ARTIGO ORIGINAL

Association between physical activity levels and polypharmacy in hypertensive patients

Associação entre níveis de atividade física e polifarmácia em pacientes hipertensos

Denise R. Bueno[1], Henrique L. Monteiro[2], Clara S. C. Rosa[3], Jamile S. Codogno[2], Rômulo A. Fernandes[2], Maria F. N. Marucci[4]

ABSTRACT

Background: exercise reduces medication usage in hypertensive people. However, different domains of physical activity (PA) have not been studied in order to analyze their relationship with the use of multiple medications, known as polypharmacy. **Purpose**: To examine the association between PA in different domains (leisure-time, locomotion and occupational) and polypharmacy in hypertensive patients. **Methods**: This is a cross-sectional study carried out with 190 hypertensive patients. Polypharmacy was defined as simultaneous use of three or more drugs. The PA domains were the independent variables: Locomotion PA (LPA), Leisure Time PA (LTPA) and Occupational PA (OPA). The multiple logistic regression was performed to analyze the associations. The Mann Whitney test determined whether medications usage differ according to each domain of PA. **Results**: The total number of drugs used ranged from 0 to 7, which represents an average of 2.35 (±1.6) drugs per person. Scores of LTPA (OR: 3.25; CI95%:1.61-6.54) and LPA (OR: 2.15; CI95%:1.09-4.25) were inversely associated with polypharmacy in hypertensive patients, in the multiple logistic regression analysis (controlled by BMI, chronic diseases, smoking, alcohol consumption and skin color). **Conclusions**: lower PA in leisure time and locomotion were associated with polypharmacy in hypertensive people.

Keywords: Hypertension. Physical Activity. Polypharmacy.

RESUMO

Introdução: o exercício reduz o uso de medicamentos em indivíduos hipertensos. Contudo, diferentes domínios de atividade física (AF) não têm sido estudados no intuito de analisar suas relações com o uso de múltiplos medicamentos, conhecido como polifarmácia. **Objetivo**: analisar a associação entre AF em diferentes domínios (tempo livre, locomoção e ocupação) e polifarmácia em indivíduos hipertensos. **Métodos**: trata-se de um estudo transversal realizado com 190 hipertensos. Polifarmácia foi definida como o uso simultâneo de três ou mais drogas. As variáveis independentes foram os domínios de AF: Locomoção (AFL); Tempo Livre (AFTL) e Ocupacional (AFO). A regressão logística múltipla foi empregada para analisar as associações. O teste de Mann Whitney foi empregado para comparar se a média de medicamentos usados diferia entre domínios de AF. **Resultados**: o número total de drogas usadas

1. Doutoranda do Programa de Pós Graduação em Nutrição em Saúde Pública, Universidade de São Paulo.
2. Docentes do Departamento de Educação Física, Unesp.
3. Doutoranda do Programa de Pós Graduação em Ciências da Motricidade, Unesp.
4. Docente do Departamento de Nutrição, Faculdade de Saúde Pública, Universidade de São Paulo.

Correspondence:
Denise Rodrigues Bueno,
Depertment of Nutrition, School of Public Health
University of São Paulo – USP
Avenida Doutor Arnaldo, 715 – Cerqueira César
CEP: 01246-904 - São Paulo - SP – Brazil

Recebido em 06/04/2015
Aprovado em 15/09/2015

variou de 0 a 7, com média de 2.35 (±1.6) por pessoa. Escores de AFTL (OR: 3.25; IC95%: 1.61-6.54) e AFL (OR: 2.15; IC95%: 1.09-4.25) foram inversamente associadas à polifarmácia em hipertensos (controlado por IMC, número de doenças crônicas, fumo, consumo de álcool e cor da pele). Conclusão: menor AF no tempo livre e de locomoção foi associada à polifarmácia em indivíduos hipertensos.

Palavras-chave: Hipertensão. Atividade Física. Polifármacos.

.

Background

The prevalence of hypertension is estimated at between 20 and 40% in adults from developing and developed nations. [1,2,3] The high risk of cardiovascular mortality in hypertensive patients [4] makes blood pressure control important for long-term survival on this population. Thus, the simultaneous prescription of different drugs (diuretics, adrenergic inhibitors, vasodilators, and beta blockers) is common in hypertensive patients, which characterizes the use of antihypertensive drugs as a common behavior.[5] Nevertheless, the use of more than one drug and their interactions have adverse effects on health, increase hospitalization and emergency care,[6,7] and hence, an increased burden on health care costs.[8]

Adherence to a drug-free approach to blood pressure control has been recommended, which consists of changes in lifestyle, including exercising, diet control, and alcohol and cigarette restriction.[2] In addition to obesity, indicated by a BMI ≥30kg/m^2, [9] low physical activity level (PAL) is also associated with hypertension development,[10,11] on the other hand aerobic exercises are effective in reducing both blood pressure[12,13,14] and medication intake.[15,16] Despite this, the effects of everyday activities such as occupational (OPA), locomotion (LPA) and leisure-time (LTPA) on medications intake and polypharmacy are little known.

Thus, this study aimed to analyze, in a sample of hypertensive patients, the association between levels of occupational, leisure time and locomotion physical activities and the occurrence of polypharmacy.

Material and Methods

Sample and Sampling

This study was conducted in two health centers located in the southwestern region of Bauru, Sao Paulo State of Brazil. It was estimated that approximately 835 hypertensive patients were attended by these Health Centers in the study occasion. All hypertensive were aged over 40 years and had been diagnosed with hypertension for at least 12 months. All hypertensive patients UBS's were invited to participate. However, according to sample size calculation (according to hypertension prevalence in Bauru), the age criteria and time of diagnosis, the same researcher interviewed a total of 190 subjects.

The subjects were informed about the assessment procedures and conditions for participation in the research. Subsequently, they signed a consent form approved by the Research Ethics Committee of the Faculty of Science and Technology, São Paulo State University - UNESP – Presidente Prudente Campus (No. 322-08), authorizing the use of information for scientific purposes and ensuring their confidentiality.

Polypharmacy

The number of medications was verified in the clinical record of each patient. All prescribed medications were computed, regardless of their pharmacological action, specific clinical treatment intended or diseases. There is no consensus for polyoharmacy in literature,[17] it has been shown as varying from two or more drugs[18] to nine or more drugs.[19] In this study polypharmacy was defined as the concomitant use of three or more drugs. This cutoff is commonly used in national[20] and international studies.[21,22]

Domains of Physical Activity

Physical activity was self-reported by interview using Baecke questionnaire.[23] This method has been nationally validated in male adults.[24,25] The questionnaire categorizes the daily physical activity into three domains: OPA, LTPA and LPA. Scores calculation have been described before.[23]

There is no established criterion in the literature for the PAL classification based on Baecke score.

To enable binary logistic regression analysis**,** the participants were divided into two groups: participants who scored above the median score (reference) and patients who scored below the median score.

Explanatory Variables (control)

Number of diseases such as cardiovascular and type 2 diabetes, and presence or absence of smoking and alcohol consumption, educational level (categorized as < eight years of education and ≥ eight years of education) and skin color (categorized as white or other) were self-reported in a questionnaire. Body mass index (BMI - kg/m²) was calculated using the values of body weight and height, both measured according to Lohman's protocol.[24] After calculating the BMI, patients were categorized into two groups: i) BMI <30 kg/m²; and, ii) BMI ≥ 30 kg/m².[25]

Statistical Analysis

For the univariate (chi-squared test) and multiple analysis, the dependent variable was defined as polypharmacy and the independent variables were age, smoking, BMI, type 2 diabetes, number of diseases, gender, alcohol consumption, education and ethnicity. All variables with a p value < 0.20 in the univariate analysis were selected for the multiple logistic regression model (expressed as odds ratios [OR] and 95% confidence intervals [95%CI]). Following the forward stepwise method, variables that remained significant (p < 0.05) or which adjusted the Odds Ratio (OR) by at least 10% were kept in the model. Kruskal- Wallis and Mann Whitney tests compared medication means according to the PAL in each domain due to the lack of normality in the dataset. Statistical significance for associations was considered when p < 0.05 and all analyzes were performed using SPSS 20.0 for Windows.

Results

Description of the sample

The mean age of the 130 women and 60 men was 63 (11) years. All dependent variables according to categorization, and their association with polypharmacy are presented in Table 1. The number of diseases and diabetes were the variables associated with polypharmacy in univariate analysis (p < 0.05). Among the physical activity domains, only LTPA was associated with polypharmacy (p = 0.036).

Physical activity and drugs

The total number of medications use ranged from 0 to 7 and 38% of patients reported at least three drugs on their medical prescription. The total number of drugs prescribed for the 190 patients were 446, which represents an average of 2.35 (1.6) per person. The classes of drugs were not documented according to their pharmacological action, however the most prevalent health problems observed in the sample were: hypercholesterolemia (42%), type 2 diabetes (23%), arthritis (20%), cardiac arrhythmia and heart attack event (12% each) and osteoporosis (9%). There was no difference between the sexes for drugs usage (p> 0.05).

The final logistic regression model of the risk of polypharmacy adjusted by the number of diseases and education level is presented graphics on Figure 1. LTPA (OR= 3.25; IC95%= 1.61 – 6.54) and LPA were associated (OR= 2.15; IC95%= 1.09 – 4.25)) with polypharmacy compared to groups with lower PAL in these domains (p <0.05). Type 2 diabetes was associated with polypharmacy (OR= 3.79; IC95%= 1.71 – 8.38) in this sample.

Figure 2 demonstrates the comparison between quartiles of LTPA for drugs use (mean), where lower medication use was observed with higher PA scores (i.e. 4th quartile) (p = 0.02). The differences occurred between the 1st and 3rd quartiles (p = 0.02). Between the 2nd and 3rd quartiles (p = 0.01) and between the 2nd and 4th quartiles (p = 0.04), always with the lowest means observed for the intervals with the higher scores. For the other domains studied no statistically significant differences were observed.

Discussion

The present study examined the association between different PA domains and polypharmacy in hypertensive patients. The lower PA score in leisure time and locomotion were inversely associated with polypharmacy. The average of drugs use was higher among individuals with lower PA scores in leisure time.

Table 1. Distribution of the sample according to the study variables and number of drugs and association with polypharmacy (≥ 3 drugs)

	Drugs				
	≤ 2	*≥ 3*			
	n (%)	*n (%)*			
Variables	***117 (61.6)***	***73 (38.4)***	***OR***	***CI95%***	***P***
Age					
< 60 years old	47 (64.4)	26 (35.6)	1.00		
≥ 60 years old	70 (59.8)	47 (40.2)	1.21	066 – 2.22	0.53
Smoke					
No	11 (61.1)	07 (38.9)	1.00		
Yes	106 (61.6)	66 (38.4)	1.02	0.38- 2.77	0.97
Sex					
Man	80 (61.5)	50 (38.5)	1.00		
Woman	37(61.7)	23 (38.3)	0.99	0.53 – 1.87	0.98
BMI					
< 30 kg/ m²	28 (70.0)	12 (30.0)	1.00		
≥ 30 kg/ m²	89 (59.3)	61 (40.7)	1.60	0.76 – 3.39	0.22
Education					
≥ 8 years	25 (53.2)	22 (46.8)	1.00		
< 8 years	92 (6.3)	51 (35.7)	0.63	0.32 – 1.23	0.17
Ethnic group					
White	70 (59.8)	47 (40.2)	1.00		
Others	47 (64.4)	26 (35.6)	0.82	0.45 – 1.51	0.53
Alcohol					
No	104 (60.5)	68 (39.5)	1.00		
Yes	13 (72.2)	05 (27.8)	0.59	0.20 – 1.73	0.33
Diabetes					
No	100 (68.5)	46 (31.5)	1.00		
Yes	17 (38.6)	27 (61.4)	3.45	1.71 – 6.95	0.001*
Number of diseases					
≤ 2	94 (66.7)	47 (33.3)	1.00		
≥ 3	23 (46.7)	26 (53.1)	2.26	1.17 – 4.38	0.01*
Physical Activity Score					
OPA					
Higher	68 (66.7)	34 (33.3)	1,00		
Lower	49 (55.7)	39 (44.3)	1.59	0.88 – 2.87	0.12
LTPA					
Higher	68 (68.7)	31 (31.3)	1,00		
Lower	49 (58.3)	42 (46.2)	1.88	1.04 – 2.40	0.04*
LPA					
Higher	54 (67.5)	26 (32.5)	1,00		
Lower	63 (57.3)	47 (42.7)	1.55	0.85 – 2.83	0.15

Note: BMI – body mass index; OPA – occupational physical activity; LTPA – leisure-time physical activity; LPA – locomotion physical activity. *statistical significance for univariate logistic regression

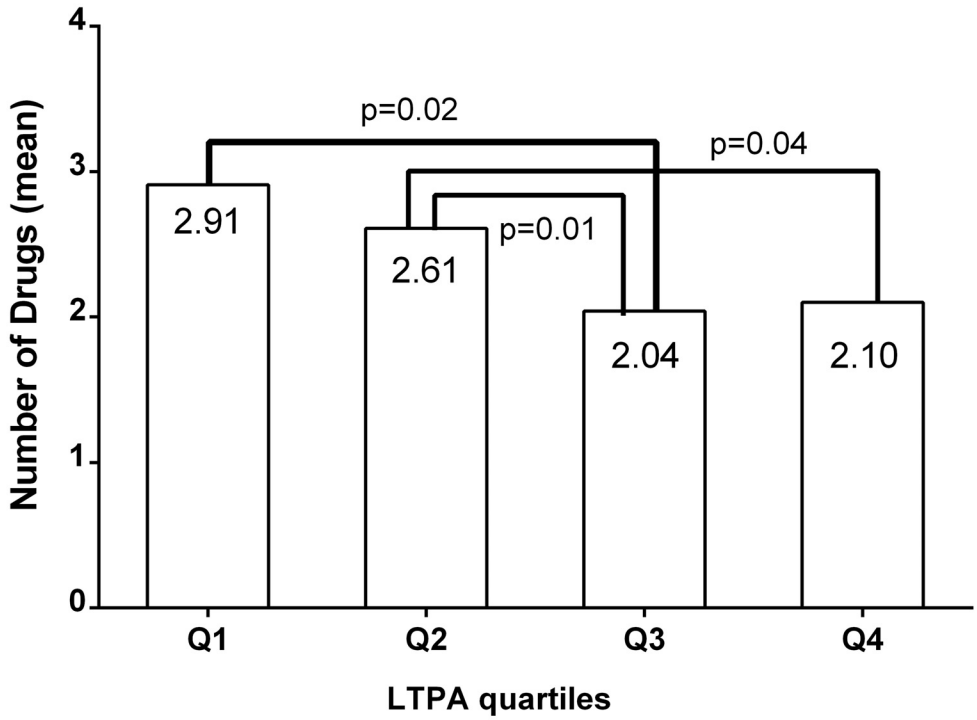

Figure 1. Means of drug use between LTPA quartiles. (Mann Whitney analysis) LTPA – leisure-time physical activity

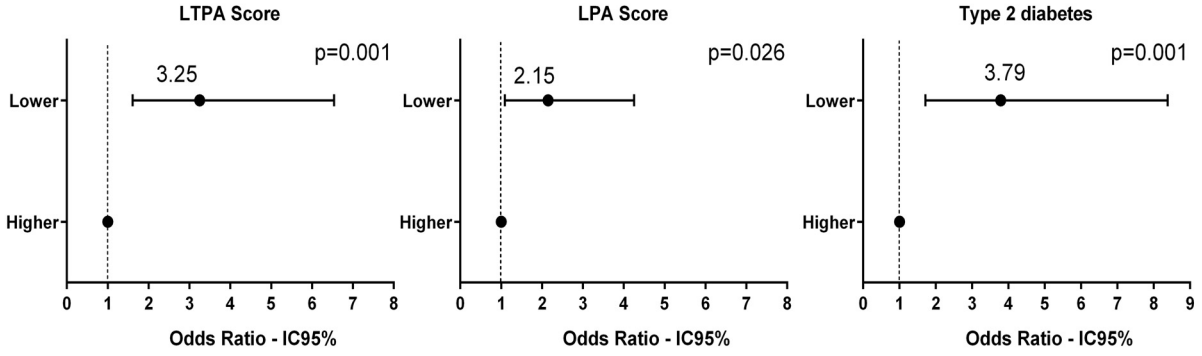

Figure 2. Final model of logistic regression to association of physical activity level in each domain (scores) and drugs use. (Logistic Regression). Odds Ratio values and interval of confidence (IC95%).

The drugs use were slightly lower than other Brazilian studies, researchers found an average of 3,2 in a study in Porto Alegre city[26] and 3,6 in São Paulo city.[27] In United States, there are reports showing that elderly people use between 2,7 and 4,2 drugs,[28] in Sweden the averages were 1,6 for subjects between 50 and 64 years old and 3,2 for those between 65 and 75 years old.[29] Polypharmacy is common in older groups[16] due to the higher prevalence of chronic diseases. Regarding this analysis, it is noteworthy that medications computed in this study were those prescribed by the doctor, therefore other drugs, self-administered by patients were not known, i.e., the number of drugs could be higher when considering that the participants could have self-medicated ,[30] which is common in the elderly.

In relation to the presence of type 2 diabetes, Carvalho et al. founded the risk of polypharmacy four times higher among elderly who self-reported this disease.[27] It is important to verify that all the above diseases, such as type 2 diabetes, have sedentary lifestyle as a risk factor and can therefore be controlled by the adoption of regular physical activity[31] which thereby reflects in a decreased of drug intake, as previously described by several studies.[32-35]

In addition, exercise causes reduction in fat percentage and body weight, components which are directly associated with the greatest need for intervention by drug therapy in hypertensive patients.[36,37] Leisure-time activities such as walking or gardening may have beneficial cardiovascular effects, even if they do not qualify as physical training.[39,40] Thus, it is expected that more physically active patients have better health outcomes and show a lower prevalence of polypharmacy. The literature has shown that exercise plays an important role in controlling chronic disease parameters, such as blood pressure.[41] Selmer et al. showed that the prevalence of hypertensive patients, without cardiovascular diseases, receiving drugs decrease 3%, 5,9% and 11,4% in agreement with a decrease of 1, 2 and 4mmHg in blood pressure, respectively.[42]

However, Fulton and Allen, points out the absence of studies which evaluated types of intervention that could be applied to reduce polypharmacy.[43] The authors mention that there is no evidence in the literature of effective measures for challenging the exacerbating prescription of medications, in addition to the issue of self-medication.

It has been shown that elderly women who walk 8,500 steps per day consume fewer medications than those who walk 6000 steps;[44] lower number of steps compared to those 10,000 found to be associated with maintenance of health and weight control in healthy adults.[45] The study conducted in southern Brazil by Bertoldi et al., showed that increase minutes of moderate and vigorous PA spent per week were associated with less medication use; in adjusted analysis, sedentary (0 minutes per week) individuals showed 23% higher medicine use in comparison to very active (>1000 minutes per week).[46] Using the recommended 150 minutes per week of moderate physical activity as a criterion for the same analyzes, inverse association between PAL and medication use was founded.[39]

Analyzing the association between physical activity level and drugs use, Bardel et al. showed that 40% of women aged between 35 and 65 years-old using drugs, reported lower LTPA ($p < 0.05$) and OPA ($p < 0.01$).[47] Our results showed no association between OPA and drugs use, contradictory to the 80% greater chance of polypharmacy (95% CI 1.1 to 2.7) in individuals who reported exercising at work, compared to individuals retired or unemployed.[27]

Our study had a cross-sectional approach, which may limit the interpretation of the results with regard to the causal relationship between PA and drug consumption. Another limitation is the estimate of PA through the use of a questionnaire, which can differ from more accurate methods and overestimate PAL. However, the method used in this research was validated for the Brazilian population and had the advantage of being low cost and enabling easy data collection.

In summary, physical activity in leisure time and locomotion were inversely associated with polypharmacy in hypertensive individuals. The treatment of patients with chronic diseases should be as effective as possible, as they will continue to use mechanisms of disease control throughout their lives, thus, physical activity should be incorporated into other methods adopted by patients.

References

1. Pereira M, Lunet N, Azevedo A, Barros H. Differences in prevalence, awareness, treatment and control of hypertension between developing and developed countries. J Hypertens. 2009;27:963-75.
2. VI Diretrizes Brasileiras de Hipertensão – DBH VI Conceituação, epidemiologia e prevenção primária (Capítulo 1). Rev Bras Hipertens. 2010;17:7-10.
3. De Macedo ME, Lima MJ, Silva AO, Alcântara P, Ramalhinho V, Carmona J. Prevalence, awareness, treatment and control of hypertension in Portugal. The PAP study. Rev Port Cardiol. 2007;26:21-39.
4. Lawes CMM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. Lancet. 2008; 371(9623):1513–8.
5. Wang YR, Alexander GC, Stafford RS. Outpatient hypertension treatment, treatment intensification, and control in Western Europe and the United States. Arch Intern Med. 2007; 167:141-7.
6. Budnitz DS, Pollock DA, Weidenbach KN, Mendelsohn AB, Schroeder TJ, Annest JL. National surveillance of emergency department visits for outpatient adverse drug events. JAMA. 2006;296:1858-66.
7. Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. N Engl J Med. 2011;365:2002-12.
8. Dib MW, Riera R, Ferraz MB. Estimated annual cost of arterial hypertension treatment in Brazil. Rev Panam Salud Publica. 2010;27:125-31.
9. Redón J, Cea-Calvo L, Moreno B, Monereo S, Gil-Guillén V, Lozano J V, et al. Independent impact of obesity and fat distribution in hypertension prevalence and control in the elderly. J Hypertens. 2008;26:1757-64.
10. Beunza JJ, Martínez-González MÁ, Ebrahim S, Bes-Rastrollo M, Núñez J, Martínez JA, et al. Sedentary Behaviors and the Risk of Incident Hypertension. The SUN Cohort. Am J Hypertens. 2007;20:1156-62.
11. Nakanishi N, Suzuki K. Daily life activity and the risk of developing hypertension in middle-aged Japanese men. Arch Intern Med. 2005;165:214-20.
12. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. Exercise and Hypertension. Med Sci Sports Exerc. 2004;36:533-53.
13. Monteiro HL, Rolim LMC, Squinca DA, Silva FC, Ticianeli CCC, Amaral SL. Efetividade de um programa de exercícios no condicionamento físico, perfil metabólico e pressão arterial de pacientes hipertensos. Rev Bras Med Esporte. 2007; 13:107-12.
14. Williams PT. Reduced diabetic, hypertensive, and cholesterol medication use with walking. Med Sci Sports Exerc. 2008;40:433-43.
15. Rolim R, Amaral S, Monteiro H. Hipertensão e exercício: custos do tratamento ambulatorial, antes e após a adoção da prática regular e orientada de condicionamento físico. Hipertensão. 2007;10:54-61.
16. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. Am J Geriatr Pharmacother. 2007;5:345-51.
17. Ramos Cedeño AM, Milián Vázquez PM, Fonseca León JL, Quirós Enríquez M. Determinación de polifarmacoterapia en pacientes geriátricos de un consultorio del médico de la familia en cienfuegos. Rev Cuba Farm. 1999, Editorial Ciencias Médicas; 2000;34:170-4.
18. Nguyen JK, Fouts MM, Kotabe SE, Lo E. Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. Am J Geriatr Pharmacother. 2006;4:36-41.
19. Almeida OP, Ratto L, Garrido R, Tamai S. Fatores preditores e conseqüências clínicas do uso de múltiplas medicações entre idosos atendidos em um serviço ambulatorial de saúde mental. Rev Bras Psiquiatr. 1999;21:152-7.
20. Barat I, Andreasen F, Damsgaard EMS. The consumption of drugs by 75-year-old individuals living in their own homes. Eur J Clin Pharmacol. 2000;56:501–9.
21. Jensen GL, Friedmann JM, Coleman CD, Smiciklas-Wright H. Screening for hospitalization and nutritional risks among community-dwelling older persons. Am J Clin Nutr. 2001; 74:201-5.
22. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. Am J Clin Nutr. 1982;36:936-42.
23. Florindo AA, Latorre MDRDDO. Validation and reliability of the Baecke questionnaire for the evaluation of habitual physical activity in adult men. Rev Bras Med Esporte. 2003;9:129-35.
24. Lohmann TG, Roche AF, Martorell R. Anthropometric Standardization Reference Manual. Human Kinetics Books, Champaign, Ill.; 1988.
25. WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000 Jan;894:i – xii, 1–253.
26. Flores VB, Benvegnú LA. Perfil de utilização de medicamentos em idosos da zona urbana de Santa Rosa, Rio Grande do Sul, Brasil. Cad Saúde Publica. 2008;24:1439-46.
27. Carvalho MFC, Romano-Lieber NS, Bergsten-Mendes G, Secoli SR, Ribeiro E, Lebrão ML, et al. Polifarmácia entre idosos do Município de São Paulo - Estudo SABE. Rev Bras Epidemiol. 2012;15:817-27.
28. Hanlon JT, Schmader KE, Ruby CM, Weinberger M. Suboptimal Prescribing in Older Inpatients and Outpatients. J Am Geriatr Soc. 2001;49:200-9.
29. Moen J, Antonov K, Larsson CA, Lindblad U, Nilsson JLG, Råstam L, et al. Factors associated with multiple medication use in different age groups. Ann Pharmacother. 2009;43: 1978-85.
30. Schmid B, Bernal R, Silva NN. Self-medication in low-income adults in Southeastern Brazil. Rev Saúde Pública. 2010; 44:1039-45.
31. Kaizu S, Kishimoto H, Iwase M, Fujii H, Ohkuma T, Ide H, et al. Impact of leisure-time physical activity on glycemic control and cardiovascular risk factors in Japanese patients with type 2 diabetes mellitus: The Fukuoka Diabetes Registry. PLoS One. 2014;9:1-9.
32. Avery L, Flynn D, van Wersch A, Sniehotta FF, Trenell MI. Changing physical activity behavior in type 2 diabetes: a systematic review and meta-analysis of behavioral interventions. Diabetes Care. 2012;35:2681-9.

33. Mora S, Cook N, Buring JE, Ridker PM, Lee IM. Physical activity and reduced risk of cardiovascular events: Potential mediating mechanisms. Circulation. 2007;116:2110-8.

34. Shih M, Hootman JM, Kruger J, Helmick CG. Physical activity in men and women with arthritis National Health Interview Survey, 2002. Am J Prev Med. 2006;30:385-93.

35. Borer KT. Physical activity in the prevention and amelioration of osteoporosis in women : interaction of mechanical, hormonal and dietary factors. Sports Med. 2005;35:779-830.

36. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension. 2006;47:296-308.

37. Hirani V, Zaninotto P, Primatesta P. Generalised and abdominal obesity and risk of diabetes, hypertension and hypertension-diabetes co-morbidity in England. Public Health Nutr. 2008;11:521-7.

38. Lee LL, Watson MC, Mulvaney CA, Tsai CC, Lo SF. The effect of walking intervention on blood pressure control: A systematic review. Int J Nurs Stud [Internet]. 2010;47:1545-61. Available from: http://dx.doi.org/10.1016/j.ijnurstu.2010.08.008

39. Melzer I, Benjuya N, Kaplanski J. Effects of Regular Walking on Postural Stability in the Elderly. Gerontology. 2003; 49: 240-5.

40. Weuve J, Kang JH, Manson JE, Breteler MMB, Ware JH, Grodstein F. Physical activity, including walking, and cognitive function in older women. JAMA. 2004;292:1454-61.

41. Kokkinos PF, Giannelou A, Manolis A, Pittaras A. Physical activity in the prevention and management of high blood pressure. Hell J Cardiol. [Internet]. 2009;50(1):52–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19196621

42. Selmer RM. Cost and health consequences of reducing the population intake of salt. J Epidemiol Community Health. 2000;54:697-702.

43. Fulton MM, Allen ER. Polypharmacy in the elderly: a literature review. J Am Acad Nurse Pract. 2005;17:123-32.

44. Silva LJ da, Azevedo MR, Matsudo S, Lopes GS. Association between levels of physical activity and use of medication among older women. Cad Saúde Publica. 2012;28:463-71.

45. Tudor-Locke C, Hatano Y, Pangrazi RP, Kang M. Revisiting "how many steps are enough?". Med Sci Sports Exerc. 2008;40(7 Suppl):S537–43.

46. Bertoldi AD, Hallal PC, Barros AJD. Physical activity and medicine use: evidence from a population-based study. BMC Public Health. 2006;6:224.

47. Bardel A, Wallander M-A, Svärdsudd K. Reported current use of prescription drugs and some of its determinants among 35 to 65-year-old women in mid-Sweden. J Clin Epidemiol. 2000;53:637-43.