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Objectively measured physical activity and polypharmacy among community-dwelling Brazilian older adults

Physical activity and polypharmacy

Abstract

Background: Previous observations regarding association between physical activity and use of medicines among older adults are derived from self-reported physical activity. This study aimed to evaluate the association between objectively measured physical activity (PA) and polypharmacy among older adults with multimorbidity in Southern Brazil.

Methods: Included 875 non-institutionalized elderly people, aged ≥60 years. Prescribed medicines used in the 15 days prior to the interview, socioeconomic data and the presence of comorbidities were self-reported. Accelerometers were used to evaluate PA following the interview.

Results: Prevalence of polypharmacy (≥ 5 medicines) was 38.3% (95%CI: 35.0-41.5), those belonging to the lowest tertile of PA used more medicines. We observed a significant inverse association for polypharmacy between men belonging to the second and third tertiles of physical activity for objectively measured overall PA and light PA compared with the most inactive tertile. For women, the association between physical activity and polypharmacy was significant for overall, light and moderate-to-vigorous PA only in the third tertile.

Conclusions: Overall, light and moderate-to-vigorous PA were inversely associated to polypharmacy and differed by gender. Promotion of physical activity in elderly may be an effective intervention to reduce the number of medicines used independent of the number of comorbidities.

Keywords: physical activity, accelerometry, aging, epidemiology, gerontology

Introduction

The global number of older people has grown exponentially during the last decades and estimated to double by year 2050[1]. Multimorbidity and thus the concomitant prescription of medicines known as polypharmacy is common among this group of the population[2, 3]. Polypharmacy can be defined in several ways, the most commonly used is the concomitant use of five or more medicines, wich was the definition used in this paper[4, 5] and is commonly associated with older people[6] and multimorbidity[7].

Major problems with polypharmacy are medicine interactions and side effects including multiple prescriptions from several physicians leading to increased risks of prescription bias[2, 8]. Recent studies in Brazil[3, 4] have estimated the prevalence of polypharmacy to around 18%[3, 4] in older adults.

The literature recognizes the important role of physical activity (PA) on chronic diseases prevention[9]. Worldwide, it is estimated that physical inactivity causes 9% of premature mortality with higher effect in the burden of disease from coronary heart disease, type 2 diabetes, breast and colon cancers[9]. For older adults, there are additional benefits such as improvement in functional independence and cognition[10].

PA is also recognized as an important lifestyle factor for secondary prevention of non-communicable chronic diseases[11]. PA improves general health profile among patients with chronic kidney disease[12], could decrease the incidence of chronic kidney disease in diabetic patients[13] and may have survival benefits among adults who have had a stroke[14]. Thus, PA may reduce the use of medicines and polypharmacy, as previously suggested[15-17].

Although there is some evidence of an inverse relationship between PA and use of medicines among older adults[16, 17], previous observations are derived from data on self-reported physical activity that is prone to recall and social desirability bias. In general, current guidelines recommend older people should do at least 150 minutes to 300 minutes a week of moderate-intensity, or 75 minutes to 150 minutes a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity[18]. Thus, this study is aimed to examine the association between objectively-measured physical activity by accelerometry and polypharmacy among community-dwelling older adults with multimorbidity in Pelotas, Brazil.

Methods

This cross-sectional study was conducted in Southern Brazil (Pelotas, RS) between January and August 2014. According to Brazilian figures (IBGE) the city of Pelotas had about 340,000 inhabitants in 2014, 93% of them living in the urban area, and approximately 50,000[19] – individuals aged 60 years or over. This study included non-institutionalized older adults who were inhabitants of the urban area of Pelotas. Exclusion criteria were institutionalized individuals (at long-term care institutions for older people, long hospital stay, or prison) at the time of the research and those with some cognitive or physical (in case of anthropometric measurements and exams) impairment that made it impossible to answer the questionnaire or absence of a caregiver to help in the interview.

Sampling process was performed in multiple stages. First, the city was divided into 469 areas distinguished according to the population mean income IBGE[19]. The total number of households was 107,152 and it was necessary to include 3,745 houses to achieve the number of 1,646 individuals necessary to achieve all aims of the study (this study evaluated different health, socioeconomic and behavioral aspects of the older adults). From the 469 areas, 133 were selected, with approximately 300 households, and 30 were systematically drawn in each of them. The number of households was estimated based on a previous figure of 0.43 elderly people/household IBGE[19]. It was expected to interview at least 12 elderly people per area, resulting in a total sample of approximately 1,700 older adults.

Female interviewers previously trained to interview and take anthropometric measurements applied a questionnaire about several aspects of health. Self-reported morbidities (yes/no) were obtained by the questionnaire which included: high blood pressure, diabetes, heart problems, heart failure, lung disease (asthma, bronchitis or emphysema), arthritis, Parkinson's disease, kidney failure, hypercholesterolemia, seizures, stomach ulcer, osteoporosis, urinary incontinence, constipation, fecal incontinence, depression, glaucoma, deafness, difficulty swallowing, insomnia, fainting, rhinitis, speaking disorders, stroke, obesity, mental disorders and cancer. This study included only elderly who reported at least two of these morbidities.

The elderly were also asked to have their weight and knee height measured. The weight was measured using a digital scale (Tanita UM-080, Tanita, Tokyo, Japan) and the knee height was measured with a portable pediatric wooden stadiometer to estimate their height using equations suggested by Chumlea, since accurate measurement of height is difficult in older adults because of the reduction in height that occurs during the ageing process[20]. Obesity was classified according to WHO criterion based on body mass index (BMI) ≥ 30 kg/m[21].

Socioeconomic and demographic characteristics were: sex (males/females); age (60-69/70-79/≥80 years); schooling (highest level achieved) – collected in years of study (none/1-3/4-7/8-10/≥11); economic level (A-B/C/D-E) – according to criteria of the Brazilian Association of Research Companies (ABEP)[22] which considers the possession of certain consumer goods, the head of the household's schooling, and the presence of maid; marital status (with a partner/without a partner). Behavioral variables were: current smoking (yes/no) – daily cigarette consumption during more than one month; alcohol intake (yes/no) – consumption of at least one alcohol drink in the last 30 days.

We investigated the number of medicines used in the 15 days prior to the interview. We asked the respondents to show the packaging or the prescription of the medicine used. For every medicine, we asked the following question: "Who has prescribed this medicine for you?". The answers were: "physician or dentist" or "someone else". Subsequently, the medicines were classified into pharmacological groups using the Anatomical Therapeutic Chemical classification system (ATC)[23] in the levels 1 (anatomical group) and 5 (chemical name). Polypharmacy was considered as the use of five or more medicines[4, 5] prescribed by a physician or dentist.

GENEActiv® accelerometers (Activinsights Ltd, Kimbolton, Cambs, UK, http://www.geneactiv.org) were used to evaluate objectively measured physical activity following the interview. It is a waterproof device which measures acceleration in three axes and provides raw data expressed in gravitational equivalent units (1000mg=1*g*). Participants were invited to wear the accelerometer on their non-dominant wrist for the next 7 days, 24 hours per day, including during water-based activities. The research team was responsible for attaching and collecting the accelerometers from the elderly' households as described in previous publication[24]. Bed-bound and disabled older adults were omitted from the PA measurement.

Accelerometers were initialized to collect data in 85.7 Hz time resolution. Data were processed in GENEActiv software and analyzed using the R-package GGRI (https://cran.r-project.org/web/packages/GGIR/vignettes/GGIR.html#citing-ggir). Raw data were calibrated to local gravity[25], scored for non-wear based on periods greater than 60 minutes of low acceleration variability (SD <13 m*g*) and abnormally high values were censored[26]. Participants providing fewer than two days of measurement were excluded from the analyses. Activity-related acceleration was calculated using the Euclidian Norm (vector magnitude of the three axes) minus 1 g ($\sqrt{x^2 + y^2 + z^2} - 1g$) as described elsewhere[27]. Invalid data segments were imputed – within individual – by the mean of similar time of day data points from other days of the measurement.

Activity intensities (light and moderate-to-vigorous) were estimated from 5-s aggregated time-series. Overall physical activity was expressed by the daily mean of acceleration (mg) as evaluated elsewhere[26, 28, 29]. Time spent in acceleration between 50 and 99 mg defined daily time in light physical activity (LPA), while activities with acceleration higher than 100 mg were considered as moderate to vigorous physical activity (MVPA)[29, 30]. MVPA in a 5 min-bout – defined as five consecutive minutes in which participants spent at least 80% of this time in MVPA – was considered.

All statistical analyses were performed with Stata 13.0 software (StataCorp, College Station, TX, USA). Absolute and relative frequencies of main characteristics were described according to the presence of polypharmacy. BMI, overall acceleration, LPA and MVPA were shown in means and standard deviations. Most common medicine classes were described according to ATC codes. All statistical associations were tested stratified by sex since both physical activity and polypharmacy are different in males and females. Crude association of overall acceleration, time spent in LPA and time spent in MVPA with number of medicines used (0, 1, 2, 3, 4, ≥ 5) was performed using the Pearson's Chi Squared test. Prevalence ratios for polypharmacy according to every PA exposure with respective 95% confidence intervals were obtained by Poisson's regression with adjust for robust variance considering three models: (1) crude; (2) adjusted for age, economic level, schooling, marital status, alcohol intake and smoking status; and (3) additionally adjusted for number of morbidities. Significance level was set at 5%.

The study was submitted to consideration and approved by the Research Ethics Committee of the School of Medicine of Federal University of Pelotas. Informed consent was obtained from all participants or their caregivers prior the interview.

Results

A total of 1844 elderly people were invited to participate of which 1451 were interviewed (78,7%). Of these, 1250 reported multimorbity (two diseases or more). Among the elderly with multimorbity, 875 provided valid accelerometry data and were included in the current study. Prevalence of polypharmacy was 38.3% (95%CI: 35.0; 41.5).

Characteristics of the individuals according to multimorbidity and polypharmacy status is shown in Table 1. Elderly with polypharmacy were generally older, classified in the economic level C, less likely to be smoker and alcohol drinker. They also had higher prevalence of heart diseases, diabetes, joint and lung diseases, depression, kidney disease and higher BMI in comparison to elderly without polypharmacy.

The most common pharmacological groups used were of cardiovascular system (44.7%), alimentary tract and metabolism (19.1%), and nervous system (15.0%). Hydrochlorothiazide, simvastatin, losartan, enalapril, atenolol, omeprazole, metformin and acetylsalicylic acid were the most frequently used medicines (Supplementary Table S1).

Number of medicines used in relation to the tertiles of PA variables for elderly men and women are shown in Figures 1 and 2, respectively. The number of medicines used decreased according to increase in the overall, light and moderate-to-vigorous PA ($p<0.001$).

Table 2 shows the association of physical activity with polypharmacy among elderly men with multimorbidity: unadjusted (Model 1); adjusted for age, economic level, schooling, marital status, alcohol intake and smoking status (Model 2); and additionally adjusted for number of morbidities (Model 3). Polypharmacy was significantly lower in tertiles 2 and 3 of overall, light and moderate-to-vigorous PA compared with the reference group (tertile 1) in crude and adjusted models. Adjusted model 3 indicates 35-38% lower frequency of polypharmacy among elderly men who practice more physical activity, except on moderate-to-vigorous PA.

In elderly women, polypharmacy was significantly lower only in the 3rd tertiles of overall, light and moderate-to-vigorous PA compared with the reference group (tertile 1) in crude and adjusted models. Adjusted models 3 indicates 31% lower frequency of polypharmacy among female elderly who practice more overall PA, 25% lower among more light PA and 41% lower among more moderate-to-vigorous PA (Table 3).

Discussion

This study aimed to evaluate the cross-sectional association between objectively-measured overall, light and moderate-to-vigorous PA and polypharmacy among community-dwelling elderly with multimorbidity living in the urban area of Pelotas, Southern Brazil. Generally, our findings indicated lower frequency of polypharmacy among elderly males and females classified in the highest tertiles of all PA variables, exception in the result for moderate-to-vigorous PA among males – where lower prevalence ratio was found also in the second tertile.

The prevalence of polypharmacy among older adults in other countries range from 20 to 40% in Argentina[31], 20% in Malaysia[32]**,** 23% in Iran[33] and 69% in the southern region of the United States[34]. Considering the Brazilian population, the prevalence of polypharmacy in our study (38%) was similar to that found in São Paulo city (36%)[35] and higher to Porto Alegre (27%)[36] and Rio de Janeiro (32.7%)[37]**.** All previous studies used the same definition of polypharmacy (use of five medicines or more).

In a population-based study (PNAUM)[3], the prevalence of polypharmacy varied according to the morbidity. Among older people with three diseases, the prevalence of polypharmacy was 37%**,** very closely to 38% found in us study, it which included only elderly who reported two or more morbidities. The highest prevalence of polypharmacy among the elderly (25%) was found in the Southern region of Brazil[3].

Seven of the ten most commonly medicines used by Brazilian elderly individuals in a national-based study[3] were listed in our Table 2 as the most commonly medicines used.

Studies exploring the relationship between PA and polypharmacy among older adults are scarce. Previous studies from Germany and France found an inverse association of self-reported PA in three life domains (leisure, household and occupational activity) with polypharmacy among older adults with multimorbidity[17, 38]. In Brazil, old males and females who did not achieve at least 150 min/week in leisure-time PA reported around 95% and 43% higher prevalence of continuous use of at least two medicines[16]. Likewise, the number of steps/day was inversely related to medication usage in Brazilian older women who attended to community physical-activity programs in São Paulo[39].

Although with no specific information regarding polypharmacy or medicines use, a study from Brazil found that PA was inversely associated with expenditure on medication among older adults[40]. The same was seen in other Brazilian study carried out with older adults enrolled in basic healthcare units that found physical activity slightly attenuated the costs of medication due to type 2 diabetes mellitus[41]. These studies estimated the PA by self-report. From our knowledge, the current study is the first to describe these associations using objectively measured PA from accelerometers.

PA may decrease the use of medication because it prevents chronic diseases and it is also an adjuvant treatment in the secondary prevention[11]. For instance, PA reduces blood pressure, triglyceride concentrations, and blood cholesterol concentrations; raises high-density lipoprotein cholesterol concentrations; reduces heart rate; increases stroke volume; and improves endothelial function[42]. PA is also recognized in the prevention and management of chronic obstructive pulmonary disease[43], osteoporosis[44], and many other diseases.

Our study is limited by its cross-sectional design, evaluating the outcomes and exposures at the same time, and thus prone to reverse causality. Although adjusting for number of diseases may not fully account for this, the association of objectively measured PA variables with lower prevalence of polypharmacy remained. However, we cannot fully exclude the possibility that the number of prescriptions is likely to be increased the more severe and number of diseases is and that, in turn, is more likely to also impact negatively on PA. In addition, the prescription is also a behavior that has its determinants which is not always related to the patient himself. The culture of overdiagnosis and overprescribing is a reality in many healthcare systems[45], including Brazilian one.

Strengths include a population-based study that took into consideration different areas of the city and elderly people from different social backgrounds. Data regarding elderly people and physical activity is highly relevant when we face the aging process of the populations and the costs associated with that, such as, hospitalization, home care, use of medicines and others. Further, the use of accelerometers is the main strength of the current study, since questionnaires are prone to bias and usually able to only estimate the moderate-to-vigorous PA but not light PA.

In conclusion, higher levels of overall, light and moderate-to-vigorous physical activity were associated to lower prevalence of polypharmacy.

Perspective

The findings reinforce the biological plausibility of the association between PA and disease prevention. As an active daily routine can promote health, it can consequently, reduce polypharmacy. The observed association between light PA and polypharmacy indicates the beneficial use of accelerometers in this population since moderate-to-vigorous PA are less practiced in the elderly and light PA is hard to be obtained from self-reported instruments.

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References

1. United Nations. *World Population Ageing*; 2015.

2. Lavan AH, Gallagher PF, O'Mahony D. Methods to reduce prescribing errors in elderly patients with multimorbidity. *Clin Interv Aging* 2016**,** 11, 857-66.

3. Ramos LR, Tavares NU, Bertoldi AD, Farias MR, Oliveira MA, Luiza VL, Pizzol TD, Arrais PS, Mengue SS. Polypharmacy and Polymorbidity in Older Adults in Brazil: a public health challenge. *Rev Saude Publica* 2016**,** 50, (suppl 2), 9s.
4. Nascimento RCRM, Alvares J, Guerra AAJ, Gomes IC, Silveira MR, Costa EA, Leite SN, Costa KS, Soeiro OM, Guibub IA, Karnikowskin MGO, Acurcio FA. Polypharmacy: a challenge for the primary health care of the Brazilian Unified Health System. *Rev Saude Publica* 2017**,** 51, (suppl 2), 19s.
5. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr* 2017**,** 17, (1), 230.
6. Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. *European journal of clinical pharmacology* 2014, 70, (5), 575-581.
7. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *The Lancet* 2012, 380, (9836), 37-43.
8. Perez-Jover V, Mira JJ, Carratala-Munuera C, Gil-Guillen VF, Basora J, Lopez-Pineda A, Orozco-Beltran D. Inappropriate Use of Medication by Elderly, Polymedicated, or Multipathological Patients with Chronic Diseases. *Int J Environ Res Public Health* 2018, 15, (2).
9. Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Lancet Physical Activity Series Working, G. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012, 380, (9838), 219-29.
10. Taylor D. Physical activity is medicine for older adults. *Postgrad Med J* 2014, 90, (1059), 26-32.

11. Giannuzzi P, Mezzani A, Saner H, Bjornstad H, Fioretti P, Mendes M, Cohen-Solal A, Dugmore L, Hambrecht R, Hellemans I, McGee H, Perk J, Vanhees L, Veress G. Working Group on Cardiac, R. Exercise Physiology. European Society of, C., Physical activity for primary and secondary prevention. Position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *Eur J Cardiovasc Prev Rehabil* 2003, 10, (5), 319-27.

12. Aucella F, Valente GL, Catizone L. The role of physical activity in the CKD setting. *Kidney Blood Press Res* 2014, 39, (2-3), 97-106.

13. Lin HC, Peng CH, Chiou JY, Huang CN. Physical activity is associated with decreased incidence of chronic kidney disease in type 2 diabetes patients: a retrospective cohort study in Taiwan. *Prim Care Diabetes* 2014, 8, (4), 315-21.

14. Loprinzi PD, Addoh O. Accelerometer-Determined Physical Activity and All-Cause Mortality in a National Prospective Cohort Study of Adults Post-Acute Stroke. *Am J Health Promot* 2017, 890117117720061.

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

16. Ribeiro AS, Pereira LC, Silva DRP, Dos Santos L, Schoenfeld BJ, Teixeira DC, Cyrino ES, Guedes DP. Physical Activity and Sitting Time are Specifically Associated With Multiple Chronic Diseases and Medicine Intake in Brazilian Older Adults. *J Aging Phys Act* 2018, 1-19.

17. Volaklis KA, Thorand B, Peters A, Halle M, Heier M, Strasser B, Amann U, Ladwig KH, Schulz H, Koenig W, Meisinger C. Physical activity, muscular strength, and polypharmacy among older multimorbid persons: Results from the KORA-Age study. *Scand J Med Sci Sports* 2018, 28, (2), 604-612.

18. U.S. Department of Health and Human Services. *Physical Activity Guidelines for Americans*, 2nd edition. Washington, DC: U.S. Department of Health and Human Services; 2018.
19. Instituto Brasileiro de Geografia e Estatística, Censo 2010. In IBGE: Rio de Janeiro, 2010.
20. Chumlea WC, Guo S. Equations for predicting stature in white and black elderly individuals. *Journal of Gerontology* 1992, 47, (6), M197-M203.
21. World Health Organization. *Physical status: The use of and interpretation of anthropometry, Report of a WHO Expert Committee.* In *World Health Organization*: Geneva, 1995.
22. ABEP, Associação Brasileira de Empresas e Pesquisas. In http://www.abep.org/.
23. WHO, Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC classification and DDD assignment*. Oslo; 2000.
24. Ramires VV, Wehrmeister FC, Böhm AW, Galliano L, Ekelund U, Brage S, Silva ICM. Physical activity levels objectively measured among older adults: a population-based study in a Southern city of Brazil. *International Journal of Behavioral Nutrition and Physical Activity* 2017, 14, (13), 1-9.
25. van Hees VT, Fang Z, Langford J, Assah F, Mohammad A, da Silva IC, Trenell MI, White T, Wareham NJ, Brage S. Autocalibration of accelerometer data for free-living physical activity assessment using local gravity and temperature: an evaluation on four continents. *J Appl Physiol (1985)* 2014, 117, (7), 738-44.
26. van Hees VT, Renstrom F, Wright A, Gradmark A, Catt M, Chen KY, Lof M, Bluck L, Pomeroy J, Wareham NJ, Ekelund U, Brage S, Franks PW. Estimation of daily energy expenditure in pregnant and non-pregnant women using a wrist-worn tri-axial accelerometer. *PLoS One* 2011, 6, (7), e22922.

27. van Hees VT, Gorzelniak L, Dean Leon EC, Eder M, Pias M, Taherian S, Ekelund U, Renstrom F, Franks PW, Horsch A, Brage S. Separating movement and gravity components in an acceleration signal and implications for the assessment of human daily physical activity. *PLoS One* 2013, 8, (4), e61691.
28. White T, Westgate K, Hollidge S, Venables M, Olivier P, Wareham N, Brage S. Estimating energy expenditure from wrist and thigh accelerometry in free-living adults: a doubly labelled water study. *International Journal of Obesity* 2019, 43, (11), 2333-2342.
29. White T, Westgate K, Wareham NJ, Brage S. Estimation of Physical Activity Energy Expenditure during Free-Living from Wrist Accelerometry in UK Adults. *PLoS One* 2016, 11, (12), e0167472.
30. Hildebrand M, Van Hess VT, Hansen BH, Ekelund U. Age group comparability of raw accelerometer output from wrist- and hip-worn monitors. *Med Sci Sports Exerc* 2014, 46, (9), 1816-24.
31. Chiapella LC, Montemarani Menna J, Mamprin ME. Assessment of polypharmacy in elderly patients by using data from dispensed medications in community pharmacies: analysis of results by using different methods of estimation. *Int J Clin Pharm* 2018.
32. Ong SM, Lim YMF, Sivasampu S, Khoo EM. Variation of polypharmacy in older primary care attenders occurs at prescriber level. *BMC Geriatr* 2018, 18, (1), 59.
33. Hosseini SR, Zabihi A, Jafarian Amiri SR, Bijani A. Polypharmacy among the Elderly. *J Midlife Health* 2018, 9, (2), 97-103.
34. Rasu R, Agbor-Bawa W, Rianon N. Impact of Polypharmacy on Seniors' Self-Perceived Health Status. *South Med J* 2017, 110, (8), 540-545.

35. Carvalho MF, Romano-Lieber NS, Bergsten-Mendes G, Secoli SR, Ribeiro E, Lebrao ML, Duarte YA. Polypharmacy among the elderly in the city of Sao Paulo, Brazil - SABE Study. *Rev Bras Epidemiol* 2012, 15, (4), 817-27.

36. Flores LM, Mengue SS. [Drug use by the elderly in Southern Brazil]. *Rev Saude Publica* 2005, 39, (6), 924-9.

37. Rozenfeld S, Fonseca MJ, Acurcio FA. Drug utilization and polypharmacy among the elderly: a survey in Rio de Janeiro City, Brazil. *Rev Panam Salud Publica* 2008, 23, (1), 34-43.

38. Husson N, Watfa G, Laurain MC, Perret-Guillaume C, Niemier JY, Miget P, Benetos A. Characteristics of polymedicated (>/= 4) elderly: a survey in a community-dwelling population aged 60 years and over. *J Nutr Health Aging* 2014, 18, (1), 87-91.

39. Silva LJD, Azevedo MR, Matsudo S, Lopes GS. Association between levels of physical activity and use of medication among older women. *Cadernos de saude publica* 2012, 28, 463-471.

40. Bueno DR, de Fatima Nunes Marucci M, Gobbo LA, de Almeida-Roediger M, de Oliveira Duarte YA, Lebrao ML. Expenditures of medicine use in hypertensive/diabetic elderly and physical activity and engagement in walking: cross secctional analysis of SABE Survey. *BMC Geriatr* 2017, 17, (1), 70.

41. Kikuti-Koyama KA, Monteiro HL, Ribeiro Lemes Í, de Morais LC, Fernandes R, Turi-Lynch B, Codogno J. Impact of type 2 diabetes mellitus and physical activity on medication costs in older adults. *The International journal of health planning and management* 2019, 34, (4), e1774-e1782.

42. Stensel D. Primary prevention of CVD: physical activity. *BMJ Clin Evid* 2009, 2009.

43. Watz H, Pitta F, Rochester CL, Garcia-Aymerich J, ZuWallack R, Troosters T, Vaes AW, Puhan MA, Jehn M, Polkey MI, Vogiatzis I, Clini EM, Toth M, Gimeno-Santos E, Waschki B, Esteban C, Hayot M, Casaburi R, Porszasz J, McAuley E, Singh SJ, Langer D, Wouters EF, Magnussen H, Spruit MA. An official European Respiratory Society statement on physical activity in COPD. *Eur Respir J* 2014, 44, (6), 1521-37.

44. Harding AT, Beck BR. Exercise, Osteoporosis, and Bone Geometry. *Sports (Basel)* 2017, 5, (2).

45. Heath I. Overdiagnosis: when good intentions meet vested interests--an essay by Iona Heath. *BMJ* 2013, 347, f6361.

Table 1. Characteristics of Southern Brazilian community-dwelling elderly with multimorbidity according to polypharmacy status. The "COMO VAI?" study. Pelotas–RS, Brazil, 2014.

Characteristics	**Polypharmacy**		
	Yes	**No**	**p**
	N (%)	**N (%)**	
Males	101 (30.2)	214 (39.7)	0.005[a]
Age			<0.001[a]
60 – 69	138 (41.3)	305 (56.6)	
70 – 79	134 (40.1)	173 (32.1)	
≥ 80	62 (18.6)	61 (11.3)	
Schooling (years)			0.140[a]
None	45 (13.6)	78 (14.6)	
1 – 3	81 (24.4)	116 (21.6)	
4 – 7	115 (36.6)	165 (30.8)	
8 – 10	67 (20.2)	111 (20.7)	
≥ 11	24 (7.2)	66 (12.3)	
Economic level			0.041[a]
A/B	103 (32.5)	190 (36.5)	
C	189 (59.6)	268 (51.5)	
D/E	25 (7.9)	62 (11.9)	
Smoking	27 (8.1)	79 (14.7)	0.004[a]
Alcohol	59 (17.7)	142 (26.4)	0.003[a]
Cardiovascular diseases	173 (51.8)	129 (23.9)	<0.001[a]
Glaucoma	33 (9.9)	37 (6.9)	0.111[a]

Diabetes	130 (38.9)	84 (15.6)	<0.001[a]
Joint disease	203 (60.8)	200 (37.1)	<0.001[a]
Lung diseases	80 (24.0)	79 (14.7)	0.001[a]
Depression	68 (20.7)	77 (14.4)	0.015[a]
Kidney disease	24 (7.2)	11 (2.0)	<0.001[a]
Cancer	37 (11.1)	54 (10.0)	0.619 [a]
BMI (kg/m^2) [mean (sd)]	28.6 (0.3)	27.8 (0.2)	<0.001[b]
Overall acceleration (m*g*) [mean (sd)]	18.9 (0.4)	23.2 (0.3)	<0.001[b]
LPA (min/day) [mean (sd)]	116.0 (3.2)	143.8 (2.2)	<0.001[c]
MVPA (min/day) [mean (sd)]	6.2 (0.7)	13.0 (0.8)	<0.001[c]

BMI – Body mass index; LPA – light physical activity; MVPA – moderate-to-vigorous physical activity.

[a] Pearson's chi squared test; [b] Student's t-test; [c] Wilcoxon's rank-sum test.

Table 2. Association of physical activity with polypharmacy among elderly males with multimorbidity. The "COMO VAI?" study. Pelotas–RS, Brazil.

	Model 1		**Model 2**		**Model 3**	
	PR (95%CI)[a]	**p**	**PR (95%CI)[a]**	**p**	**PR (95%CI)[a]**	**p**
Objectively-measured overall PA – mg (tertiles)		<0.001		<0.001		0.027
1st (lower)	1.00		1.00		1.00	
2nd	0.43 (0.29; 0.63)		0.51 (0.34; 0.76)		0.62 (0.41; 0.93)	
3rd (upper)	0.40 (0.26; 0.61)		0.51 (0.32; 0.80)		0.62 (0.40; 0.98)	
Objectively-measured light PA – minutes/day (tertiles)		<0.001		0.001		0.035
1st (lower)	1.00		1.00		1.00	
2nd	0.45 (0.30; 0.67)		0.54 (0.36; 0.82)		0.63 (0.42; 0.96)	
3rd (upper)	0.42 (0.28; 0.63)		0.53 (0.35; 0.81)		0.65 (0.43; 0.99)	

Objectively-measured MVPA – minutes/day (tertiles)		<0.001		<0.001		0.024
1st (lower)	1.00		1.00		1.00	
2nd	0.43 (0.29; 0.65)		0.54 (0.36; 0.80)		0.62 (0.43; 0.89)	
3rd (upper)	0.41 (0.27; 0.62)		0.50 (0.32; 0.79)		0.68 (0.43; 1.09)	

PR: prevalence ratio, CI: confidence interval p: value p

Model 1: unadjusted; Model 2: Adjusted for age, economic level, schooling, marital status, alcohol intake and smoking status; Model 3: Adjusted for model 2 + number of morbidities.

Poisson's regression with adjustment for robust variance.

Table 3. Association of physical activity with polypharmacy among elderly females with multimorbidity. The "COMO VAI?" study. Pelotas–RS, Brazil.

	Model 1		Model 2		Model 3	
	PR (95%CI) [a]	**p**	**PR (95%CI)** [a]	**p**	**PR (95%CI)** [a]	**P**
Objectively-measured overall PA – mg (tertiles)		<0.001		<0.001		0.003
1st (lower)	1.00		1.00		1.00	
2nd	0.72 (0.59; 0.89)		0.70 (0.55; 0.89)		0.83 (0.66; 1.03)	
3rd (upper)	0.45 (0.34; 0.59)		0.48 (0.35; 0.64)		0.61 (0.46; 0.81)	
Objectively-measured light PA – minutes/day (tertiles)		<0.001		<0.001		0.041
1st (lower)	1.00		1.00		1.00	
2nd	0.66 (0.53; 0.83)		0.64 (0.49; 0.83)		0.80 (0.63; 1.01)	
3rd (upper)	0.57 (0.44; 0.73)		0.60 (0.46; 0.79)		0.75 (0.59; 0.96)	

Objectively-measured MVPA – minutes/day (tertiles)	<0.001	<0.001	0.002
1st (lower)	1.00	1.00	1.00
2nd	0.76 (0.61; 0.94)	0.74 (0.58; 0.95)	0.90 (0.71; 1.13)
3rd (upper)	0.45 (0.34; 0.60)	0.48 (0.35; 0.65)	0.59 (0.44; 0.79)

PR: prevalence ratio, CI: confidence interval, p: value p

Model 1: Unadjusted; Model 2: Adjusted for age, economic level, schooling, marital status, alcohol intake and smoking status; Model 3: Adjusted for model 2 + number of morbidities.

Poisson's regression with adjust for robust variance

Figure 1. Association between physical activity variables and number of medicines prescribed used in the 15 days prior to the interview among elderly males with multimorbidity. The ''COMO VAI?'' study. Pelotas-RS, Brazil, 2014.

Figure 2. Association between physical activity variables and number of medicines prescribed used in the 15 days prior to the interview among elderly females with multimorbidity. The ''COMO VAI?'' study. Pelotas-RS, Brazil.

Supplementary Table S1. Medicines most commonly used by the elderly with multimorbidity, according to the Anatomical Therapeutic Chemical Classification System (ATC, levels 1 and 5[a]). The "COMO VAI?" study. Pelotas–RS, Brazil, 2014.

Pharmacological Groups	N	%
C - Cardiovascular System	**1699**	**44,7**
C03AA03 - hydrochlorothiazide	248	14,6
C10AA01 - simvastatin	239	14,1
C09CA01 - losartan	213	12,5
C09AA02 - enalapril	146	8,6
C07AB03 - atenolol	136	8,0
Others	982	42,2
A – Alimentary Tract and Metabolism	**728**	**19,1**
A02BC01 - omeprazole	193	26,5
A10BA02 - metformin	159	21,8
Others	376	51,7
N - Nervous System	**570**	**15,0**
N03AE01 - clonazepam	50	8,8
N02BE01 - paracetamol	37	6,5
Others	483	84,7
B – Blood and Blood forming organs	**231**	**6,1**
B01AC06 - acetylsalicylic acid	137	59,3
B01AC04 - clopidogrel	33	14,3
Others	61	26,4
M - Musculo-skeletal System	**213**	**5,6**
M05BA04 - alendronic acid	27	12,7

M01AB55 – diclofenaco, combinations	23	10,8
Others	163	76,5
H – Systemic Hormonal Preparations	**117**	**3,1**
H03AA01 – levothyroxine sodium	97	82,9
Others	20	17,1
R – Respiratory System	**74**	**1,9**
R03AK07 - formoterol and budesonide	19	25,7
Others	55	74,3
Others[b]	**171**	**4,5**
Total	**3803**	**100**

a: Within level 5, only the drugs most used within each group were mentioned.

b: Phytotherapics, sense organs, genito-urinary system, antiinfectives for systemic use, antineoplastic, dermatological and antiparasitic agents.