetes, as well as to the predisposition to increases in serum levels of cholesterol and systolic blood pressure (SBP) and diastolic blood pressure, which are risk factors for cardiovascular disease (CVD).[1]

An analysis of Korean teenagers found that levels of total cholesterol (TC) increased significantly with increasing body mass index (BMI).[2] Furthermore, Reinehr et al[3] in Germany and May et al[4] in the USA found that obese children, when compared with those of normal weight, had higher concentrations of low density lipoprotein (LDL) and lower concentrations of high density lipoprotein (HDL). In Brazil, a positive correlation of waist circumference (WC) and BMI, with blood pressure was observed in schoolchildren in Taguatinga, Federal District.[5]

Data from the *VIGITEL Brasil 2011: Vigilância de Fatores de Risco e Proteção para Doenças Crônicas por Inquérito Telefônico* [Surveillance of risk and protective factors for chronic diseases by telephone survey][6] revealed that the proportion of overweight persons in Brazil had increased, from 42.7% in 2006 to 48.5% in 2011, while the percentage of obese persons increased from 11.4% to 15.8%. In the Federal District, in the same period, the percentage of the population that was overweight or obese increased from 39.8% to 49.2% and from 10% to 15%, respectively.[6] These data show that strategies should be implemented to curb and reduce weight gain in this population.

A way to prevent obesity in adulthood is to treat childhood overweight and obesity. Once excess weight is present in childhood and adolescence it tends to persist in older ages.[7] Further, atherosclerosis and arterial hypertension, pathological processes that start in childhood; life phase; eating habits; physical activity level (PAL); and environmental factors are determining the increase in obesity prevalence.[8]

Educative strategies should be adopted to encourage the consumption of healthy foods and to promote physical activity in childhood and adolescence. The school environment is a good place to promote a healthy lifestyle, because this is a place of intense social interaction and is appropriate for educative activities.[9] In particular, school physical education classes represent particularly suitable venues for dissemination of information, discussion, and reflection on healthy habits.

In this regard, our group has created a learning tool for use in physical education classes called an "illustrative diary" that aims to promote knowledge that will motivate students to adopt a healthy diet and to reduce sedentary behavior (watching television, playing video games, and computer use).[10] The instrument consists of a paper pad with blank squares representing each day of the week, which the students fill with figures representing their activities during the day concerning nutrition, physical activities, and sedentary behaviors. Thus, the aim of the study reported here was to evaluate the effects of a program of recreational physical activities, associated with the use of the illustrative diary, on the cardiovascular risk profile of overweight and obese schoolchildren.

Methods

Study design and sample selection

This was a pilot study with experimental delimitation conducted in Classe 46 School in Ceilândia, Federal District, Brazil. Students born between 2001 and 2003 enrolled in that school were invited to have their height and weight assessed to identify those overweight and obese for inclusion in the study. A total of 314 students attended the evaluations, of whom 84 were classified as overweight (≥85th and <95th percentile) and obese (>95th percentile) for their age and sex according to the World Health Organization's BMI classification.[11]

From the 84 children classified as overweight and obese, 34 (40%) consented to participate in the study and they were organized into two homogeneous and internally heterogeneous groups, between them, with the same number of participants, and number of males and females in each. The intervention group (IG), which comprised eight male and nine female participants, submitted to a program of recreational physical activity and orientation to healthy lifestyle using the illustrative diary, while the control group (CG), again comprising eight male and nine female participants, continued with their daily normal activities.

The parents of the schoolchildren signed informed consent in accordance with Brazilian Resolution 196/96. The research was approved by the Ethics Committee of the Catholic University of Brasilia (protocol CAAE07297412.4.0000.0029).

Evaluations

Pubertal development, weight, height, WC, cardiorespiratory fitness, blood pressure, and biochemical parameters (fasting glucose [FG], TC, LDL, HDL, and triglyceride [TG] levels) were assessed and skinfold measurements taken. In addition, the level of physical activity and eating habits were measured before and after intervention.

To measure body weight, the adolescents, wearing school uniform and barefoot, were positioned standing on a Wiso scale, model W721 (Wiso, Sportive Technology, Florianopolis, Brazil) with digital display and 100 g of precision while being asked to keep still and stand erect in the middle of the scale, with their arms along their body. For evaluation of stature, a Sanny compact stadiometer, model ES:2040 (Sanny – American Medical do Brasil, Ltda, São Bernardo do Campo, Brazil) fixed on a wall without a gap, accurate to 1 mm, was used with the teenagers barefoot and leaning against the wall, heels together, hands relaxed along the body, and head adjusted in the Frankfurt plane. BMI was determined using the formula: weight in kg/m^2). The cutoff points proposed by the World Health Organization classification were used.[11]

For evaluation of WC, a Sanny fiberglass tape with a precision of 1 mm was used. The measurement was taken from the lower circumference, located midpoint between the last rib and iliac crest. Tricipital (TR) and subscapular (SB) skinfolds were measured with a Lange Skinfold Caliper skinfold compass (Santa Cruz, CA, USA) with resolution of 5 mm. For measurement of the triciptal, the compass was placed on the back of the right arm of the adolescent, at the midpoint between the lateral projection of the acromion process and inferior margin of the olecranon. The subscapular was measured 1 cm below the inferior angle of the scapula. The %BF was estimated from the results of the sum of the TR and SB using Boileau et al's equation.[12]

Cardiorespiratory fitness, expressed as maximum oxygen uptake (VO_{2max} [$mL \cdot kg^{-1} \cdot min^{-1}$]), was obtained from a 20 m shuttle run test according to the procedure and equations outlined by Léger and Lambert.[13] This test consists of a running in a limited space of 20 m, where the students were submitted to a run in the rhythm of a sound signal. In each signal, they should reach one end marked. The signal is based on the speed (km/h), which starts with 8.5 km/h, increasing by 0.5 km/h each time, until the evaluated student can't reach one of the extremities after two consecutive signals. The test was conducted in the same school to which they belonged. The track was marked in a span of 20 m and two students took the test at a time, each one supervised by a physical education professional. Leger et al's formula was used to estimate the VO_{2max}, using the age and average speed (km/h) data. To identify the extent of pubertal development, the self-assessment method proposed by Tanner[14] was employed. This method allows the student to identify their own maturity stage by observing the development of pubic hair. Individually, each student reported to a researcher of the same sex as themselves, which image presented to them they most identified with. From their responses, each was classified as either prepubescent (stage 1), pubescent (stages 2–4), or postpubescent (stage 5).

Blood pressure was measured three times at intervals of 2 minutes. Before the first measurement, the student sat for 5 minutes. An automatic digital monitor (Omron Hem 705 CP, Omron, Tokyo, Japan) was used with clamps of suitable size with a width of approximately 40% of the arm circumference. The measurements were performed on the right arm and the mean of the three assessments was considered.

For biochemical evaluations, a technician from the Clinical Laboratory of the University of Brasilia went to Classe 46 School between 7.30 and 8.30 am to collect blood by venipuncture. The children were required to fast for 12 hours prior to having their blood collected. Blood (10 mL) was collected in a tube with a gel separator and under vacuum without anticoagulant and transported in a Styrofoam box with dry ice to the analytical laboratory of the University Hospital of Brasilia. For determination of FG, TC, HDL, LDL, and TG, the following methods were used: serum/hexokinase automated and serum/esterase-oxidase, oxidase-peroxidase and Friedewald formula. Dosage of FG was performed with an automated method (colorimetric enzymatic glucose-hexoxidase) in an ARCHITECT C8000 Analyzer (Abbott, Illinois, USA), using 5 mL of serum after being centrifuged at 3,000 rpm for 5 minutes. TC, TG and HDL were analyzed using the enzymatic colorimetric method utilising esterase-oxidase and oxidase-peroxidase, using 5 mL of serum after being centrifuged at 3,000 rpm for 5 minutes. The LDL fraction was obtained using the formula proposed by Friedewald et al.[15] The measurements were performed with the automated method on device ARCHITECT C8000 Analyzer (Abbott, Illinois, USA).

The metabolic equivalent (MET) is defined as the oxygen uptake equivalent to a sitting quietly position (3.5 $mL \cdot kg^{-1} \cdot min^{-1}$). The PAL was obtained in MET/week by using the Level of Physical Activity and Sedentary Behavior in Teenager Students questionnaire, created and validated by our group.[16] In this questionnaire students were classified into the following categories: sedentary (PAL less than 600 MET/week), irregularly active (PAL greater than 600 and less than 1,500 MET/week), active (PAL greater than 1,500 and less than 3,000 MET/week) and very active (PAL greater than 3,000 MET/week). Dietary habits were assessed by the questionnaire Risk Behaviors of Adolescents Catarinenses – COMPAC[17] in which students were asked about the weekly frequency of consumption of fruit juice, vegetables, fruits, sodas, chips, pasta, sweets, meat, rice and beans.

Intervention program

Students in the IG performed recreational physical activities and received guidance on healthy habits, in a different timetable than they normally study, during 10 weeks, with 20 sessions of 60 minutes each. Each session comprised 5 minutes of stretching, 40 minutes of basic motor recreational activities (running, jumping, and throwing), and 15 minutes recovery time, which included guidance on healthy habits and use of the illustrative diary.

Recreational activities were planned and directed by a physical education teacher to ensure that the children would be active throughout the period doing activities at a moderate to vigorous intensity (65% to 85% of maximum heart rate obtained in the described 20 m shuttle run test). During the activities, students' heart rate was monitored using a monitor Polar F1TM (Polar Electro Oy, FIN-90440 Kempele, Finland) to ensure the group was exercising within the recommended range.

In terms of the guidance on healthy habits, on the first day of the intervention, each student received a journal made of A4 paper containing pictures representing each weekday, and pages displaying various images of food (fruit, vegetables, candy, fried foods, soft drinks, fruit juice, etc), sedentary activities (watching TV, using a computer, playing video games), and active behavior (jumping rope, jogging, playing soccer, cycling, etc). Colorful pictures were used to represent healthy habits, while black and white pictures were used to represent unhealthy habits. Children were asked to paste pictures into their diary to represent the activities done and foods eaten and to write down the amount of times that they consumed each particular food and the time spent doing each activity. The parents of the students received a note explaining the diary completion activity and recommending that children should take it to school each day that a study recreational activity session was scheduled.

At the end of each recreational activity session, students showed the diary pages that they had filled in daily at home to the teacher and proper habits and inadequate health care were discussed, with the intention of motivating students to improve their lifestyle and making their diaries more colorful as a result.

Statistical analysis

Means and standard deviations were initially used for variables with parametric distribution. The Shapiro–Wilk test was performed to evaluate the variables' adherence to a normal curve, where all showed normality ($P < 0.05$). Paired and non-paired *t*-tests were used to compare data between variables. For data analysis of the questionnaire assessment of dietary habits, we used contingency tables and chi-square tests. All statistical analyses were performed using SPSS Statistics (version 17.0, IBM Corporation, Armonk, NY, USA), using a significance level of $P < 0.05$.

Results

The sample included 34 children (nine girls and eight boys in each group). The mean age of children in the IG and CG was 9.9 years and 10.1 years, respectively. Students were prepubescent and pubescent. All the girls were pubertal and 25% of the boys were prepubertal. The students were divided evenly between both groups to avoid interference of biological age in the research results.

There were no significant differences between the IG and CG in terms of anthropometric parameters, biochemical parameters, blood pressure, or VO_{2max}, both before and after the intervention. However, when comparing results within the same group, it was observed that unlike the CG, the IG showed significant differences in almost all variables, showing positive reductions in risk factors for CVD (Table 1).

The healthy lifestyle guidance offered through the illustrative diary motivated the students to include recreational physical activities in their daily routine. Before the intervention, children were classified as "irregularly active," with no significant differences between groups at pre-test ($P = 0.73$). However, after the intervention, the groups differed significantly ($P < 0.01$), with most students in the IG becoming active while those in the CG remained irregularly active (Table 2).

Analysis of the questionnaire assessing the eating habits of students in the IG and CG revealed no significant differences between them before the intervention. However, after the intervention, there were significant differences in intake of fruit juice, fruit, soft drinks, and candy (Table 3).

In analysis of the questionnaires assessing eating habits, we observed a significant increase in weekly intake of fruit juice and fresh fruit and this was associated with an equally significant decrease in intake of sodas, fries, and pasta. In addition, there was a decrease in the frequency of the weekly consumption of meat (Table 4).

Discussion

In this research, a program of recreational physical activity and orientation to healthy habits using an illustrative

Table 1 Characteristics of intervention group and control group pre- and post-intervention

Variable	Intervention (n = 17)		*P*-value	Control (n = 17)		*P*-value
	Pre	Post		Pre	Post	
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Age (years)	9.94 ± 0.83	10.00 ± 0.93	–	10.12 ± 0.86	10.12 ± 0.86	–
Weight (kg)	46.75 ± 7.49	46.25 ± 7.46	0.012*	48.05 ± 7.15	48.95 ± 8.43	0.28
Height (cm)	1.45 ± 0.9	1.46 ± 0.9	0.000*	1.48 ± 0.8	1.49 ± 0.08	0.00*
BMI (kg/m²)	22.21 ± 2.15	21.6 ± 2.08	0.000*	22.17 ± 1.08	21.89 ± 2.24	0.18
WC (cm)	70.16 ± 6.15	69.15 ± 5.84	0.001*	71.4 ± 4.93	71.14 ± 5.99	0.60
%BF	29.25 ± 4.57	28.05 ± 4.77	0.003*	29.69 ± 4.88	29.53 ± 0.61	0.61
SBP (mmHg)	106.02 ± 9.57	101.72 ± 10.37	0.000*	108.25 ± 8.8	104.74 ± 8.65	0.22
DBP (mmHg)	65.12 ± 8.25	62.92 ± 9.06	0.308	70.58 ± 11.8	65.5 ± 5.22	0.10
VO_{2max} (mL·kg^{-1}·min^{-1})	43.35 ± 2.01	44.3 ± 2.37	0.014*	42.95 ± 3.24	43.5 ± 3.51	0.10
FG (mg/dL)	84.29 ± 4.01	82.12 ± 5.38	0.153	83.71 ± 8.47	84.71 ± 8.44	0.45
TC (mg/dL)	168.82 ± 29.03	154.0 ± 26.72	0.000*	158.94 ± 32.59	153.88 ± 29.59	0.15
HDL (mg/dL)	43.29 ± 8.08	41.88 ± 7.36	0.152	40.71 ± 7.69	38.29 ± 9.02	0.09
LDL (mg/dL)	107.53 ± 28.38	99.76 ± 26.8	0.000*	101.41 ± 28.54	95.88 ± 23.92	0.17
TG (mg/dL)	90.24 ± 28.02	70.76 ± 24.85	0.002*	83.82 ± 33.46	99.0 ± 58.46	0.18

Note: *Statistically significant difference (paired *t*-test).
Abbreviations: %BF, percent body fat; BMI, body mass index; DBP, diastolic blood pressure; FG, fasting glucose; HDL, high density lipoprotein; LDL, low density lipoprotein; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol; TG, triglycerides; VO_{2max}, maximum oxygen intake; WC, waist circumference.

diary showed positive effects on the cardiovascular risk profile of overweight and obese schoolchildren aged 9 to 11 years old, reducing their BMI, WC, %BF, TC, LDL, TG, and SBP, and increasing their VO_{2max}. These results, despite the relatively short duration of the intervention, probably occurred because, aside from the 20 hours of recreational activities in school, the orientation toward healthy habits through the use of the illustrative diary encouraged them to practice physical activity every day and to adopt a healthy diet.

No child discontinued the program, which may be due to the fact that the activities were carried out at school as well as the active participation of students in discussions about healthy lifestyles generated through the illustrative diary. Another reason for this may have been that the physical activities were all recreational. Students in the CG were encouraged to conduct the pre- and post-intervention, with the idea of their participating in the program the following year. At the beginning of the program, students were not engaged in regular physical activity programs and had inadequate diets that included the consumption of fried foods, candy, pasta,

Table 2 Comparatives test of total physical activity level intra- and inter-group

Group	METs	SD	n	Paired t-test	IG/CG, independent *t*-test	
				P-value	*P*-value (pre)	*P*-value (post)
IG						
Pre	669.79	366.71	17	<0.01	0.73	<0.01
Post	1,601.38	529.67	17			
CG						
Pre	713.12	357.66	17	0.23		
Post	847.43	340.27	17			

Notes: Physical activity level classification: sedentary <600 MET/week, irregularly active >600 and <1,500 MET/week, active >1,500 and <3,000 MET/week, and very active >3,000 MET/week.
Abbreviations: CG, control group; IG, intervention group; MET, work metabolic equivalent; SD, standard deviation.

Table 3 Comparative analysis of the eating habits of schoolchildren in the intervention group (IG) and control group (CG), pre- and post-intervention

Weekly intake[a]	Pre	*P*-value	Post	*P*-value
Fruit juice	IG	0.203	IG	0.006
	CG		CG	
Fruit	IG	0.488	IG	0.004
	CG		CG	
Legumes	IG	0.203	IG	0.139
	GC		GC	
Soda drinks	IG	0.729	IG	0.002
	CG		CG	
Fries	IG	0.331	IG	0.122
	CG		CG	
Pasta	IG	0.465	IG	0.319
	CG		CG	
Candy	IG	0.396	IG	0.070
	CG		CG	
Rice and beans	IG	0.382	IG	0.587
	CG		CG	
Meat	IG	0.048	IG	0.151
	CG		CG	

Note: [a]Values were taken in days/week.

Table 4 Eating habits of schoolchildren in the intervention group (IG), pre- and post-intervention (%)

Weekly intake[a]	Situation	0 times	1–3 times	4–6 times	Every day	Twice every day	*P*-value*
Fruit juice	Pre	58.8	41.2	0.0	0.0	0.0	<0.01
	Post	17.6	11.8	70.6	0.0	0.0	
Fruit	Pre	23.5	70.6	5.9	0.0	0.0	<0.01
	Post	0.0	11.8	29.4	58.8	0.0	
Legumes	Pre	35.3	29.4	11.8	23.5	0.0	0.14
	Post	11.8	17.6	41.2	29.4	0.0	
Soda drinks	Pre	5.9	29.4	17.6	47.1	0.0	<0.01
	Post	58.8	29.4	11.8	0.0	0.0	
Fries	Pre	17.6	35.3	35.3	11.8	0.0	<0.05
	Post	64.7	11.8	17.6	5.9	0.0	
Pasta	Pre	29.4	58.8	5.9	5.9	0.0	<0.05
	Post	70.6	17.6	11.8	0.0	0.0	
Candy	Pre	5.9	17.6	17.6	47.1	0.0	<0.01
	Post	5.9	47.1	47.1	0.0	0.0	
Rice and beans	Pre	0.0	0.0	5.9	23.5	70.6	0.15
	Post	0.0	0.0	0.0	52.9	47.1	
Meat	Pre	0.0	41.2	23.5	35.3	0.0	0.01
	Post	0.0	5.9	76.5	17.6	0.0	

Notes: [a]Values were taken in days/week; *significant in answer proportions comparison between pre- and post-intervention (chi-square test).

and soda drinks, and a low intake of vegetables, fruit and fruit juice. The orientation toward healthy habits through an illustrative diary motivated students in the IG to perform physical activities every day, increasing their activity level from irregular to active, as well as encouraged students to consume more fruit juice and fresh fruit and less soda drinks, fried foods, pasta and candy.

These findings corroborate Duncan et al's results.[18] In their study, they also found changes in the PALs and eating habits of schoolchildren in New Zealand after 6 weeks of a program called "Healthy Homework." This program was designed for the physical education curriculum, with the goal of increasing physical activity and healthy eating through school homework that required children to receive weekly booklets with guidelines on various healthy activities that they were to realize.

Poor dietary and low PAL are important contributing factors to obesity and risk factors for CVD. Knowledge on benefits of healthy eating and the importance of physical activity for health is very important for the prevention and treatment of obesity. Schools are conducive to the implementation of health education programs; therefore, teachers should develop interactive and enjoyable strategies for use with their classes to disseminate information to encourage the adoption of a healthy lifestyle.[19]

After the intervention, the lipid profile of the IG improved for all measures, except HDL. These results are consistent with other short-term studies of overweight and obese children and adolescents who have combined diet and exercise.[20,21] Although there was a reduction in FG in the IG and an increase in FG in the CG, these results were not significant.

A study on lifestyle intervention conducted in Germany with overweight children aged 8–16 years old improved participants' dietary pattern and was effective in reducing excess weight, %BF, and WC.[22] Leite et al examined the effects of 12 weeks of a program of physical activity and nutritional counseling on obese adolescents and found a reduction in body weight, BMI, WC, TG, and SBP in the adolescents who had more than one risk factor for CVD.[23] These findings are in agreement with our results.

Cardiorespiratory capacity is represented by VO_{2max} and its value decreases in children with overweight and obesity, being strongly associated with the clustering of cardiovascular risks factors.[24] This observation was explained by the fact that this population participates in organized physical education less than their non-obese peers.[25] In our study, there was a significant increase (2.2%; $P < 0.01$) in VO_{2max} in the IG after the intervention, that may be due to an increase of PAL.

The positive results of this study underscore the importance of physical activity combined with orientation toward healthy habits, as well as the benefits of using an illustrative diary, against obesity and other risk factors for CVD, and may be used as subsidies for implementation of interventional programs in schools strategies.

A limitation of this study was the use of subjective methods to measure dietary habits and PAL, thus the extent to which the stated dietary habits and PAL reflect actual habits may be questioned. However, reproducible and validated questionnaires were used to minimize this problem.

Conclusion

The program was effective in reducing risk factors for CVD and the use of an illustrative diary for 10 weeks may have been the key to this result, since the students were motivated to change their poor eating and physical activity habits to healthy ones and increase their PALs.

Future studies should be carried out to evaluate the behavior of the students, to know if the introduced concepts were still in use and if it had affected their PAL. Future studies may require a greater number of students to show a complete set of variables that may be changed within the proposed program.

Disclosure

The authors declare no conflicts of interest in this work.

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