Acute and Chronic Effects of Exercise

Cost-effectiveness analysis of physical exercise program among hypertensive patients in the Brazilian National Healthcare System: real-life data

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Abstract - Objective The study aimed to perform a cost-effectiveness analysis comparing the treatment based on traditional drug therapy (TDT), in relation to alternative treatment based on combined TDT and exercise program (TDT +E) in real-life condition. **Methods:** The health outcomes monitored during the investigation were metabolic (glucose, cholesterol, and triglycerides) and body composition (weight, body mass index [BMI] and body fat percentage [%BF]) parameters of individuals within each group. Healthcare expenditures from each participant were estimated including information registered in medical records during 12 months of follow-up. **Results:** The intervention group showed economic advantages in comparison to control group for triglycerides, cholesterol, weight, BMI and body fat percentage and corresponding to savings of US$7.63/mg/dL, US$5.20/mg/dL, US$31.21/kg, US$69.38/kg/m^2 and US$19.32/%BF. Results were maintained even after sensitivity analyzes. **Conclusions:** Exercise programs might be cost-effectiveness to public health interventions among hypertensive patients in primary health care facilities, due to reduced metabolic and body composition variables, which are risk factors for chronic diseases.

Keywords: cost-effectiveness, exercise, dyslipidemias, healthcare costs.

Introduction

The increase in life expectancy has been accompanied by an increase in the prevalence of non-communicable chronic diseases[1], a matter of especial concern in low and middle-income countries[2] due to the occurrence of double burden of disease[3]. Non-communicable chronic diseases were responsible for 72% of all deaths in Brazil in 2013, cardiovascular diseases were the main causes. In 2019, the cardiovascular diseases were responsible for 28.2% of the deaths in the country[5].

Physical inactivity is an aggravating factor in the upsurge of non-communicable chronic diseases, being directly related to the development of several health problems, including hypertension, type 2 diabetes and obesity[6], which in turn represent significant expenditures to the public health system[7-11].

On the other hand, the practice of regular physical activity minimizes the physiological effects and progression of non-communicable chronic diseases, being considered an important strategy for health promotion, non-drug control of diseases and protection from risk factors[6,12,13]. In primary care settings, the National Institute for Health and Care Excellence (NICE) provides specific guidelines for promotion of physical activity to countries belonging to the United Kingdom[14]. In fact, a study recently conducted in London showed that programs encouraging the practice of physical activities would result in resource savings by reducing the significant number of cases of non-communicable chronic diseases and their aggravating factors[15].

In Brazil, the National Health Promotion Policy (PNPS) was instituted in 2006, which incorporates physical activities practice promoting quality of life[16]. Regarding primary health care, the physical education professional could be included in a multidisciplinary team called Family Health Support Center (NASF)[17]. Researchers have shown that an exercise program for hypertensive and diabetic patients, attended in the NASF, is effective in reducing the use of medication, systolic and diastolic blood pressure, and even improving quality of life[18].

However, most published studies related to the practice of physical activities and health costs are from developed countries. In developing countries, such as Brazil, where there is one of the largest, government-funded health systems, few studies have verified the effectiveness and costs of a systematized exercise program, as well as its potential impact on the reduction of costs for public health services.

Thus, the aim of the present study was to conduct a cost-effectiveness analysis, in real-life condition, comparing the treatment usually offered by Primary Healthcare Units (PHU) to hypertensive patients (traditional drug therapy - TDT) with an alternative treatment (TDT and exercise program - TDT+E), using measures of effectiveness related to metabolic variables (glucose, cholesterol and triglycerides), body composition (weight, body mass index [BMI] and body fat percentage [%BF].

Methods

Sample

The study was approved by the Ethics Research Committee of the Sao Paulo State University (process number: 241.291/2013) and was carried out between the years 2014 and 2015. The sample included individuals attended in primary care within the Brazilian National Healthcare System, residents in the city of Presidente Prudente (~200,000 inhabitants), Western region of the São Paulo state, Brazil. The patients were assigned into two groups for comparison of interventions for 12 months: TDT (n = 20), and TDT+E (n = 29).

The cost-effectiveness analysis performed was based on estimation of cost-effectiveness ratio (CER) and incremental cost-effectiveness ratio (ICER) between two groups, considering direct costs at primary health care level and health outcomes based on estimation of health outcomes using health system perspective[19-20].

The Brazilian National Health System offers universal health care coverage funded by the government, including integral care at primary, secondary and tertiary complexity levels. The primary health care is supplied within medical facilities (PHU) covering individuals living in a geographically circumscribed area, and focusing on the promotion of health, monitoring, and prevention of diseases, including physician consultations, diagnostic exams, vaccines, and prescribed medicines.

Two PHU were selected by local authorities (Municipal Department of Health) to be included in the longitudinal study, considering the high number of daily appointments for patients. Enrollment of patients was conducted during 30 days in each PHU from year to year. All patients with appointments scheduled during the designated 30 days period were initially considered eligible to participate in the study.

The sample size calculation was based on previous data[21] using Student t-test equation, accounting for the mean difference of US$2.08 between physically active (SD = 0.48) and sedentary (SD = 1.36) patients regarding health expenditures, power of 80%, alpha error of 5%, and addition of 100% of sample losses throughout the intervention. The minimum sample size estimated was 20 patients in each group (n_{total} = 40).

Those who met the established inclusion criteria were invited to participate in the intervention group. Likewise, a group with the same characteristics was formed and accompanied during the follow-up. The inclusion criteria were: i) to have active registration in the PHU; ii) age ≥ 50 years, age range associated with the onset of non-communicable chronic diseases in the state of São Paulo[22], as well as higher probability of death in low- and middle-income countries[23]; iii) diagnosis of hypertension; iv) to be classified as physically inactive (individuals reporting no engagement in physical activities/sports in the leisure time); v) to sign the consent form.

The study exclusion criteria were: i) did not meet at least one inclusion criterion; ii) did not obtain medical clearance to perform the exercise sessions; iii) present a physical disability that made it impossible to participate in training sessions; iv) patients with a participation rate of less than 70% in training sessions; v) control group participants who became active during the study were excluded from the analyzes.

Patients selected for participation in the exercise program were cleared by a physician before starting the intervention.

Initially, 27 adults agreed to participate in the intervention group (TDT+E), all meeting the inclusion criteria and had medical clearance to practice exercises. In the TDT+E, 7 adults were excluded due to low adherence to training sessions (patients with participation rate lower than 70% were excluded from data analysis). In parallel, 29 adults accepted to compose the control group, throughout the study, no member of the TDT group failed to meet the requirements and was excluded from the sample.

Thus, the final sample included 49 adults, 20 adults from TDT+E group (n = 7 (35%) men and n = 13 (65%) women) and 29 adults from TDT group (n = 10 (34.5%) men and n = 19 (65.5%) women).

Socio-demographic and lifestyle variables

Information on the diagnosis of hypertension and other non-communicable chronic diseases was assessed through a questionnaire[24]. Regarding physical activity, we used a questionnaire composed of 16 Likert-scale questions considering three domains of physical activity (occupational physical activity; sport/exercise during leisure-time; physical activity during leisure-time and locomotion)[25]. Individuals who reported no engagement in sports/exercise during leisure-time were considered physically inactive. Also, the following information was collected during the interview: i) age; (ii) sex; and iii) systolic (SBP) and diastolic (DBP) blood pressure at rest (following the protocol of the VI Brazilian Guidelines on Hypertension[26]).

Health outcomes

The variables of health outcomes considered in the calculation of the cost-effectiveness ratio and incremental cost-effectiveness ratio were metabolic variables (glucose, cholesterol, and triglycerides) and body composition variables (weight, body mass index [BMI] and body fat percentage [%BF]). This information was collected at baseline and after 12 months of follow-up.

Metabolic variables were measured using a portable device (Roche brand, Accutrend Plus model), an instrument validated by the national literature[27]. Body mass index (BMI) was calculated using measurements of weight and height and was calculated according to Lohman et al. (1988)[28]. The %BF was verified through bioelectrical impedance (Inbody brand, model 230) following the manufacturer's recommendations.

Due to the use of hypertensive drugs by the participants, blood pressure was not included as one of the health outcomes.

Treatment protocols

Individuals in the TDT group followed traditional drug therapy, following medical recommendations. The participant's level of physical activity was assessed every six months[25]. If any of the patients started a physical activity program during the 12-month follow-up, they were excluded from the group and data analysis.

Individuals in the TDT+E group also followed a protocol of traditional drug therapy, combined with a systematic physical exercise program. The exercise protocol followed the VI Brazilian Guidelines for Hypertension[29].

In the beginning of the exercise session, the patient's blood pressure was measured, and patients with SBP > 160 mm/Hg and/or DBP > 105 mm/Hg were not allowed to participate in the exercise session for that day. Patients diagnosed with diabetes mellitus also had glycemic values assessed before exercise sessions, and individuals taking insulin should have values > 100 mg/dL to be able to participate in the session[30].

Each exercise session started with stretching, followed by aerobic exercise [approximately 30 min walking, intensity maintained between 65% and 75% of maximal heart rate, controlled by heart rate monitor (POLAR mark, model FT1)], resistance training (free weights, approximately 25 min) including different muscle groups with sets of 8 to 15 repetitions until moderate fatigue[29], ending the session with stretching exercises. Patients using beta-blockers had exercise intensity controlled using the Borg Rating of Perceived Exertion Scale, target zone ranging from 12 to 13[31].

The sessions were held three times a week, in each session four to six resistance exercises were performed, so that in all sessions exercises for lower and upper limbs were performed. The exercises were organized as follows, considering the different muscle groups: session 1: Chest, Triceps, Quadriceps, Abs; session 2: Latissimus dorsi, biceps brachii, hamstrings, abs and session 3: Deltoid, gastrocnemius, hip adductors and abductors. The exercises were reformulated every three months.

The proposed program lasted 12 months, and patients with participation rate lower than 70% were excluded from data analysis.

Direct healthcare costs

Direct healthcare costs attributable to primary care services provided for patients within each group were estimated including items registered in medical records during 12 months of follow-up[11,12,21]. Healthcare expenditures included: i) medication obtained in the health care facility; ii) laboratory tests performed; iii) clinical consultation: health professionals consultations (medical, nursing and physical therapy), and screening before and after appointments and iv) patient care services: costs associated with management and operation of the PHU were considered in the estimation of direct costs, including medication withdrawal at pharmacy (in this case, it was considered the costs to maintenance a worker responsible for dispensation of medication- pharmaceutical salary), and administrative costs (human resources, electricity, water and telephone bills).

Prices of healthcare procedures used by patients during the follow-up period were based on information from standard tables for reimbursement of services provided to the municipal government. Direct healthcare costs were estimated for each patient during the 12-month period. Subsequently, the average cost per patient in each group was verified, considering the 12-month follow-up period.

The exercise professional was provided by the research group that conducted the research, thus, to calculate the direct costs related to the exercise program (TDT+E group) were based on the monthly salary of the exercise professional if this professional would be hired by the Municipal Department of Health of the city of Presidente Prudente, considering the number of hours worked in the exercise program per month multiplied by the value corresponding to one hour of service. Exercise sessions lasted one hour and were performed three times a week, resulting in 12 h per month.

Costs related to the place for execution, material used in the physical exercise program, as well as costs of program incentive, recruitment and outreach materials were not computed, since the training sessions were held on the premises of the UBS and the material used, of a permanent nature, were provided by the research group responsible for the study.

Monetary values were updated according to the official Brazilian inflation index (Extended National Consumer Price Index, IPCA), and converted into US dollars (US$) using the official exchange rate for January 2019, published by the Brazilian Central Bank[32].

Statistical analyses

The data were analyzed using descriptive statistics (mean, standard deviation, median and interquartile range). Student's t-test for independent samples (variables with normal distribution) or Mann-Whitney test, otherwise, were used to verify the difference between TDT and TDT+E groups in the initial part of the study. A chi-square test was used to assess categorical data. Statistical significance (p-value) was set at values lower than 5%, using BioEstat software (version 5.0).

Regarding the cost-effectiveness analysis, cost-effectiveness ratios (CER) were calculated by dividing the average cost per patient in each group in relation to variations between baseline and end of follow-up for each health outcome. Incremental cost-effectiveness ratio (ICER) was calculated by dividing the differences in the average costs between intervention (TDT+E) and control (TDT) groups in relation to the differences in health outcomes between groups[19,20].

Cost-effectiveness indicates a therapeutic option with better clinical results per monetary unit spent. Thus, the health outcomes selected in the present study should present a negative variation between the beginning and end of the follow-up period as an ideal clinical result (improvement in the patient's health status).

The robustness of CER and ICER results was assessed using univariate, multivariate and probabilistic sensitivity analyses regarding effects from potential changes in main determinants of costs and health outcomes.

The univariate sensitivity analysis was performed using isolated variations in healthcare costs. CER and ICER were recalculated based on the variation of $\pm$ 100% in costs of the following items: clinical consultations, patient care services, laboratory tests, medications, and exercise program.

The multivariate sensitivity analysis considered discrete variations in the costs of exercise program in six categories (ranging from 0 to double the actual value estimated in the study) combined with variation in health outcomes (triglycerides, cholesterol, glucose, weight, BMI and %BF) within groups. The range of health outcomes (shocks) was adjusted within values close to the actual, minimum and maximum values according to the literature (values and literature references[30,33,34] were given in the figures for each outcome.

The probabilistic sensitivity analysis was performed based on Monte Carlo simulations to confirm trends from intervention and control groups. The simulations were estimated using mean and variance of annual health care costs within each group based on γ distribution, and mean and variance of each health outcome within each group based on normal distribution.

Simulations provided 10,000 cases in the intervention group and 10,000 cases in the control group for analysis of distribution of ICER values, which indicate probabilities of occurrence of diverse cost-effectiveness ratio scenarios in the comparison of control and intervention groups due to changes in probabilities of costs and outcomes.

Results

Initially, 27 adults were included in the Intervention group (TDT+E) and 29 in the control group (TDT). In the TDT+E, 7 adults were excluded due to low adherence to training sessions. There was no sample loss for the TDT. Thus, the sample consisted of 49 adults divided into two groups, according to the type of treatment. The Intervention group (TDT+E) consisted of 20 adults [n = 7 (35%) men, and n = 13 (65%) women] and the control group (TDT) consisted of 29 adults [n = 10 (34.5%) men and n = 19 (65.5%) women]. Of the patients of the TDT+E group, 9 (45%) used beta-blockers.

Table 1 presents the characteristics of the groups at baseline, and it shows the similarity between them. Robust differences were identified only in glucose levels (p = 0.016); however, the prevalence of diabetes was not different between groups (p = 0.523).

Healthcare expenditures at baseline are presented in Table 2. There were no robust differences between groups regarding healthcare expenditures.

CER and ICER are presented in Table 3. Healthcare expenditures and health outcomes are presented in annual mean values. Negative CER values show cost-effective treatment, and positive values indicate not cost-effective treatment during the 12 months of follow-up. For triglicerides, both groups were cost-effective, but TDT+E had an advantage considering that the decrease of one unit of triglycerides (mg/dL) resulted in higher savings (3.17 US$/mg/dL for TDT vs. 3.90 US$/mg/dL for TDT+E). For glucose, none of the groups was cost-effective; however, the increase of one unit of glucose resulted in higher expenditures for the TDT group when compared to the TDT+E group (6.79 US$/mg/dL vs. 5.75 US$/mg/dL, respectively). TDT+E group was cost-effective for cholesterol (161.18 US$/mg/dL for TDT vs. 17.49 US$/mg/dL for TDT+E). For body composition variables, TDT+E presented a synergistic effect that resulted in reduction of body composition measures during the 12 months of follow-up, and the decrease of one unit of weight, BMI and body fat percentage resulted in reduction of health expenditures of 123.69 US$/kg, 266.26 US$/kg/m^2 and 70.78 US$/%BF, respectively.

Table 1 - Characteristics of the sample at baseline according to groups.

	Groups		p-value*
	TDT+E (n = 20) **Mean (SD) Median (IR)**	**TDT (n = 29)** **Mean (SD) Median (IR)**	
Age (years)	62.82 (8.46)	67.01 (9.35)	0.116
	60.77 (10.79)	67.20 (10.29)	
Weight (kg)	72.60 (13.20)	77.42 (14.54)	0.242
	74.75 (18.45)	79.10 (17.05)	
BMI (kg/m^2)	30.26 (5.95)	31.32 (5.81)	0.539
	29.36 (5.69)	31.13 (9.49)	
Body fat percentage (%)	40.08 (8.52)	40.21 (10.28)	0.964
	38.20 (16.10)	39.60 (17.13)	
Blood pressure Systolic (mmHg)	135.79 (16.32)	143.71 (27.34)	0.226
	133.00 (17.00)	144.00 (45.00)	
Diastolic (mmHg)	78.79 (20.63)	80.43 (11.36)	0.848
	81.00 (19.00)	80.00 (13.00)	
Biochemical exams Cholesterol (mg/dL)	198.95 (27.84)	188.75 (38.21)	0.313
	195.00 (34.00)	173.00 (43.50)	
Triglycerides (mg/dL)	138.25 (53.39)	148.31 (64.49)	0.568
	122.00 (57.00)	139.00 (92.00)	
Glucose (mg/dL)	112.15 (48.83)	146.93 (46.49)	0.016
	97.00 (62.00)	146.00 (61.00)	
HPA (escore)	6.78 (1.68)	5.95 (0.93)	0.054
	6.68 (2.91)	5.87 (1.31)	
Presence of NCD	n (%)	n (%)	**
Dyslipidemia	7 (35.00%)	14 (48.27%)	0.529
Diabetes Mellitus	5 (25.00%)	11 (37.93%)	0.523

* = Student's t-test; ** = chi-square test; TDT = traditional drug treatment; E = exercise program; SD = standard deviation; IR = interquartile range; BMI = body mass index; HPA = habitual physical activity; NCD = non-communicable chronic diseases.

Table 2 - Healthcare expenditures at baseline according to treatment groups.

Healthcare expenditure (US$)	Group		p-value*
	TDT+E (n = 20) **Mean (SD) Median (IR)**	**TDT (n = 29)** **Mean (SD) Median (IR)**	
Clinical consultation	13.10 (8.87)	13.36 (9.35)	0.758
	11.02 (9.53)	10.27 (10.53)	
Laboratory test	3.36 (6.99)	3.63 (7.44)	0.476
	0.00 (0.00)	0.00 (0.00)	
Medications	22.86 (31.95)	13.64 (13.16)	0.931
	13.05 (14.84)	10.02 (8.29)	
Patient care services	5.59 (2.23)	4.22 (1.95)	0.300
	3.94 (2.98)	3.61 (2.58)	
Overall	43.93 (33.57)	34.87 (22.53)	0.319
	38.16 (25.41)	23.89 (26.20)	

* = Mann-Whitney; TDT = traditional drug treatment; E = exercise program; SD = standard deviation; IR = interquartile range.

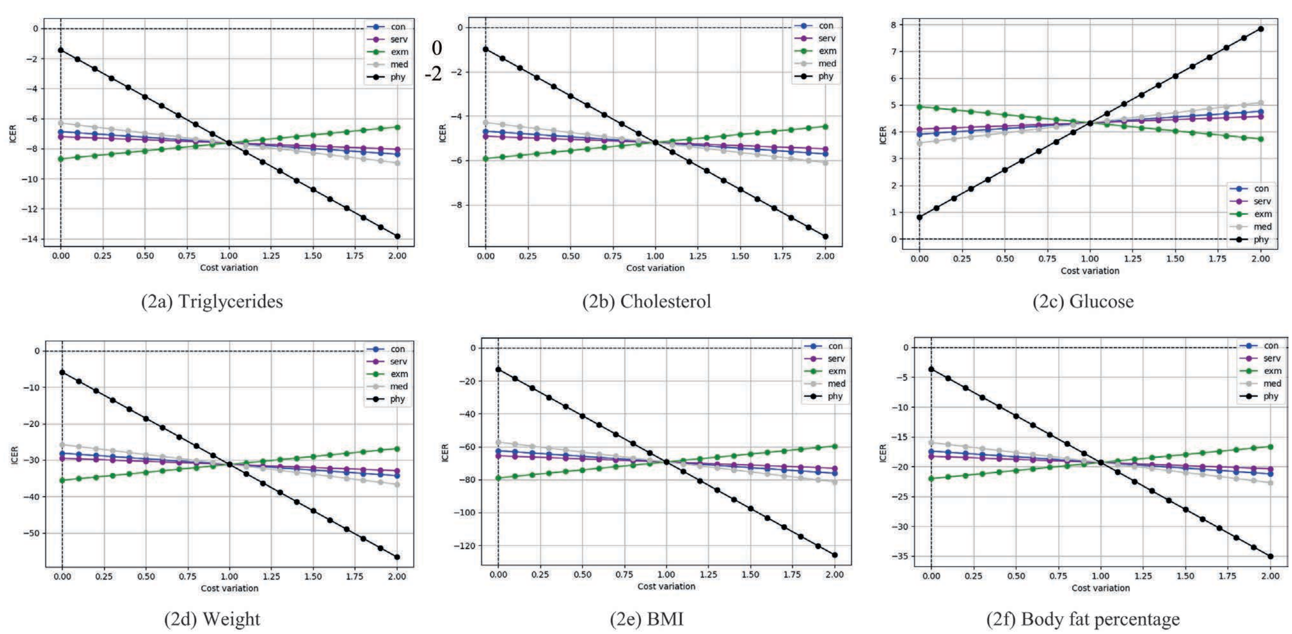
Table 3 - Cost-effectiveness and incremental cost-effectiveness analyses considering metabolic and body composition variables.

Outcome	Treatment	Baseline mean	Follow-up mean	Mean cost 12 months (US$)	Effectiveness mean diff.	CER US$/outcome units	ICER
Tryglicerides (mg/dL)	TDT (n = 29)	148.31	122.03	83.37	-26.28	-3.17	-7.63
	TDT+E (n = 20)	138.25	106.85	122.45	-31.40	-3.90	
Cholesterol (mg/dL)	TDT (n = 29)	188.75	189.27	83.37	+0.52	+161.18*	-5.20
	TDT+E (n = 20)	198.95	191.95	122.45	-7.00	-17.49	
Glucose (mg/dL)	TDT (n = 29)	146.93	159.21	83.37	+12.28	+6.79*	+4.33*
	TDT+E (n = 20)	112.15	133.45	122.45	+21.30	+5.75*	
Weight (kg)	TDT (n = 29)	77.42	77.68	83.37	+0.26	+318.12*	-31.21
	TDT+E (n = 20)	72.60	71.61	122.45	-0.99	-123.69	
BMI (kg/m^2)	TDT (n = 29)	31.32	31.42	83.37	+0.10	+806.18*	-69.38
	TDT+E (n = 20)	30.26	29.80	122.45	-0.46	-266.26	
Body fat percentage (%)	TDT (n = 29)	40.21	40.50	83.37	+0.29	+284.44*	-19.32
	TDT+E (n = 20)	40.08	38.35	122.45	-1.73	-70.78	

TDT = traditional drug therapy; E = exercise program; CER = cost-effectiveness ratio; ICER = incremental cost-effectiveness ratio; * = not cost-effective; BMI = body mass index.

When considering the ICER analyses (difference in costs with health services and difference in health outcome variations), the implementation of an exercise program for users of the Brazilian National Healthcare System is an advantageous intervention in decreasing triglycerides, cholesterol, weight, BMI, body fat percentage and costs when compared to the traditional treatment.

Figure 1 presents the results of the univariate sensitivity analyses, showing changes of ICER according to costs variation of metabolic and body composition variables. It is important to notice that ICER ratio tended to decrease with increases in costs with exercise professionals, consultations, other services and medications for all health outcomes, except glucose. This means that increases in costs result in increased differences between intervention and control groups, favoring the ratio cost for outcome units of the exercise intervention.



(2a) Triglycerides (2b) Cholesterol (2c) Glucose

(2d) Weight (2e) BMI (2f) Body fat percentage

Figure 1 - Univariate sensitivity analyses of ICER in relation to variations in health care costs. Presidente Prudente, SP, Brazil, 2015. ICER = incremental cost-effectiveness ratio; BMI = body mass index; con = health professionals consultations; serv = Costs associated with management and operation; exm = exams; med = medication; phy = exercise professional.

Costs with exams presented diverse behavior: ICER usually increased according to the increase in the cost of exams, except in the case of glucose. Additionally, the effects on glucose levels showed inverse trends, showing an increase of ICER ratios according to increases in costs with exercise professionals, consultations, other services and medications, which indicates that rising costs of these items increase positive differences in incremental cost-effectiveness ratios, i.e, increases in outcomes and costs that maintain the cost-effective scenario for the intervention.

The same findings were confirmed in the multivariate sensitivity analyses for metabolic (Figure 2) and body composition variables (Figure 3). When the variation in triglycerides, cholesterol, glucose, weight, BMI, and % BF is closer to the minimum value, the ICER dispersion ratio is higher, and when the variation is closer the the maximum values for the same health outcomes, the ICER dispersion ratio is close to zero.

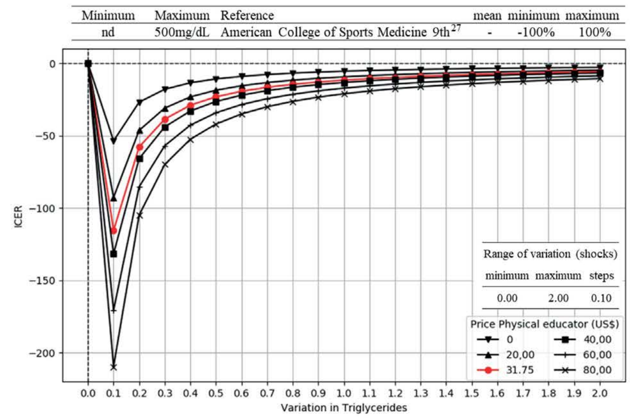
Metabolic health outcomes showed advantages in the probabilistic sensitivity analyses for triglycerides and cholesterol (53.41% and 55.52%, respectively). Body composition outcomes showed advantages for weight, BMI and %BF (63.65%, 64.42%, 71.26%, respectively). These values represent the sum of the percentage showing better outcomes - negative value in difference effectiveness. Glucose outcomes had an inverse pattern (worse health outcomes and higher costs, approximately 40% of cases in the computational simulations), showing the dominance of the traditional drug therapy and reinforcing the need of monitoring the evolution of this health outcome in long-term physical activity interventions (Figure 4).

Discussion

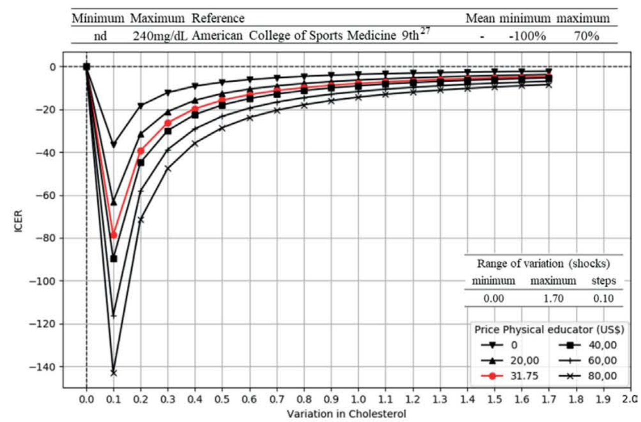
The present study found through real-life that traditional drug treatment combined with a 12-month exercise program for hypertensive adults showed better metabolic and body composition outcomes when compared to the traditional drug treatment alone and it proved to be a financially effective strategy for the Brazilian National Health System.

It is well known that metabolic and body composition risk factors are associated with hypertension[35], and this combination is expensive for health systems due to increases in expenditures[36]. Thus, minimizing the effects of metabolic and body composition risk factors among hypertensive patients may be an advantageous alternative to reduce healthcare costs within primary healthcare settings[37-40], consist of a cost-effective prevention strategy according to the findings of this study.

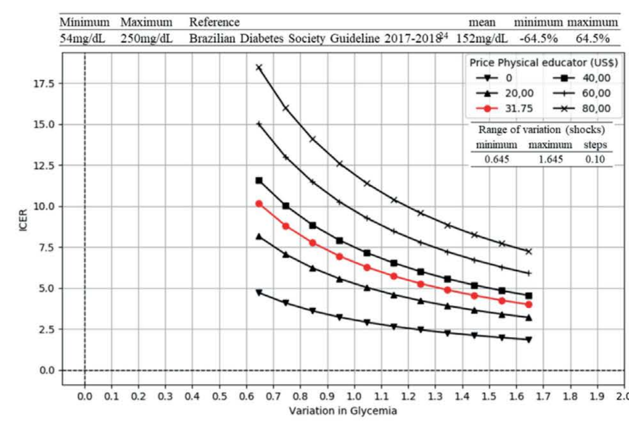
The results also showed that the combined intervention (exercise + drug treatment) was superior to the drug treatment alone for reductions in triglycerides



(2a) Triglycerides



(2b) Cholesterol

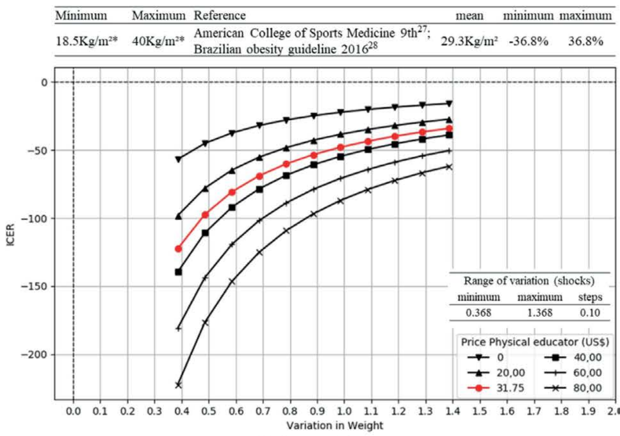


(2c) Glucose

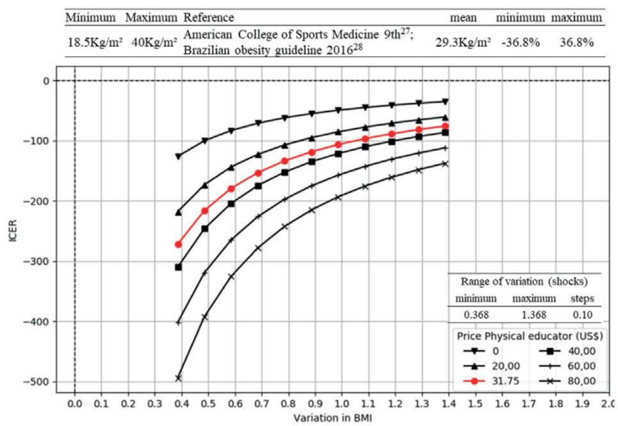
Figure 2 - Multivariate sensitivity analysis of ICER in relation to variations in health care costs of patients in the sample, according to metabolic variables. Presidente Prudente, SP, Brazil, 2015. ICER = incremental cost-effectiveness ratio.

(31.40 mg/dL vs. 26.28 mg/dL), cholesterol (7.00 mg/dL), weight (0.99 kg), BMI (0.46 kg/m^2) and body fat percentage (1.73%).

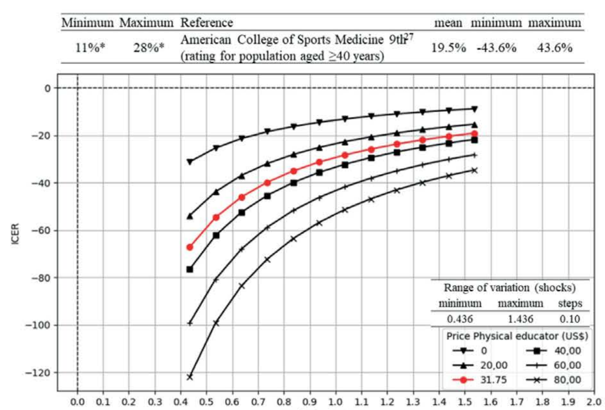
Similarly, a study evaluating 163 individuals aged 52 years old in the United Stats of America found that subjects engaged in physical exercises improved plasma



(3a) Weight



(3b) BMI



(3c) %BF

Figure 3 - Multivariate sensitivity analysis of ICER in relation to variations in health care costs of patients in the sample, according to body composition variables. Presidente Prudente, SP, Brazil, 2015. CER = cost-effectiveness ratio; BMI = body mass inde; %BF = body fat percentage; *For the analysis of the WEIGHT variable, the same reference values as the BMI were considered; **the value used refers to % BF in man, in the sensitivity analysis model, there is no distinction between sex when shocks are performed (variations in outcome).

lipid variables, including cholesterol and triglycerides concentrations, and that such changes were maximized as a result of weight loss[41]. Other study conducted in Portugal with adults over 60 years of age showed that pharmacologic drugs of the statin type combined with a 24-month exercise program were more effective to manage cholesterol and BMI (reduction of 5% and 1%, respectively) than the isolated drug treatment (no differences, $p > 0.05$)[42].

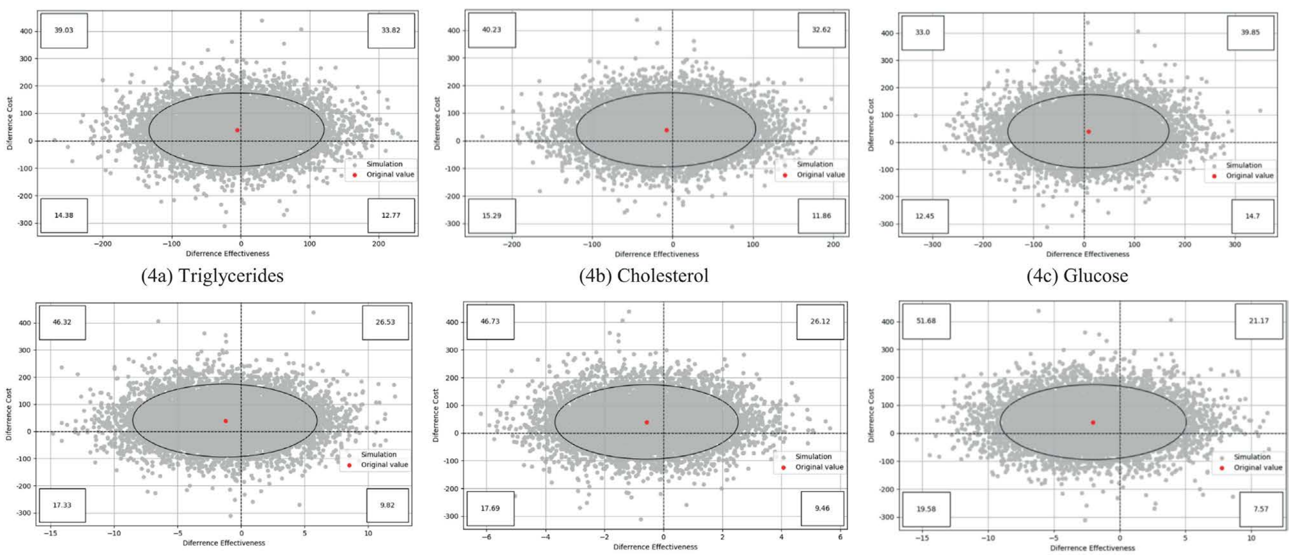
In parallel, it is worth mentioning that reductions in metabolic variables, such as those included in this studied, are associated with a reduced risk of cardiovascular events[43], a fact that may also be associated with the reduction of expenses in secondary and tertiary public health care. In Brazil, a study carried out with cardiac patients with a mean age of 61±10 years attended at a public hospital, between the years 2000 and 2015, showed that the average costs per hospitalization were US$ 1,976 per patient[44] Expenses that could be saved due to public health prevention actions.

Therefore, knowing the benefits of exercise for health outcomes, we decide to test if an exercise program could also be cost-effective for universal health systems. With the current findings, it is possible to confirm that having an exercise science professional in the primary healthcare setting would result in savings of US$ 7.63, US $ 5.20, US$ 31.21, US$ 69.38 and US$ 19.32 for each unit reduced of triglycerides, cholesterol, weight, BMI and body fat percentage, respectively.

The higher impact was generated by variations in the costs of exercise science professionals. It was a result expected in the analysis due to the central role of the professional in the intervention. Previous studies have shown that physical inactivity is associated with higher expenditures with health services[12,45]. Among adults aged > 65 years, attended by the Brazilian National Healthcare System, those who do not perform systematic exercise or sport spend 1.57 times more with medications than those who perform, in addition, the authors found that individuals who presented less physical activity in different domains of physical activity (work, sport and leisure time) presented health expenses 2.12 times higher[12]. Additionally, physical inactivity allied to obesity increases the likelihood of spending with medication in 3.01 times and overall health expenditures in 3.08 times[45].

The results of this study represent important evidence for public health, and may also contribute to public sector decision-making processes in Brazil. In the probabilistic sensitivity analysis based on potential variations in individuals' characteristics and health care costs attributable to patients within each group, the simulations have shown that differences among individuals within each group did not change the results for most health outcomes investigated. Better outcomes indicated a negative value in difference effectiveness, demonstrating a higher probability of favorable effects due to intervention combining traditional medication treatment and physical exercise.

Evidence for the cost-effectiveness of physical activity interventions in primary health care settings is



(4a) Triglycerides (4b) Cholesterol (4c) Glucose

(4d) Weight (4e) BMI (4f) Body fat percentage

Figure 4 - Probabilistic sensitivity analysis from computational simulation scenarios from changes in healthcare costs, physical exercise program costs, and health outcomes of patients, according to metabolic and body composition variables. Presidente Prudente, SP, Brazil, 2015. BMI = body mass index.

scattered[46], which makes it difficult to compare the results. There is plenty of evidence from cost-effectiveness analysis in studies performed in developed countries, e.g., the United States, Australia, and the United Kingdom, especially in pharmacological treatments, including potential estimates of impact from new treatments[47]. Hence, the originality of this study should be emphasized in showing that physical exercise can also be an advantageous strategy for primary healthcare regarding health promotion and disease prevention.

Also, knowing that behavioral changes can be sustained for decades[48], evidence shown in this study may be used to encourage actions in public health for the reduction of exposure to risk factors through regular physical exercise.

Limitations

The main limitations of the study refer to sample representativeness at the local level and lack of information on metabolic and body composition measures of patients after the end of the follow-up period. In addition the lack of randomization of the patients into the two groups, and the presence of other diseases that could be potential factors that affect the results. Finally, the costs related to the place for execution, material used in the physical exercise program, as well as costs of program incentive, recruitment and outreach materials were not computed.

On the other hand, it is worth mentioning that this study presents a good research design, by comparing intervention and control groups, besides presenting originality when implementing a 12-month intervention in the primary healthcare setting.

Conclusions

Our study contributes to filling the gap in knowledge by showing that exercise intervention programs for hypertensive patients reduced metabolic and body composition variables, which are risk factors for chronic diseases, and proving to be a cost-effective strategy for public health systems.

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