









Epidemiology

## Cost-utility analysis of traditional drug therapy with and without exercise program for hypertensive patients in real-life data primary health care

Monique Yndawe Castanho Araujo<sup>1</sup> , Flávia Mori Sarti<sup>2</sup> , Bruna Camilo Turi-Lynch<sup>3</sup> , Dayane Cristina Queiroz<sup>1,4</sup> , Valéria Juday Santos Neves<sup>5</sup> , Murilo Mazzotti Silvestrini<sup>2</sup> , Jamile Sanches Codogno<sup>1,4</sup> 

<sup>1</sup>Universidade Estadual Paulista “Julio de Mesquita Filho”, Departamento de Educação Física, Grupo de Estudos em Saúde Atividade Física e Economia, Presidente Prudente, SP, Brazil

<sup>2</sup>Universidade de São Paulo, São Paulo, SP, Brazil <sup>3</sup>Lander University, Department of Physical Education and Exercise Science, Greenwood, SC, United States of América <sup>4</sup>Universidade Estadual Paulista “Julio de Mesquita Filho”, Departamento de Educação Física, Programa de Pós-Graduação em Ciências do Movimento, Presidente Prudente, SP, Brazil <sup>5</sup>Universidade Anhembi Morumbi, São Paulo, SP, Brazil.

Associate Editor: Danilo Silva , Universidade Federal de Sergipe, São Cristóvão, SE, Brazil. E-mail: danilorpsilva@gmail.com.

**Abstract - Aim:** The study aimed to conduct a cost-utility analysis of traditional drug therapy (TDT) provided for hypertensive patients at primary care in comparison to the protocol based on combination with an exercise program (TDT+E) in real-life conditions, adopting a health system perspective. **Methods:** Longitudinal study based on enrollment of 49 hypertensive adults distributed into two groups, for 12 months. Quality-adjusted life years were estimated using health-related quality of life. Direct health care costs were calculated including inputs and human resources in primary care from medical records. Sensitivity analysis was performed based on multivariate and probabilistic scenarios. **Results:** Incremental cost-effectiveness ratios of TDT+E in comparison to TDT were +79.69. Sensitivity analysis showed that TDT+E presented advantages considering uncertainties. **Conclusion:** Our findings show that exercise programs may improve quality of life and life expectancy among hypertensive patients.

**Keywords:** cost-utility analysis, exercise, physical activity, QALY, quality of life, healthcare costs, hypertension.

### Introduction

Cardiovascular diseases result in approximately 17.5 million annual deaths<sup>1</sup>. Approximately 45% of mortality due to cardiovascular disease is attributable to hypertension<sup>2</sup>, leading to a heavy financial burden due to the use of health care services<sup>3,4</sup>. There is a high prevalence of hypertension among adult populations worldwide, particularly in low- and middle-income countries, which tend to have a lack of infrastructure and human resources available in the national health system<sup>5</sup>.

Statistical opinion published by the American Heart Association described that, from 2013 to 2014, about 75.2 million Americans were diagnosed with arterial hypertension, and that these incurred US\$ 51.2 billion in direct and indirect expenses<sup>6</sup>. In Brazil, the study developed in 2018 estimated costs attributable to arterial hypertension of more than 2 billion per year, considering the costs of hospitalizations, outpatient procedures, and medi-

cations distributed by the Brazilian National Health Service to treat this disease<sup>7</sup>.

Hypertension is considered one of the main preventable causes of disease, premature mortality, and disability worldwide. Recent studies summarize the harmful impacts of hypertension on well-being, and health-related quality of life<sup>8,9</sup>, including increases in disability-adjusted life years<sup>10</sup>. On the other hand, there is evidence of enhanced effectiveness from innovative health care strategies for hypertension treatment in developed countries, particularly the United Kingdom, including exercise programs<sup>11-14</sup>, such as a 12 week for physical activity with 30-45 min sessions that focused on building endurance, strength, balance, and flexibility<sup>13</sup>, as also a population trial which aimed to encourage the practice of 3,000 steps/d (approximating a 30 min walk) on five or more days weekly with 12 months of follow-up with and without nurse support<sup>12</sup>.

Primary health care interventions designed to reduce individuals' exposure to risk factors, such as physical inactivity, have shown improvements in perception of health-related quality of life and gains in quality-adjusted life year (QALY), consequently reducing expenditures in national health systems<sup>11-18</sup>. Considering this perspective, in some countries most of the population visits primary health care annually, making this an ideal setting for intervening to increase physical activity, which could lead to better cost-effectiveness.

A Brazilian study, carried out with the population served by the public health network, verified the benefits of physical activity on quality-adjusted life years (QALY) and observed a more advantageous cost-utility relationship for the group that did not undergo any drug treatment and was considered physically active (US\$ 0.12/QALY), followed by the group that underwent drug treatment combined with physical activity (US\$ 3.21/QALY) and, later, by the group that underwent only drug treatment (US\$ 3.92/QALY)<sup>19</sup>. However, it should be noted that this study was based on self-reported information.

Despite the high prevalence of hypertension<sup>20</sup>, there is a lack of information on the application of evidence-based methods in decision-making processes for public policy in developing nations, especially considering primary care services, responsible for the treatment and monitoring of hypertensive patients. Therefore, we emphasize the importance and originality of this proposal in hypothesizing that an exercise program adapted to the reality of Brazilian primary care, for the population with arterial hypertension, can be cost-effective in improving the perception of health-related quality of life and gains in the QALY.

Therefore, the present study aimed to conduct a cost-utility analysis, in real-life conditions, of the treatment usually supplied to hypertensive patients in primary care services in Presidente Prudente municipality, Brazil, based on traditional drug therapy (TDT) in comparison to alternative treatment including exercise program (TDT+E).

## Methods

### *Study design*

Economic assessment of longitudinal intervention study comparing traditional drug therapy (TDT) and drug therapy combined with exercise (TDT+E) among hypertensive adults ( $\geq 50$  years old) within primary health care units.

### *Sample*

The sample included patients of primary care services provided by the Brazilian National Health Service in Presidente Prudente (~200,000 inhabitants; Human Development Index = 0.806), located in the western region of

Sao Paulo state, Brazil. The patients were assigned into two groups for comparison of interventions during 12 months: TDT ( $n = 20$ ), and TDT+E ( $n = 29$ ).

Two Basic Healthcare Units were selected by local authorities (Municipal Department of Health) to perform the longitudinal study, considering the high number of daily appointments for patients. Enrollment of patients was performed for 30 days at each Basic Healthcare Unit from year to year. All patients with appointments scheduled during the 30 days enrollment period were initially considered eligible to participate in the study.

After first contact for enrollment, the inclusion criteria considered for participation in the study were: i) active registration in the Basic Healthcare Unit; ii) age  $\geq 50$  years, life stage associated with the onset of non-communicable chronic diseases among Brazilian adults<sup>21</sup>, and higher probability of death in low- and middle-income countries<sup>22</sup>; iii) medical diagnosis for hypertension; iv) reported not participating in physical activities/sports in the leisure time; v) signed written 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.

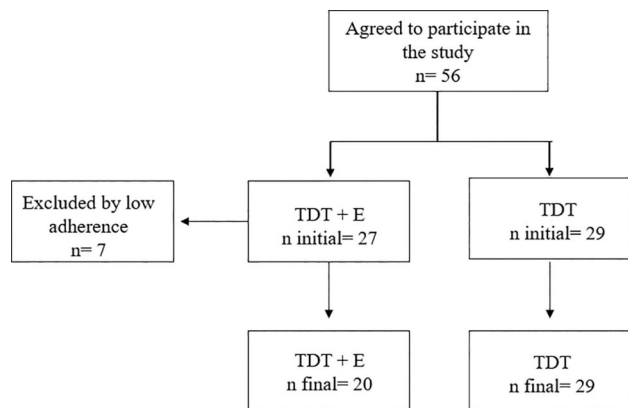
Patients selected for participation in the study had a physician consultation in order to be released for participation in the exercise intervention. The study was approved by the Ethics Research Committee of the Sao Paulo State University (process number: 241.291/2013).

### *Sample size*

The sample size calculation was based on previous data<sup>23</sup> using Student's t-test equation, accounting for a 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% for sample losses throughout the intervention. The minimum sample size estimated was 20 patients in each group ( $n_{\text{total}} = 40$ ).

Initially, 27 adults agreed to participate in the intervention group (TDT+E), all meeting the inclusion criteria and having medical clearance to practice exercises. In the TDT+E, 7 adults were excluded due to low adherence to training sessions (patients with a participation rate sub than 70% were excluded from data analysis). In parallel, 29 adults were 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 (Figure 1).

Thus, the final sample included 49 adults, 20 adults from TDT+E group ( $n = 7$  (35%) men and  $n = 13$  (65%)



**Figure 1** - Flowchart containing sample loss during follow-up. Obs.: TDT+E = traditional drug therapy combined with exercise; TDT = traditional drug therapy; n = number of participants.

women) and 29 adults from TDT group (n = 10 (34.5%) men and n = 19 (65.5%) women).

### Variables

Trained researchers performed personal interviews<sup>24</sup> to register patients' data regarding sociodemographic and lifestyle dimensions (age, sex, among others), including health status: i) diagnosis of hypertension and other chronic diseases; ii) age of diagnosis, and iii) use of medication.

Physical inactivity was assessed using Baecke's<sup>25</sup> questionnaire, comprised 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). Individuals who did not report physical activities in the dimension of sports/exercise during leisure time were considered insufficiently active (inclusion criteria).

In addition, the patient's resting blood pressure (systolic, SBP, and diastolic, DBP) was taken out before the interviews began, following the protocol of the VI Brazilian Guidelines on Hypertension<sup>26</sup>. Body mass index (BMI) was calculated by dividing the patient's weight by height squared ( $\text{kg/m}^2$ ), using the patient's measurements of weight and height<sup>27</sup>.

### Health outcomes related to the quality of life

The estimation of quality-adjusted life years was based on health-related quality of life aspects, assessed using the EuroQoL Group Descriptive System - EQ-5D (1990) questionnaire, an instrument validated for the Brazilian population by Andrade et al.<sup>28</sup>.

The questionnaire is based on a classification system capable of describing the health-related quality of life in five different dimensions: i) mobility; ii) self-care; iii) usual activities; iv) pain/discomfort, and v) anxiety/depression. Utility values range from -0.1755 to 1 (according to the EuroQol group for the Brazilian popula-

tion), which are considered worst and best health status, respectively. The utility values obtained were used to weigh the patient's life expectancy, estimated using the individual's birth year, in order to calculate his/her quality-adjusted life years (QALY).

### Direct health care costs

Direct health care 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<sup>23,29</sup>. Healthcare expenditures included medication obtained in the health care facility, diagnostic exams performed, health professionals' consultations (medical, nursing, and physical therapy), and screening before and after appointments.

Overhead costs associated with the management and operation of the Basic Healthcare Unit were considered in the estimation of direct costs, including medication withdrawal at the pharmacy, and administrative costs (human resources, electricity, water, and telephone bills).

Prices of health care 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 health care costs were estimated for each patient during the 12 months.

Direct costs related to the exercise program (alternative supplementary treatment) were incorporated into direct health care costs in the case of patients assigned to the TDT+E group. The direct costs of the exercise program were based on the monthly wage of the exercise professional, 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, the 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 to January 2019 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.

### Protocol on health strategies (TDT and TDT+E)

Individuals in the TDT group followed traditional drug therapy, following medical recommendations without regular physical exercise. They were assessed every six months to investigate physical activity level<sup>25</sup>, and

patients who started any physical activity program during the 12 month follow-up were excluded from data analysis.

Individuals in the TDT+E group also followed a protocol of traditional drug therapy, combined with a protocol of systematic physical exercise. The exercise protocol followed the VI Brazilian Guidelines for Hypertension<sup>26</sup>. At the beginning of exercise sessions, 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. 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<sup>30</sup>.

Exercise sessions started with stretching, followed by aerobic exercise [30 min walking, intensity maintained between 65% and 75% of maximum heart rate, controlled using a heart rate monitor (POLAR mark, model FT1)]. Patients using beta-blockers had exercise intensity controlled using the Borg Rating of Perceived Exertion Scale, with target zone ranging from 12 to 13<sup>31</sup>. In sequence, the patients performed resistance training (free weights, approximately 25 min) including different muscle groups with sets of 8 to 15 repetitions until moderate fatigue<sup>26</sup>, ending the session with stretching exercises.

The sessions were held three times a week, in each session four to six resistance exercises were performed, so in all sessions exercises for sub 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 program was performed during 12 months of follow-up, and patients with participation rates sub than 70% were excluded from data analysis.

### *Statistical analysis*

The descriptive statistics were composed of mean, standard deviation, median and interquartile range. The difference between groups in the initial part of the study was analyzed using Student's t-test for independent samples or the Mann-Whitney test. Categorical data were assessed using the  $\chi^2$  test. Statistical significance (p-value) was set at values sub than 5%, using BioEstat software (version 5.0).

The economic analysis comparing the two strategies was performed using the cost-effectiveness ratio (CER) and incremental cost-effectiveness ratio (ICER). Cost-utility analysis indicates the therapeutic option with additional health outcomes per monetary unit of cost. The health outcomes selected in the present study should present a positive variation between the beginning and end of

the intervention as an ideal clinical result (improvement in the patient's health status).

Considering that the health outcome of the study refers to additional life expectancy and changes in quality of life in the future, there were three scenarios estimated for sensitivity analysis regarding discount rates in cost-utility ratios: without discount rate, and application of annual discount rates of 3% to 5% on patients' additional quality-adjusted life years.

Finally, a multivariate sensitivity analysis was performed using the Python platform to verify the robustness of CER and ICER results regarding potential changes (shocks) in the main components of costs and health outcomes. Simultaneous variations in patients' costs and health outcome (QALY) of patients ranging from -100% to +100% were applied to estimate diverse scenarios that may alter the cost-utility ratios initially identified in the deterministic case (real situation), focusing especially on costs of physical activity intervention, which was the main difference between groups.

In addition, Monte Carlo simulations were performed to confirm trends in the comparison between control and intervention groups, resulting in 10,000 cases of patients in group intervention and 10,000 cases of patients in group control. The cost estimates were based on the mean and variance of annual health care costs within each group using  $\gamma$  distribution and health outcomes estimates were based on the mean and variance of changes in QALY within each group using the normal distribution.

Finally, the net monetary benefit (NMB) of the physical exercise intervention was assessed to project its acceptability curves. For this calculation, it was considered the acceptable threshold cost of the intervention (physical exercise program), was applied in the interval from US\$ 0 to US\$ 200, based on discrete changes of US\$ 1.

The NMB of individuals in each group, according to the acceptable threshold cost of the intervention value, were compared to estimate the proportion of cases with higher NMB in each group, allowing the design of acceptability curves. That is, the curves point out the probability of higher outcomes with sub intervention costs in comparison to global health care costs for each group.

## **Results**

The sample included 49 adults distributed into two groups, according to the type of treatment. TDT+E group consisted of 20 adults (n = 7 (35%) men and n = 13 (65%) women) and the TDT group consisted of 29 adults (n = 10 (34.5%) men and n = 19 (65.5%) women). Of the patients in the TDT+E group, 9 (45%) used beta-blockers. [Table 1](#) presents the characteristics of the groups at baseline, showing similar characteristics between groups.

**Table 1** - General information at baseline according to the type of treatment.

	Groups			p-value*
	TDT+E (n = 20)	TDT (n = 29)		
	Mean (SD)	Mean (SD)		
	Median (IR)	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 <sup>2</sup> )	30.26 (5.95)	31.32 (5.81)		0.539
	29.36 (5.69)	31.13 (9.49)		
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)		
HPA (score)	6.78 (1.68)	5.95 (0.93)		0.054
	6.68 (2.91)	5.87 (1.31)		
Utility	0.66 (0.20)	0.66 (0.18)		0.984
	0.66 (0.27)	0.64 (0.20)		
QALY (base case)	13.73 (6.08)	11.98 (5.22)		0.287
	12.87 (8.18)	10.92 (8.06)		
Diseases	n (%)	n (%)		p-value**
Dyslipidemia (yes)	7 (35.1%)	14 (48.27%)		0.529
Diabetes Mellitus (yes)	5 (25.1%)	11 (37.93%)		0.523

\*= Student's t-test

\*\*= chi-square test; TDT = traditional drug treatment; TDT+E = traditional drug treatment plus exercise program; SD = standard deviation; IR = interquartile range; BMI = body mass index; HPA = habitual physical activity; QALY = quality adjusted life year.

Direct health care costs at baseline, presented in Table 2, show no statistically significant differences between the two intervention groups.

**Table 2** - Direct health care costs at baseline according to the type of treatment group.

Variables	Groups			p-value*
	TDT+E (n = 20)	TDT (n = 29)		
	Mean (SD)	Mean (SD)		
	Median (IR)	Median (IR)		
Health care costs (US\$)				
Clinical consultation	13.10 (8.87)	13.36 (9.35)		0.758
	11.02 (9.53)	10.27 (10.53)		
Diagnostic exams	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)		
Overhead	5.59 (2.23)	4.22 (1.95)		0.300
	3.94 (2.98)	3.61 (2.58)		
Total direct costs	43.93 (33.57)	34.87 (22.53)		0.319
	38.16 (25.41)	23.89 (26.20)		

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

The CER and ICER of the two groups are presented in Table 3, considering the scenarios with discount rates of 3% and 5% per year. Positive values of CER show effective treatment over the 12 month follow-up.

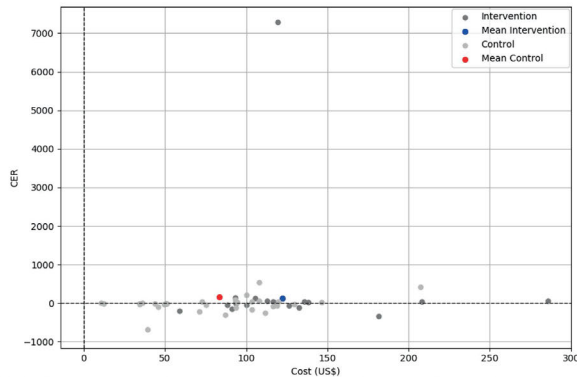
Both treatments showed an increase in QALY over the 12 months of follow-up. Although the mean annual cost of the TDT group (US\$ 83.37) was sub than that of the TDT+E group (US\$ 122.45), it was observed that an improvement unit in QALY cost US\$ 163.42 per year in the TDT group and US\$ 122.38 per year in the TDT+E (base case) group, the latter being more advantageous.

Figure 2 shows the results of the deterministic scenario, representing the diverse cost-effectiveness ratios per QALY according to the cost levels of patients in the sample, including variations in discount rates (none, 3%, and

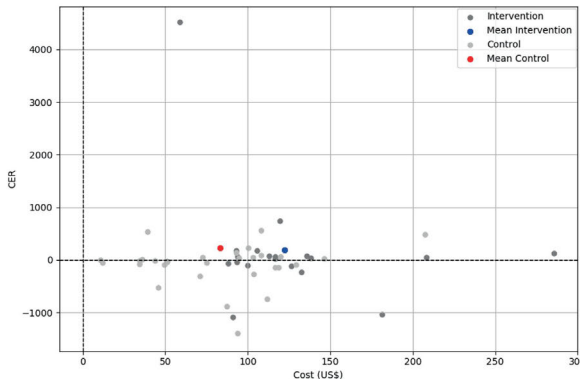
**Table 3** - Cost-utility analysis, according to the intervention group.

Treatment	Discount rate	QALY		Mean cost 12 months (US\$)	Effectiveness (Mean diff. QALY)	CER US \$/QALY	ICER US \$/QALY
		Baseline Mean	Follow up Mean				
TDT (n = 29)	Base case	11.98	12.49	83.37	+0.51	+163.42	+79.69
TDT+E (n = 20)	Base case	13.73	14.73	122.45	+1.00	+122.38	
TDT (n = 29)	3%	6.74	7.10	83.37	+0.36	+233.64	+142.58
TDT+E (n = 20)	3%	7.07	7.70	122.45	+0.63	+194.08	
TDT (n = 29)	5%	4.71	4.99	83.37	+0.28	+300.64	+219.10
TDT+E (n = 20)	5%	4.69	5.15	122.45	+0.46	+268.72	

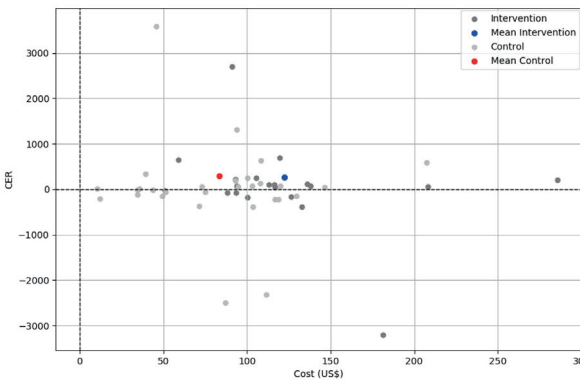
TDT = traditional drug treatment; TDT+E = traditional drug treatment plus exercise program; Diff = difference; QALY = quality adjusted life year; CER = cost-effectiveness ratio; ICER = incremental cost-effectiveness ratio.



(1a) Physical exercise program costs and QALY without discount rate.



(1b) Physical exercise program costs and QALY with a 3% discount rate.

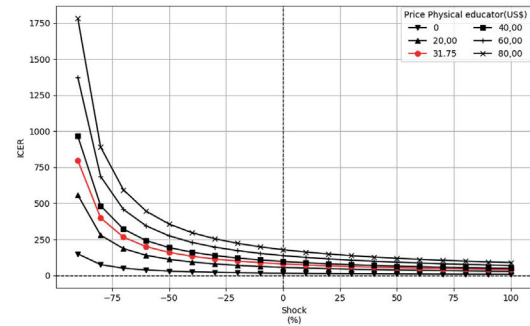


(1c) Physical exercise program costs and QALY with a 5% discount rate.

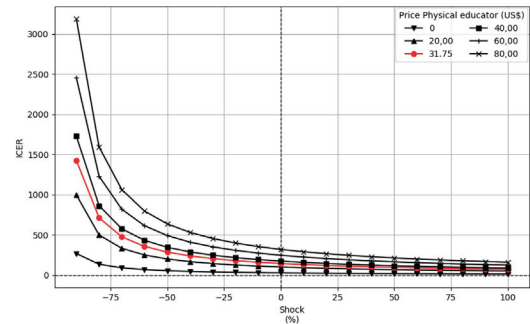
**Figure 2** - Cost-Effectiveness Ratios (CER) per QALY in the deterministic scenario of the sample. Obs.: QALY = Quality-Adjusted Life Years; QALY 3% = QALY with 3% discount rate; QALY 5% = QALY with 5% discount rate; cont = control group; interv = intervention group.

5% per year). The control group presents sub costs than the intervention group, and the mean differences in health outcomes are negligible at first. Increases in discount rates resulted in a reduction of the variability of health outcomes in groups control and intervention.

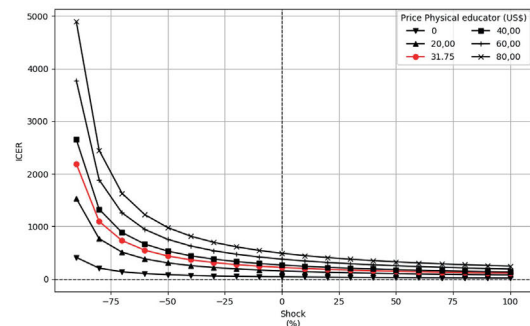
Figure 3 presents the results of multivariate sensitivity analysis deriving from significant variations in healthcare costs and health outcomes (Quality Adjusted Life Years), including variations in discount rates (none, 3%, and 5% per year). Considering changes in the cost of



(2a) Changes in physical exercise program costs and QALY without discount rate.



(2b) Changes in physical exercise program costs and QALY with a 3% discount rate.



(2c) Changes in physical exercise program costs and QALY with a 5% discount rate.

**Figure 3** - Multivariate sensitivity analysis scenarios from changes in health care costs, physical exercise program costs, and QALY. Obs.: ICER = Incremental Cost-Effectiveness Ratio; QALY = Quality-Adjusted Life Years.

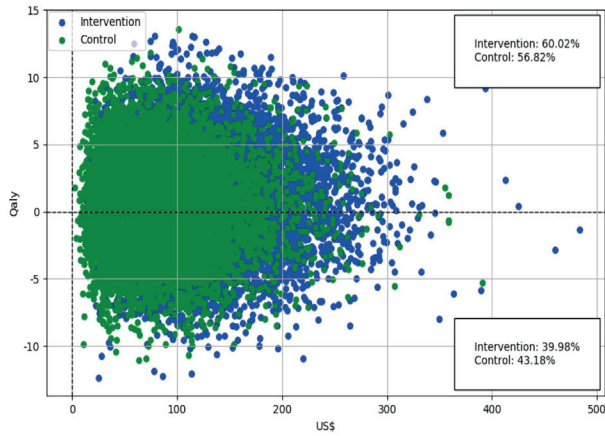
physical education professionals in primary health care, we projected changes in values for payment of the professionals and QALY in relation to ICER results. The increase in costs with physical education professionals showed an increase in ICER at negative shocks in QALY; however, shocks closer to 0 and higher positive shocks in QALY tended to present gradually similar results in ICER. Changes in discount rates only increased the magnitude of differences between initial points of ICER.

It is important to notice that the differences in costs per QALY between groups increase according to discount rates at sub negative variations in health outcome (from approximately US\$ 1,750 without a discount rate to more than US\$ 5,000 with a 5% discount rate); however, positive changes in health outcome (QALY) mitigate the differences in costs.

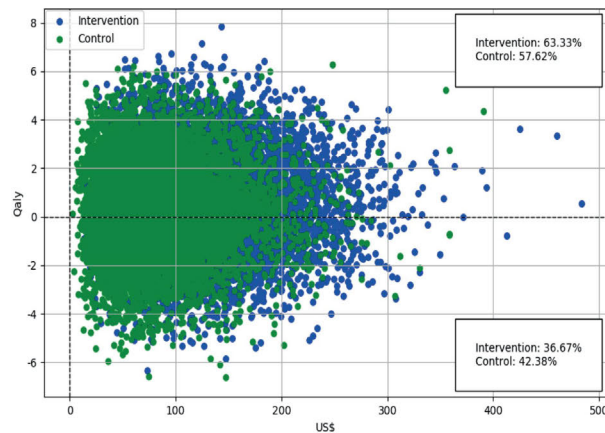
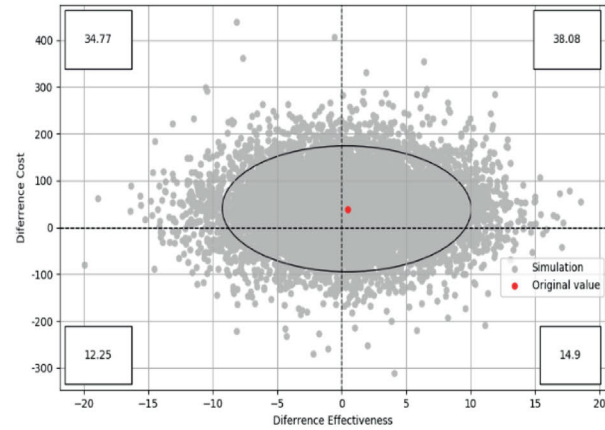
Regarding probabilistic sensitivity analysis, results of the Monte Carlo simulations (Figure 4) indicated that the intervention group had higher effectiveness in most scenarios, compared to the control group (from 52.98% of

cases without a discount rate to 54.07% of cases with 5% discount rate).

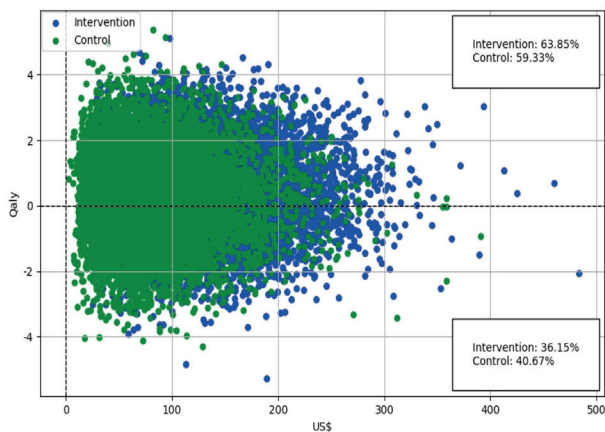
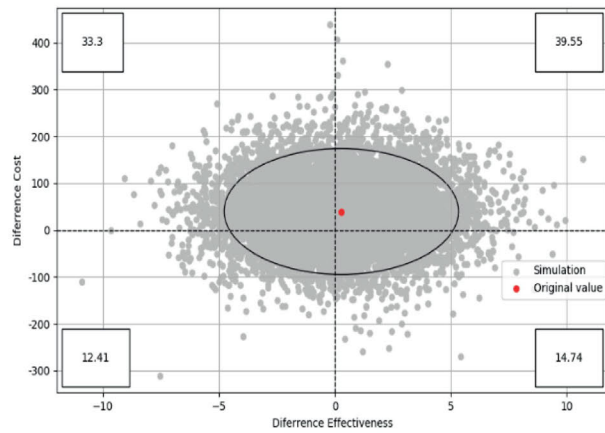
The exercise program is dominant in approximately 15% of the scenarios simulated with or without a discount



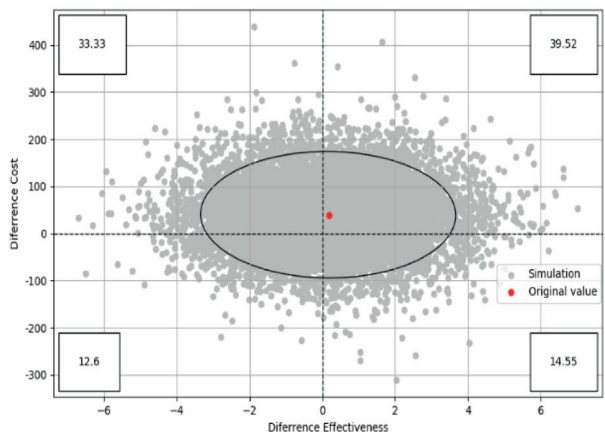
(3a) Simulations based on QALY without discount rate.



(3b) Simulations based on QALY with a 3% discount rate.



(3c) Simulations based on QALY with a 5% discount rate.



**Figure 4** - Probabilistic sensitivity analysis scenarios from changes in health care costs, physical exercise program costs, and QALY. Obs.: QALY = Quality-Adjusted Life Years.

rate, being cost-effective with higher QALY associated with higher costs in approximately 39% of the scenarios and cost-effective with sub QALY and sub costs in approximately 12% of simulations.

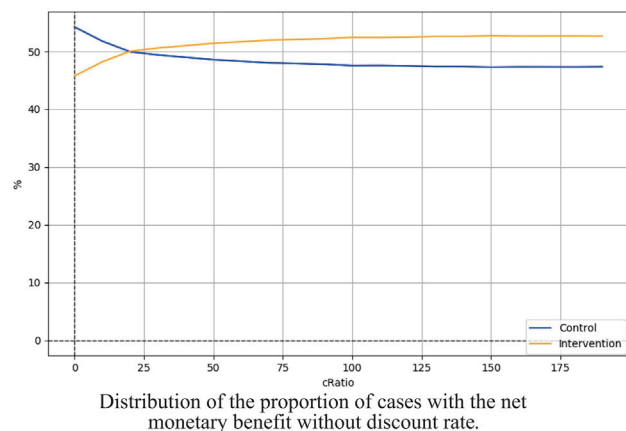
Finally, it is important to notice that the acceptability curves estimated with Monte Carlo simulations showed cutoff points in favor of the physical exercise intervention at US\$ 20 per capita (without discount rate) (Figure 5); US \$ 25 per capita (3% discount rate) and US\$ 38 per capita (5% discount rate), i.e., the lowest intervention costs allowing the probability of higher outcomes that compensate differences in global health care costs.

The results of net monetary benefit indicated that willingness to pay for physical activity intervention compensated health care costs due to increases in effectiveness, showing an advantage in investments to promote physical activity that minimizes health care costs attributable to problems due to hypertension.

## Discussion

The main finding of the present study indicates through real-life data that traditional drug treatment combined with an exercise program for adults with hypertension was effective in improving the quality of life, and QALY, although it also resulted in increased direct health care costs within the health system. However, incremental cost-utility ratios showed benefits in relation to traditional drug treatment, considering the best and worst scenarios in the analysis of uncertainties.

Regarding the average costs of interventions per participant, we found that the mean annual cost of the TDT group was US\$ 83.37 and of the TDT+E group US\$ 122.45 found were higher than those observed by another Brazilian study carried out with a population also served by the public health network (US\$ 56.07 for those who underwent drug treatment only and US\$ 49.06 for those who underwent drug treatment and were classified



**Figure 5** - Acceptability curves from estimates of Net Monetary Benefit (NMB) in simulations. Presidente Prudente, 2015.

as physically active)<sup>19</sup>. However, it is worth mentioning that our results include costs with the exercise program, which, in this case, was not verified in the aforementioned study, since the information on the level of physical activity was self-reported.

Regarding CER, we observed that traditional drug treatment resulted in additional QALY, although showing higher cost-utility. The result is similar to findings from a study based on probabilistic simulations performed in China, indicating that government incentives to reduce hypertension through drug treatment could lead to gains of 1.2 million QALY annually with good cost-utility, considering that the increment of one unit of QALY would cost US\$ 9,000 (sub than the limit established by national simulations, US\$ 11,900)<sup>32</sup>.

The effectiveness of the drug treatment in increasing QALY was maximized when combined with the exercise program. Although the effectiveness of the traditional drug treatment provided an average gain of 0.51 QALY per year, the combination of medication with exercise showed an average gain of 1.0 QALY per year (96% higher). Evidence shows that regular practice of exercise improves self-assessment of health status and QALY among hypertensive patients<sup>13,14,17</sup>. In Texas, a 10 week exercise program among adults aged  $\geq 55$  years, mostly hypertensive (73%), found an average of 0.159 QALY<sup>13</sup>. However, few studies specifically evaluate the cost-utility of drug treatment combined with an exercise program for hypertensive patients.

The improvements in quality of life and QALY might be explained by the training protocol used in the present research. It is well established that both aerobic and combined aerobic with resistance exercise generate improvements in physiological parameters, including aerobic capacity<sup>33</sup>, reduction of blood pressure in individuals with systemic hypertension<sup>34</sup>, and increase of muscular strength<sup>35</sup>, besides being the most important modifiable protective factor of lifestyle<sup>34</sup> providing better overall mobility in adults<sup>36</sup>.

Cost-utility measures have been tools used by public managers for decision-making considering the financial expenditures required to implement innovative health strategies for improvement of population quality of life<sup>11,12,15-18</sup>. However, most studies focus on strategies based on incentives and/or counseling for the adoption of physical activity, not necessarily giving conditions for enrolling in exercise programs guided and monitored by physical education professional<sup>11,12,14,17,18</sup>.

However, it is worth mentioning that incentives and/or counseling regarding the practice of physical activity have been pointed out as useful strategies to increase levels of physical activity among users of primary health care, being also cost-effective in comparison to the traditional treatment<sup>11</sup>. Previous studies have been conducted in developed countries, especially in the National Health



Service in the United Kingdom<sup>11,12,14,17,18</sup>, which have established widely accepted thresholds for the incremental cost-utility ratio of £ 20,000 to £ 30,000 per QALY gained<sup>37</sup>.

A population study using information from 5,248 Brazilian municipalities showed that primary health care strategies for the promotion of health and prevention of chronic diseases had positive effects on the reduction of hospitalization rate and mortality due to hypertension. In this sense, a 1% increase in the coverage of primary health care strategies reduced hypertension mortality rates by 0.2% and promoted a decrease of 0.4% in average hospital length of stay due to hypertension<sup>38</sup>.

Although the Brazilian National Health Service presents similarities to the National Health Service of the United Kingdom (i.e., health services publicly funded by the government), there are no official cut-off points to establish cost-utility thresholds for consideration in the case of exercise programs implemented in primary health care. A study published in Brazil showed that there were high expectations from the healthcare business industry regarding an official stipulation of a financial threshold by the Brazilian government, in order to ensure economic returns through lawsuits enforcing the adoption of health care innovations within the publicly funded national health system, which may lead to misallocation of resources<sup>39</sup>.

Additionally, considering disparities between Brazil and United Kingdom referring to socioeconomic, demographic, and geographical characteristics, there are some questions to be addressed in terms of direct comparability with data presented in the study. Research regarding the economic assessment of health interventions in Brazil has been progressing in the last decade; however, it is important to point out that some studies performed in Brazil still lack adherence to standards evaluation and protocols in economics that could provide parameters with expected quality.

Aiming to elucidate the national literature to policy-makers and health agencies considering the implementation of the exercise program, even presenting comparability with a previous study, we must be cautious in affirming the possible feasibility of implementing exercise programs, since, in the Brazilian scenario, considerations about decision-making in public policies must be based on willingness to pay.

Therefore, it would be advisable that research performed in Brazil should give some attention to this matter within the Brazilian context due to its extreme importance for national public policies, especially considering the wide array of evidence on direct gains in disease prevention, benefits in health promotion and additional quality of life resulting from exercise interventions, and consequently minimizing health care costs<sup>20,21,23,29</sup>.

The present study has some limitations, including a lack of randomization of the patients into the intervention

groups, and the presence of other diseases that could be potential factors affecting the results obtained. Also, it is not possible to isolate the impacts of aerobic and resistance training on health outcomes. Finally, the costs related to the place for execution, the 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 the originality of the study regarding research design, encompassing follow-up of patients in primary health care and implementation of the intervention during 12 months, as well as a comparison of results between intervention and control groups.

In addition, we can infer that this is a strong and important study for the Brazilian context, as it is methodically suited to the recently published Guidelines for Utility Measurement for Economic Analysis<sup>40</sup>, regarding the choice of data collection instrument. In addition, the document in question makes clear the need for sensitivity analyses, which consider any potential differences in utility estimates. Therefore, as mentioned throughout the discussion, even finding it is difficult to compare the data found with previous national studies, this study is innovative and can be a reference for managers in decision making.

## Conclusion

Our study contributes to filling the gap in knowledge by showing that exercise programs might show high cost-utility within primary health care settings dealing with public health interventions, besides improving QALY among hypertensive patients.

## Funding

This study was financed by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) process number: 476244/2013-7.

## Conflict of interest

The authors declare that there are no conflicts of interest.

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#### *Corresponding author*

Monique Yndawe Castanho Araujo. Universidade Estadual Paulista “Julio de Mesquita Filho”, Departamento de Educação Física, Presidente Prudente, SP, Brazil.  
E-mail: mo\_castanho@hotmail.com.

*Manuscript received on April 21, 2022*

*Manuscript accepted on July 11, 2022*



Motriz. The Journal of Physical Education. UNESP. Rio Claro, SP, Brazil  
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