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The Impact of Multimorbidity Patterns on Changes in Physical Activity and Physical Capacity Among Older Adults Participating in a Year-Long Exercise Intervention

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This study investigated the impact of multimorbidity patterns on physical activity and capacity outcomes over the course of a year-long exercise intervention, and on physical activity 1 year later. Participants were 314 physically inactive community-dwelling men and women aged 70–85 years, with no contraindications for exercise at baseline. Physical activity was self-reported. Physical capacity measurements included five-time chair-stand time, 6-minute walking distance, and maximal isometric knee-extension strength. The intervention included supervised and home-based strength, balance, and walking exercises. Multimorbidity patterns comprised physician-diagnosed chronic disease conditions as a predictor cluster and body mass index as a measure of obesity. Multimorbidity patterns explained 0%–12% of baseline variance and 0%–3% of the change in outcomes. The magnitude and direction of the impact of unique conditions varied by outcome, time point, and sex. Multimorbid older adults with no contraindications for exercise may benefit from multimodal physical training.

Keywords*:* physical training, physical functioning, physical performance, chronic conditions, community-dwelling

Multimorbidity and physical inactivity are two strongly interrelated challenges facing aging populations globally. Physical inactivity is a risk factor for many chronic conditions (Bauman et al., 2016; Piercy et al., 2018) and for multimorbidity, which is typically defined as more than one chronic condition in the same individual (Johnston et al., 2019; Xu et al., 2017). One detrimental outcome of both physical inactivity and multimorbidity is the development of functional limitations, which compromise older adults' mobility and can lead to disability and loss of independence (Bauman et al., 2016; Ryan et al., 2015). It is; therefore, crucial to find successful strategies to promote physical activity and functioning among older adults.

Physical activity guidelines encourage older adults to engage in aerobic, muscle strengthening, and balance-enhancing physical activity several times per week, or to be as physically active as their chronic conditions allow (Bull et al., 2020; Piercy et al., 2018). Regular physical activity is recommended in the prevention and treatment of many chronic conditions (Pedersen & Saltin, 2015; Piercy et al., 2018). Physical activity guidelines for people with chronic conditions are broadly similar to those for general and older adult populations (Dempsey et al., 2020). The current recommendations are, however, limited to only a few chronic conditions, and less is known about benefits of physical activity among older adults with multimorbidity. Due to the limited evidence, exercise recommendations are currently lacking in the clinical treatment guidelines for multimorbidity (Muth et al., 2019). However, a recent meta-analysis suggested that exercise is safe and beneficial for multimorbid individuals (Bricca et al., 2020). Since older adults with multimorbidity tend to be less physically active than their healthier counterparts (Keats et al., 2017; Steeves et al., 2019), promoting physical activity may substantially benefit their health and functioning.

Earlier research has suggested that exercise interventions can increase physical activity and improve physical capacity in community-dwelling older adults (DiPietro et al., 2019; Sansano-Nadal et al., 2019). This has been supported by our previous studies (Savikangas et al., 2021; Sipilä et al., 2021). During a year-long multicomponent intervention that included physical and cognitive training, older adults increased both their physical activity and their physical capacities, including aerobic endurance, muscle strength, and lower-extremity functioning (Savikangas et al., 2021; Sipilä et al., 2021). These benefits may have extended beyond the intervention period, as the participants reported a higher physical activity category after the 1-year follow-up period than at baseline (Savikangas et al., 2021). However, the effects of exercise-based interventions may not be similar for healthy older adults or those with underlying chronic disease conditions. The increase in the level of physical activity has been suggested to be somewhat smaller in older adults with multimorbidity (Chase, 2015). The evidence on whether multimorbid older adults can increase their

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physical capacity to a similar extent as healthy older adults is, however, limited. Furthermore, while both the prevalence and patterns of multimorbidity, exercise efficacy, and the associations of physical activity and capacity with multimorbidity may differ between men and women (Abad-Díez et al., 2014; Jones et al., 2021; Keats et al., 2017; Welmer et al., 2012), research is lacking on whether the impacts of multimorbidity on training outcomes may also differ between men and women.

Therefore, the aim of this exploratory post hoc analysis of a randomized controlled trial was to investigate the impact of multimorbidity patterns comprising 17 chronic disease conditions and obesity on physical activity and physical capacity in older men and women who did not meet the current physical activity recommendations at baseline. More specifically, the aims were to investigate the impact of multimorbidity patterns on the participants' baseline level of physical activity and physical capacity and on changes in their physical activity and capacity over the course of a year-long multicomponent exercise intervention, and on physical activity 1-year later.

Materials and Methods

Study Design

This study is an exploratory post hoc analysis of a randomized controlled trial (ISRCTN52388040). The main aim of the PASSWORD study was to investigate whether physical and cognitive training had greater effects on gait speed, executive functions, and falls than physical training alone in physically inactive community-dwelling older adults. The study protocol and main results have been published previously (Sipilä et al., 2018, 2021). The study was approved by the Ethics Committee of the Central Finland Health Care District (14/12/2016, ref: 11/2016) and conducted in accordance with the Declaration of Helsinki. All participants signed a written informed consent before enrolling in the study.

Participants

Older adults aged 70–85 years and residing in Jyväskylä, Central Finland, were recruited from a population-based random sample. The recruitment process and study flow have been described in detail elsewhere (Savikangas et al., 2021; Sipilä et al., 2021). Briefly, participants were eligible for the study, if they did not meet the physical activity recommendations current at the time of the study, were able to walk 500 m without assistance, and had a Mini-Mental State Examination score of ≥24. Exclusion criteria were a severe chronic condition and/or medication affecting cognitive and/or physical function, including cancer; a severe musculoskeletal, lung, renal or cardiovascular disease; diabetes with insulin medication; a severe psychotic disorder, cognitive impairment or disease affecting cognition; or a serious neurological disease or disorder. Furthermore, participants were excluded if they had other medical, psychological, and/or behavioral factors that were contraindications for physical training or could have interfered with participation, such as a severe vision or hearing problem, excessive alcohol consumption, or other family member participating in the study. Between February 2017 and March 2018, 314 participants were recruited and randomized to receive either physical and cognitive training ($n = 155$) or physical training only ($n = 159$). Of these, 291 participated in the 12-month measurements and 288 returned the 1-year follow-up questionnaire. Data collection ended in April 2020. The study flow is shown in Figure 1.

Measurements

Multimorbidity Patterns

Chronic disease conditions were self-reported at the baseline health examination and verified from the integrated national patient registry (Effica database) by the study physician, who coded the conditions according to the *International Classification of Diseases, Tenth Revision* classification (World Health Organization, 2004). For further analysis, conditions were classified into 17 indicator variables (Fortin et al., 2017). Body mass index (BMI, kg/m^2) was used as a measure of obesity as per Fortin et al. (2017) with the exception that we used it as a continuous instead of dichotomous measure. As BMI has been recognized as a suboptimal marker of adiposity in older adults (Batsis et al., 2016), additional analyses were performed using body fat percent as a marker of obesity instead of BMI. Fat percent was measured with dual-energy X-ray absorptiometry (LUNAR Prodigy, GE Healthcare). The categorization of chronic disease conditions is shown in detail in Supplementary Table S1 (available online).

Physical Activity

Participants responded to a one-item, 7-scale questionnaire on their current physical activity at baseline, and at 6 months during and 12 months immediately after the intervention, and at the 1-year follow-up (24 months from baseline). Participants were asked to select the highest response option that described their current physical activity on a scale ranging from 0 (*I do not move more than is necessary in my daily chores*) to 6 (*I participate in competitive sports and maintain my fitness through regular training*; Hirvensalo et al., 1998).

Physical Capacity

Aerobic endurance was measured with the 6-minute walking test (6-min walk, in meters; ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002), which was performed indoors in a 20-m long hallway at a comfortable pace. Lower-extremity muscle power was assessed with the five-time chair-stand test, in which participants were asked to stand up as quickly as possible from a chair five times in succession. A shorter time (in seconds) indicates better performance (Guralnik et al., 1994). The 6-min walk and chair-stand tests were performed at baseline and at 6 and 12 months thereafter. Muscle strength was assessed at baseline and 12 months thereafter as maximal isometric knee-extension strength (in kilograms) on the side of the dominant hand using an adjustable dynamometer chair (Good Strength, Metitur Ltd.; Portegijs et al., 2008).

Descriptive Characteristics

Sex and age were drawn from the national population registry. Appendicular lean mass (in kilograms) was measured with dual-energy X-ray absorptiometry. Education, marital status, smoking status, self-perceived current health, and difficulties in outdoor mobility were self-reported. Global cognition was assessed with the Mini-Mental State Examination (score range 0–30; Folstein et al., 1975).

Interventions

The interventions used have been described in detail previously (Savikangas et al., 2021; Sipilä et al., 2018, 2021). Two supervised physical therapy sessions were organized weekly: one for strength

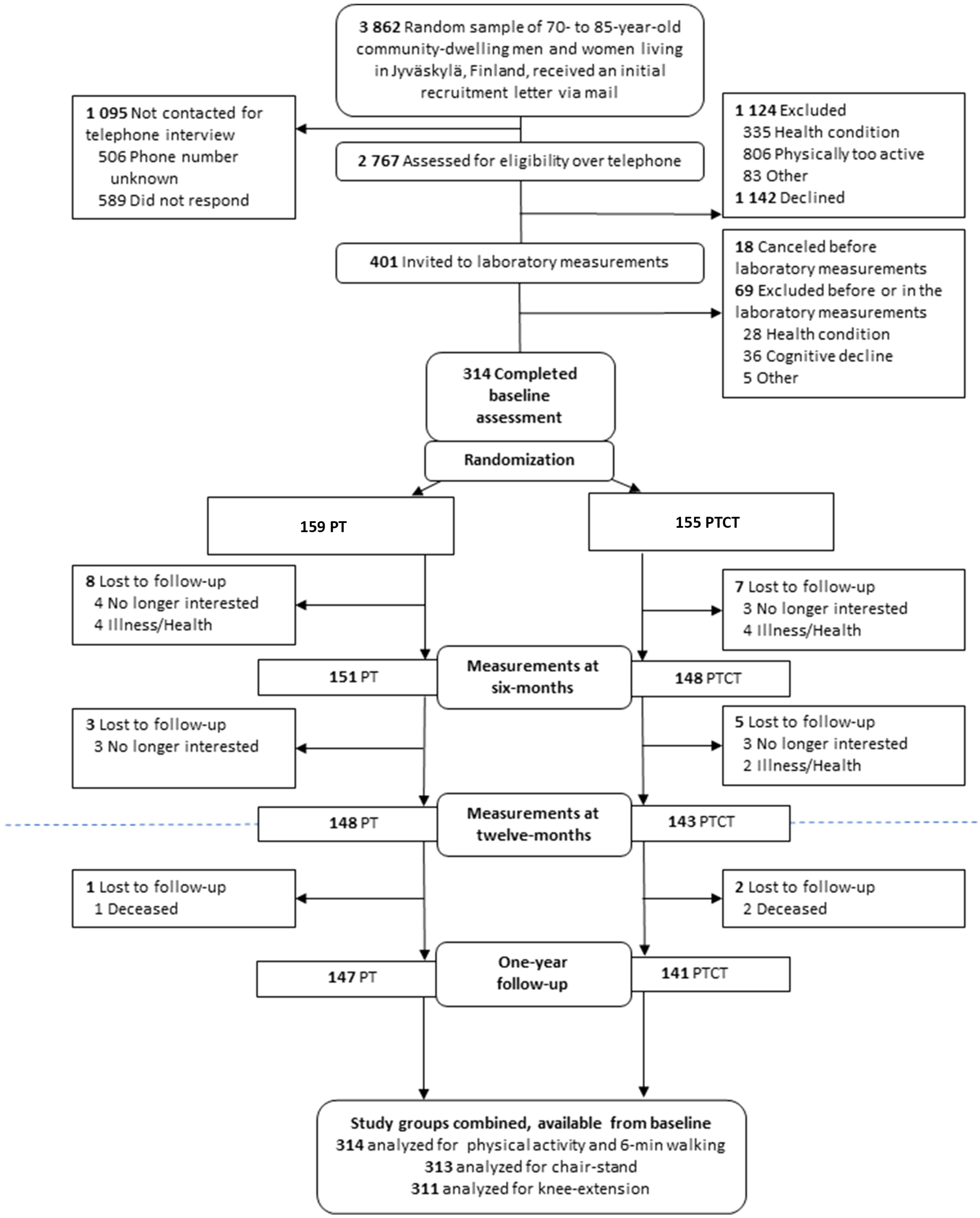

Figure 1 — Flowchart of the study. PT = physical training; PTCT = physical and cognitive training.

and balance and one for walking and dynamic balance. The strength training took place at senior gyms equipped with machines utilizing air pressure technology and aimed at increasing muscle strength and power with an emphasis on the lower body. Each session consisted of warm-up, eight to nine strength exercises, and standing balance exercises. Walking and dynamic balance exercises were performed on an outdoor walking path or, during the winter months, in a sports hall. The sessions included a warm-up with walking balance exercises followed by a continuous walk of 10–20 min at a hard to somewhat hard intensity (rating of perceived exertion 13–14; Borg, 1982). In addition, participants received a progressive home exercise program, with target training frequency two to three times per week, which included strength, balance, and flexibility exercises. Participants were also encouraged to accumulate 150 min of moderate aerobic activity per week in bouts of ≥10 min. Training loads and difficulty of the balance tasks were increased progressively, while training periods varied in volume, intensity, and training specificity during the intervention year. Adherence was recorded from resistance training machines, supervisor logs, and physical activity diaries, and has been reported previously (Sipilä et al., 2021).

The cognitive training for the physical and cognitive training group targeted executive functions. Training was performed on an in-house developed computer program adapted from a program previously used among older adults (Ngandu et al., 2015). Target training frequency was three to four times per week.

Potential adverse events were carefully tracked with questionnaires every 3 months, and participants had the possibility to visit the study nurse and/or physician, if necessary, during the intervention year. Adverse events have been reported previously: approximately 10% of participants perceived some intervention-related adverse events, most of which were minor, for example, transient muscle, and joint pain (Savikangas et al., 2021; Sipilä et al., 2021).

Statistical Analyses

Study groups were combined for the present analysis, since no between-group differences had been found for changes in physical activity (Savikangas et al., 2021) or capacity (Sipilä et al., 2021) in previous studies. Three participants were not analyzed for knee-extension ($n = 311$) and one for chair-stand ($n = 313$) due to missing data at baseline. Participant characteristics are presented as mean and *SD* for continuous variables and as frequencies (n) and percentages (%) for categorical variables. Differences between men and women were tested with independent samples t test for continuous variables, Fisher's exact test for dichotomous categorical variables, and exact Pearson's chi-squared test for the other categorical variables. Similar tests were used to assess differences between participants who remained in the study at 12 months and those who dropped out. To investigate if differences in body composition had an impact on differences in physical capacity outcomes between men and women, estimated marginal means and their *SE* were calculated for the 6-min walk, chair-stand, and knee-extension tests, adjusted for appendicular lean mass. Descriptive analyses were performed in SPSS Statistics (version 26.0 and 28.0).

The effects of multimorbidity patterns on the physical activity and capacity outcomes were analyzed by generalized estimating equation (GEE) linear models with unstructured working correlation and maximum quasi-likelihood estimation. GEE models can account for all available data, meaning that excluding participants with missing data in a longitudinal study is not necessary, and hence we included all participants with valid baseline data in the outcome of interest in each analysis ($n = 311$–314). Data were expected to be missing at random. Men and women were analyzed separately due to differences observed in the preliminary analyses. Models included the main effects of time, age, BMI, and chronic disease conditions as main predictors and the interaction effects of BMI and chronic disease conditions with time to assess their relationship to change in outcomes. Specifically, we used the multiparameter Wald test to assess the combined effect arising from the cluster of chronic disease condition variables, BMI + chronic disease conditions as a combined predictor cluster, the interaction effects of time-by-BMI, time-by-chronic disease conditions, and time-by-BMI + chronic disease conditions. For these parameter clusters, we calculated an effect size (ES) estimate corresponding to the squared semipartial correlation that can be interpreted as the change in model R^2 attributable to the cluster variables. Finally, the analyses were repeated with fat percent as a measure of obesity instead of BMI.

Results are presented as unstandardized regression estimates (Est) and *SE*, except for effects including the predictor cluster of chronic disease conditions for which ES are presented. Unlike regression estimates, ES does not indicate if the relationship is positive or negative. The correlations among the chronic disease condition indicator variables were assessed, and the magnitude of the correlation was <.2 in 95% and 98% of the correlations in men and women, respectively (Supplementary Figure S1 [available online]). GEE and correlation analyses were performed in the R programming environment (version 4.1.1, R Core Team, 2021). The function *geeglm* from the *geepack* package (version 1.3.2) was utilized for the GEE analyses (Højsgaard et al., 2005) and *pheatmap* (version 1.0.12) for the correlation heatmaps (Kolde, 2019).

Results

Baseline Characteristics

Participants were on average 74.5 years old and had a BMI of 27.9 kg/m^2 (Table 1). Two-hundred and six (66%) participants had two or more chronic disease conditions (range 0–6). The median number of conditions was two in both men and women. Men more often had prevalent hyperlipidemia, cardiovascular diseases (including angina pectoris, myocardial infarction, atrial fibrillation, and poor circulation in the lower limbs), diabetes, and chronic urinary tract problems than women, whereas women more often had arthritis/arthrosis and thyroid disorders than men.

The median physical activity category was two in both men and women (range 0–5 in men and 0–4 in women). However, men and women differed in all the physical capacity outcomes and most of the descriptive characteristics (Table 1). Differences in all the physical capacity outcomes remained statistically significant even after adjusting for appendicular lean mass, although attenuated for the 6-min walk and knee-extension tests. Participants who dropped out before the 12-month measurements did not differ from those who remained in the study in any sociodemographic or health-related variable, including chronic disease conditions ($p \geq .1$, data not shown).

The Impact of Multimorbidity Patterns on Physical Activity and Capacity

The results of the GEE analyses are shown in Tables 2 and 3 for men and women, respectively. Chronic disease conditions had a small but significant impact on baseline physical activity and the 6-min walk in both men and women, and on knee-extension in women. The explained variance of these outcomes ranged from less than 1% to 12% ($p < .001$ to .011). In men, the explained variance was not notably higher when the combined effect of chronic disease conditions and BMI was assessed, except that the impact on knee-extension became statistically significant and the effect size estimate was nearly twice as high (ES = 0.11, $p < .001$). In women, the ES of the combined cluster of chronic disease conditions and BMI on physical activity and the 6-min walk at

Table 1 Participant Characteristics, Mean (*SD*), or Frequency (%) at Baseline in Full Study Sample and by Sex

	All ($N = 314$)	Men ($n = 126$)	Women ($n = 188$)	p[a]
Age, years, mean (*SD*)	74.4 (3.8)	74.4 (3.9)	74.5 (3.8)	.787
Height, m, mean (*SD*)	1.66 (0.09)	1.74 (0.06)	1.60 (0.06)	<.001
Weight, kg, mean (*SD*)	76.9 (14.2)	84.3 (12.5)	71.9 (13.1)	<.001
BMI, kg/m^2	27.9 (4.7)	27.9 (3.6)	28.0 (5.3)	.869
ALM, kg, mean (*SD*)	19.3 (4.3)[b]	23.7 (2.9)[b]	16.4 (2.0)	<.001
Fat percent, mean (*SD*)	36.2 (8.2)[b]	30.2 (6.0)[b]	40.1 (7.0)	<.001
Married/living with a partner, *n* (%)	199 (63)	103 (82)	96 (51)	<.001
Education, *n* (%)				.028
High	66 (21)	21 (17)	45 (24)	
Medium	200 (64)	78 (62)	122 (65)	
Low	48 (15)	27 (21)	21 (11)	
Smoking status, *n* (%)				<.001
Never	191 (61)	56 (44)	135 (72)	
Former	109 (35)	61 (48)	48 (26)	
Current	14 (4)	9 (7)	5 (3)	
Perceived health good/very good, *n* (%)	141 (45)	57 (45)	84 (45)	>.999
No difficulties in outdoor mobility, *n* (%)	245 (78)	104 (82)	141 (75)	.127
MMSE, score, mean (*SD*)	27.6 (1.5)	27.4 (1.4)	27.8 (1.5)	.075
Physical activity and capacity				
Physical activity, mean (*SD*)[e]	1.96 (1.26)	2.02 (1.35)	1.93 (1.20)	.544
6-min walk, m, mean (*SD*)[f]	475.4 (81.7)	502.4 (89.9)	457.3 (70.3)	<.001
Adjusted for ALM, EMM (*SE*)		481.0 (10.7)	471.6 (7.8)	<.001
Chair stand, s, mean (*SD*)[g]	13.9 (3.5)[b]	12.6 (2.6)	14.8 (3.8)[b]	<.001
Adjusted for ALM, EMM (*SE*)		12.5 (0.4)	14.8 (0.3)	<.001
Knee-extension, kg, mean (*SD*)[h]	37.0 (12.0)[c]	47.2 (10.0)[d]	30.3 (7.6)[b]	<.001
Adjusted for ALM, EMM (*SE*)[h]		40.5 (1.1)	34.6 (0.8)	<.001
Chronic disease conditions				
Number of chronic conditions, mean (*SD*)	2.2 (1.4)	2.3 (1.4)	2.1 (1.4)	.224
Hypertension, *n* (%)	164 (52)	65 (52)	99 (53)	.908
Hyperlipidemia, *n* (%)	127 (40)	61 (48)	66 (35)	.020
Arthritis/arthrosis, *n* (%)	72 (23)	18 (14)	54 (29)	.003
Cardiovascular disease, *n* (%)	68 (22)	37 (29)	31 (16)	.008
Pulmonary disease, *n* (%)	40 (13)	13 (10)	27 (14)	.307
Chronic musculoskeletal conditions, *n* (%)	38 (12)	12 (10)	26 (14)	.292
Diabetes, *n* (%)	38 (12)	22 (18)	16 (8)	.021
Thyroid disorder, *n* (%)	38 (12)	3 (2)	35 (19)	<.001
Chronic urinary problem, *n* (%)	30 (10)	27 (21)	3 (2)	<.001
Stroke and transient ischemic attack, *n* (%)	17 (5)	7 (6)	10 (5)	>.999
Heart failure, *n* (%)	16 (5)	9 (7)	7 (4)	.198
Cancer, *n* (%)	12 (4)	7 (6)	5 (3)	.234
Depression or anxiety, *n* (%)	10 (3)	2 (2)	8 (4)	.326
Colon problem, *n* (%)	9 (3)	3 (2)	6 (3)	.745
Osteoporosis, *n* (%)	6 (2)	2 (2)	4 (2)	>.999
Stomach problem, *n* (%)	3 (1)	2 (2)	1 (0)	.567
Kidney disease or failure, *n* (%)	2 (1)	2 (2)	0 (0)	.160

Note. ALM = appendicular lean mass; MMSE = Mini-Mental State Examination score; EMM = estimated marginal mean; BMI = body mass index.
[a]Independent samples *t* test for continuous variables, Fisher exact test for dichotomous categorical variables, and Pearson's chi-squared test for other categorical variables. [b]Missing, $n = 1$. [c]Missing, $n = 3$. [d]Missing, $n = 2$. [e]Current physical activity category, range 0–6 as follows: (0) I do not move more than is necessary in my daily chores, (1) I go for casual walks and engage in light outdoor recreation one to two times a week, (2) I go for casual walks and engage in light outdoor recreation several times a week, (3) I engage one to two times a week in brisk physical activity (e.g., yard work, walking, cycling) to the point of perspiring and some degree of breathlessness, (4) I engage several times a week (3–5) in brisk physical activity (e.g., yard work, walking, cycling) to the point of perspiring and some degree of breathlessness, (5) I do keep-fit exercises several times a week in a way that causes rather strong shortness of breath and sweating during the activity, and (6) I participate in competitive sports and maintain my fitness through regular training. [f]Six-minute walking distance in meters. [g]Five-time chair-stand test time in seconds. [h]Maximal isometric knee-extension strength in kilograms.

Table 2 Impact of Chronic Disease Conditions, Obesity, and Time on Physical Activity and Capacity Outcomes in Men

		Physical activity[a]			6-min walk[b]			Chair stand[c]			Knee-extension[d]		
Effect	**Time point (months)[e]**	**Est**	***SE* (Est)**	***p*[f]**	**Est**	***SE* (Est)**	***p*[f]**	**Est**	***SE* (Est)**	***p*[f]**	**Est**	***SE* (Est)**	***p*[f]**
Time	6	1.64	0.86	.057	–48.05	36.47	.188	–0.27	1.09	.806	—	—	—
	12	0.17	1.12	.880	48.06	23.93	.045	–1.82	1.14	.111	0.76	3.54	.830
	24	1.85	1.44	.200	—	—	—	—	—	—	—	—	—
BMI	—	–0.05	0.04	.167	–8.85	2.13	<.001	0.02	0.06	.799	0.70	0.22	.001
Time-by-BMI	6	–0.03	0.03	.285	2.65	1.24	.033	–0.02	0.04	.568	—	—	—
	12	0.01	0.04	.843	–0.10	0.90	.913	0.02	0.04	.695	0.09	0.13	.526
	24	–0.02	0.05	.623	—	—	—	—	—	—	—	—	—

		Physical activity		6-min walk		Chair stand		Knee-extension	
		ES	***p*[g]**	**ES**	***p*[g]**	**ES**	***p*[g]**	**ES**	***p*[g]**
CDC	—	0.05	<.001	<0.01	<.001	0.06	.336	0.06	.089
CDC + BMI	—	0.06	<.001	<0.01	<.001	0.06	.325	0.11	.001
Time-by-CDC	6	0.01	.064	<0.01	<.001	<0.01	.050	—	—
	12	0.01	.017	<0.01	.004	<0.01	<.001	<0.01	<.001
	24	0.03	<.001	—	—	—	—	—	—
Time-by-CDC + BMI	6	0.01	.002	<0.01	<.001	<0.01	.050	—	—
	12	0.01	.012	<0.01	.004	<0.01	<.001	<0.01	<.001
	24	0.03	<.001	—	—	—	—	—	—

Note. Est = generalized estimating equations coefficient estimate; *SE* (Est) = standard error of coefficient estimate; ES = squared semipartial correlation effect size estimate; BMI = body mass index; CDC = chronic disease conditions.
[a]Current physical activity category, range 0–6. [b]Six-min walking distance in meters. [c]Five-time chair-stand test time in seconds. [d]Maximal isometric knee-extension strength in kilograms. [e]Reference time point 0 months. [f]*p* value for coefficient estimate. [g]*p* value for effect group.

Table 3 Impact of Chronic Disease Conditions, Obesity, and Time on Physical Activity and Capacity Outcomes in Women

		Physical activity[a]			6-min walk[b]			Chair stand[c]			Knee-extension[d]		
Effect	**Time point (months)[e]**	**Est**	***SE* (Est)**	**p^f**	**Est**	***SE* (Est)**	**p^f**	**Est**	***SE* (Est)**	**p^f**	**Est**	***SE* (Est)**	**p^f**
Time	6	0.59	0.51	.251	57.17	14.97	<.001	−1.20	0.78	.122	—	—	—
	12	1.12	0.54	.038	59.63	28.35	.035	−3.19	1.60	.047	5.90	1.78	.001
	24	2.48	0.58	<.001	—	—	—	—	—	—	—	—	—
BMI	—	−0.05	0.01	<.001	−5.18	0.68	<.001	0.03	0.06	.539	0.11	0.10	.277
Time-by-BMI	6	0.02	0.02	.309	−0.72	0.55	.188	0.02	0.03	.577	—	—	—
	12	0.00	0.02	.990	−0.46	0.98	.640	0.06	0.06	.295	−0.06	0.06	.328
	24	−0.03	0.02	.107	—	—	—	—	—	—	—	—	—

		Physical activity		6-min walk		Chair stand		Knee-extension	
Effect	**Time point (months)**	**ES**	**p^g**	**ES**	**p^g**	**ES**	**p^g**	**ES**	**p^g**
CDC	—	0.02	.011	0.03	<.001	0.05	.092	0.07	.002
CDC + BMI	—	0.12	<.001	0.09	<.001	0.06	.044	0.07	.002
Time-by-CDC	6	0.01	<.001	<0.01	.018	<0.01	.229	—	—
	12	0.02	<.001	<0.01	.007	0.01	.042	0.01	.010
	24	0.01	.047	—	—	—	—	—	—
Time-by-CDC + BMI	6	0.03	<.001	<0.01	.007	<0.01	.277	—	—
	12	0.03	<.001	<0.01	<.001	0.01	.042	0.01	.008
	24	0.01	.002	—	—	—	—	—	—

Note. Est = generalized estimating equations coefficient estimate; *SE* (Est) = standard error of coefficient estimate; ES = squared semipartial correlation effect size estimate; BMI = body mass index; CDC = chronic disease conditions.

[a]Current physical activity category, range 0–6. [b]Six-min walking distance in meters. [c]Five-time chair-stand test time in seconds. [d]Maximal isometric knee-extension strength in kilograms. [e]Reference time point 0 months. [f]*p* value for coefficient estimate. [g]*p* value for effect group.

baseline was small but three to six times greater than the impact of chronic disease conditions alone. The combined impact of chronic disease conditions and BMI did not explain more of the variance of baseline knee-extension than chronic disease conditions alone, whereas their combined impact on the chair-stand test performance at baseline was statistically significant in contrast to the impact of either one alone (ES = 0.06, $p = .044$).

Chronic disease conditions had a small but significant impact on changes in all outcomes, the explained variance being 3% at the maximum, across all the measurements in both men and women (ES < 0.01 to 0.03, $p < .001$ to .05). In contrast, BMI did not have a significant impact on the development of any physical activity or capacity outcome over time (time-by-BMI interaction effect $p > .1$ for all), except for the 6-min walk in men at 6 months ($p = .033$). The joint cluster of chronic disease conditions and BMI explained a similar amount of the variance, that is, 3% at the maximum, in the development of any outcome in comparison to the cluster of chronic disease conditions alone. In women, only the ESs of the combined cluster of chronic disease conditions and BMI on the change in physical activity at 6 and 12 months were slightly higher than the ESs of chronic disease conditions alone (ES = 0.03, $p < .01$, and ES ≤ 0.02, $p < .01$, respectively).

The results of the analyses including fat percent as the indicator of obesity are shown in Supplementary Tables S2 and S3 (available online) for men and women, respectively. The results differ only slightly from those with BMI as the indicator of obesity. In men, the joint cluster of chronic disease conditions and fat percent explained at the maximum two percentage points more of the variance in any outcome at baseline compared with chronic disease conditions alone. In women, the joint cluster of chronic disease conditions and fat percent explained three to seven times more of the variance in physical activity and the 6-min walk, but only one percentage point more variance in the chair-stand and knee-extension tests at baseline compared to chronic disease conditions alone. The results for changes in physical activity and capacity were mainly similar to those of the analyses conducted with BMI. That is, the joint cluster of chronic disease conditions and fat percent did not explain more variance in the changes of the outcomes than the cluster of chronic disease conditions alone, except that among women the joint cluster explained a greater proportion of the variance of changes in physical activity.

The Associations of Unique Chronic Disease Conditions With Physical Activity and Capacity

The ES of the cluster of chronic disease conditions does not indicate whether the effects of the multimorbidity patterns on the outcomes are positive or negative. This can be explored from the condition-specific results, which are presented in detail in Supplementary Tables S4 and S5 (available online) and are relatively unaffected by collinearity in our data due to the low correlations among the condition indicators. The magnitude and direction of the impact of different conditions varied according to the outcome, sex, and time point, with only a few conditions showing consistent results for one or more outcomes.

The Associations of Unique Chronic Disease Conditions With Physical Activity and Capacity at Baseline

In men, both diabetes and pulmonary diseases were associated with notably lower baseline physical activity ($B = -1.03$ and -1.11, $SE = 0.32$ and 0.34, respectively; Supplementary Table S4 [available online]). Only a few significant associations were found at baseline between unique chronic conditions and physical capacity. Arthritis/arthrosis was associated with lower knee-extension strength ($B = -2.82$, $SE = 2.14$), whereas hyperlipidemia was associated with shorter ($B = -35.45$, $SE = 14.75$) and heart failure with longer 6-min walk distance ($B = 30.85$, $SE = 15.35$).

Among women, pulmonary diseases were related to higher baseline physical activity (main effect of condition $B = 0.54$, $SE = 0.25$; Supplementary Table S5 [available online]). Arthritis/arthrosis was negatively associated with all the physical capacity outcomes, that is, knee-extension strength, 6-min walk, and chair-stand ($B = -2.27$, $SE = 1.13$; $B = -19.67$, $SE = 8.07$, and $B = 1.19$, $SE = 0.65$, respectively). In addition, diabetes and heart failure were associated with a slightly better performance in the chair-stand test at baseline ($B = -0.46$, $SE = 0.88$, and $B = -2.45$, $SE = 1.10$, respectively).

The Associations of Unique Chronic Disease Conditions With Changes in Physical Activity and Capacity

In men, diabetes and pulmonary diseases were associated with a greater increase in physical activity during the study (condition-by-time interaction at 24 months: $B = 1.17$, $SE = 0.38$ and $B = 1.09$, $SE = 0.57$, respectively; Supplementary Table S4 [available online]). The time interactions for both conditions indicated that the initial difference in physical activity at baseline, favoring those without these conditions, declined notably during the study. In contrast, arthritis/arthrosis was associated with a lower increase in strength during the study ($B = -2.83$, $SE = 1.17$), indicating that the initial difference favoring those without arthritis/arthrosis became greater during the study.

In women, pulmonary diseases were associated with a lower increase in physical activity throughout the study (condition-by-time interaction at 24 months, $B = -0.86$, $SE = 0.30$; Supplementary Table S5 [available online]). The time interactions indicated that the initial difference in physical activity at baseline favoring those with pulmonary disease was considerably reduced during the study. In contrast, hyperlipidemia showed a positive association with the changes in all the physical capacity outcomes (e.g., time interaction at 12 months for knee extension: $B = 1.59$, $SE = 0.76$; Supplementary Table S5 [available online]). The negative association between arthritis/arthrosis and the 6-min walk test strengthened during the study (interaction with time at 6 and 12 months: $B = -13.43$, $SE = 8.58$ and $B = -12.92$, $SE = 8.66$, respectively), whereas the initial difference in chair-stand test performance diminished during the study (interaction with time at 6 and 12 months: $B = 0.96$, $SE = 0.47$, and $B = -1.41$, $SE = 0.52$, respectively). In addition, diabetes was associated with a greater improvement in the chair-stand test performance during the study (time interactions at 6 and 12 months: $B = 0.23$, $SE = 0.41$, and $B = -1.24$, $SE = 0.55$, respectively), that is, the small initial difference in chair-stand time in favor of those with diabetes increased during the study.

Discussion

In this exploratory analysis, we found that multimorbidity patterns, including chronic disease conditions and BMI, explained at most 12% of the variance at baseline and 3% of the variance in the changes in the physical activity and physical capacity outcomes among older men and women participating in a year-long multicomponent exercise intervention. The magnitude and direction of the impact varied according to chronic disease condition, outcome, sex, and time point. In general, most conditions did not have a substantial impact on physical activity, aerobic endurance, or on muscle strength or power. These findings suggest that multimorbid older adults who do not have contraindications for exercise may benefit from physical training following the physical activity recommendations for older adults.

Our findings support the evidence from systematic reviews suggesting that exercise interventions may lead to increased physical activity among older adults (Grande et al., 2020; Sansano-Nadal et al., 2019). While the increase has been proposed to be slightly smaller in older adults with chronic disease conditions than in healthier peers (Chase, 2015), the present results do not show a clear negative impact of chronic disease conditions. In general, the impact of multimorbidity patterns on weekly physical activity was minor thus, probably not clinically meaningful. The main effect of multimorbidity patterns explained a greater proportion of physical activity at baseline than of change in physical activity over time, indicating that the baseline impact of multimorbidity patterns remained relatively stable over the course of the intervention and follow-up. One potential explanation for multimorbidity patterns not being a significant predictor of change may be the relatively strict health-related exclusion criteria applied in the study, that is, the participants mostly had mild-to-moderate multimorbidity patterns, which may not have notably limited their engagement in intensive exercise, thereby allowing them to benefit from the intervention. The intervention itself, which included both intensive supervised exercises and self-administered physical activity adapted to individual's physical fitness level, may have been well-suited for this population.

In general, our results complement the findings from a recent meta-analysis, restricted to seven chronic diseases, which suggested that multimorbidity patterns do not compromise exercise-related improvements in physical capacity (Bricca et al., 2020). In the present study, the impact from chronic disease conditions was stronger among men while obesity was a stronger indicator for women. The results were relatively similar for all the measured aspects of physical capacity, including aerobic endurance, muscle strength, and power. In men, BMI was a stronger predictor of muscle strength than chronic disease conditions, showing a positive association. In contrast, in women, BMI was a stronger predictor of aerobic endurance than chronic disease conditions, showing a negative association. These differences between men and women may be explained by the possibility that higher BMI is related to higher muscle mass particularly in men, whereas BMI may be more strongly correlated with body fat in women than in men (Gallagher et al., 1996). This was supported by our finding that, in contrast to BMI, fat percent did not show a positive association with muscle strength but had a negative association with muscle power at baseline. In contrast, the combined impact of chronic disease conditions and fat percent was slightly greater than that of chronic disease conditions and BMI, especially on physical activity in women. However, the differences in the results for BMI and fat percent were mostly minor, and despite the suggestion that BMI is a suboptimal indicator of obesity in older adults (Batsis et al., 2016), our results suggest that BMI continues to be useful in the context of physical activity and capacity, although its limitations should be borne in mind.

Research on the relationships of multimorbidity with physical activity and capacity has been challenged by the heterogeneity of the definitions of multimorbidity (Johnston et al., 2019; Willadsen et al., 2016). The aggregation and combination of conditions may affect the health-related outcomes of multimorbidity (Salive, 2013; Wei et al., 2016) by introducing condition-specific interactions. Therefore, we investigated multimorbidity as a cluster of chronic disease conditions instead of treating multimorbidity as a count of conditions. We found mainly small coefficients for the unique condition indicators and that the associations tracked inconsistently over time points, which may explain the overall small ESs of the multimorbidity patterns on physical activity and capacity.

Interestingly, some conditions had a negative impact on physical activity and capacity outcomes, as expected, whereas others had positive effects on some of the outcomes. Moreover, the effects varied between men and women. For example, in women, pulmonary diseases were associated with a higher baseline level of physical activity but with a lower increase during the study. In men, however, the results were the opposite. The discrepancy between men and women may be explained by differences in baseline physical activity: women with pulmonary diseases had on average a notably higher initial physical activity level compared to men with pulmonary diseases. It is known that asthmatic symptoms may worsen with more intense physical activity and limit possibilities for engaging in higher volume or intensity activity (Panagiotou et al., 2020). Thus, there may have been more room for increasing physical activity in men compared with women. Furthermore, it was not surprising that conditions which may cause musculoskeletal pain had some impact on physical capacity outcomes, but the results were inconsistent. In men, arthritis and/or arthrosis was associated with an increasing negative impact on muscle strength. In women, these conditions were related to consistently lower muscle strength and less improvement in aerobic endurance but greater improvement in muscle power than in women without arthritis/arthrosis. This partially supports previous research suggesting that while, for example, osteoarthritis and rheumatoid arthritis compromise physical functioning, patients may improve their physical capacities with exercise (Bennell & Hinman, 2011; Cooney et al., 2011). It is, however, important to recognize that older adults with, for example, osteoarthritis may perceive relief from joint pain as a motivator but, also perceived, or expected pain as a barrier to exercise (Gay et al., 2018; Petursdottir et al., 2010).

The major strength of the present study is the investigation of multimorbidity as a cluster of chronic disease conditions instead of a count or a categorized count. This allowed us to determine the combined contribution of the conditions to the variance in the physical activity and capacity outcomes and to assess the burden arising from multimorbidity. Using the Wald test for conditions as a cluster allowed us to overcome potential problems related to correlations among the indicators. In our data, the indicator correlations were low, and hence we also assessed the unique contributions of single conditions.

One important limitation of this study is its exploratory nature, and that the power considerations were not extended to the analyses of the present study. Due to the complexity of the potential interactions between the conditions and the low frequency of many conditions, the results for single conditions must be interpreted with caution. Furthermore, we could not investigate the effects of different combinations of conditions on physical activity and capacity due to the variety of combinations. Future studies with larger or more focused samples are thus required to investigate the impact of interactions between specific conditions. Further limitations are that data on prevalent conditions were only available at baseline and that medications were not considered. The discrepancies in the findings may at least partly be a result of changes in conditions during the study or differences in medication status. Furthermore, participants who were physically active or had very severe chronic diseases were excluded from the PASSWORD study. It is thus likely that some chronic disease conditions were over- or underrepresented in the present sample, thereby limiting the generalizability of the results to older adults who met all the inclusion and none of the exclusion criteria. While persons presenting with contraindications to intensive exercise were excluded from this study, it would be important to investigate if those with more severe multimorbidity patterns would increase their physical activity and capacity as a result of engaging in multimodal physical activity at an intensity safe for them, or if those with mild-to-moderate multimorbidity who are already physically active would benefit from additional exercise. From a health promotion perspective, however, this was an ideal study population, since the participants were physically inactive at baseline, and thus could benefit from increasing their physical activity and exercise, and in most cases their chronic disease conditions were at a stage where physical activity and exercise are recommended as a mode of treatment.

Conclusion

This exploratory study showed that multimorbidity patterns had a very small but statistically significant impact on physical activity and capacity in older adults participating in a year-long multicomponent exercise intervention. However, the ESs were small, and the impact of multimorbidity patterns on change in the outcomes over time was minor. Previous research has suggested that interventions promoting physical activity may be less effective in multimorbid older adults than in healthier peers (Chase, 2015) hence, it is encouraging that multimorbidity patterns did not have a notably negative impact on the beneficial effects of exercise. Based on our current findings, many chronic disease conditions that are not contraindications for relatively intense exercise can be assumed not to have a major effect on changes in physical activity and capacity. Despite the lack of physical activity recommendations for people with multimorbidity (Muth et al., 2019), older adults are encouraged to engage in aerobic, muscle strengthening, and balance-enhancing activities to the extent allowed by their chronic disease conditions (Piercy et al., 2018). Multicomponent training following the physical activity recommendations for older adults may also support the functional independence of multimorbid older adults.

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