

Multimorbidity and physical activity profiles: results of the SMILE community cohort study

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Abstract

Background: Physical Activity has emerged as the key treatment option for a wide range of chronic diseases. Many adults aged 55 and up suffer from multiple chronic diseases. Behavioral change is driven by stimulating specific physical activity behaviors, such as walking. Knowing which behaviors are common among which patients may inform interventions. This study describes the types of physical activity performed in a representative, community-based Dutch sample of adults with multimorbidity. We hypothesize that chronic disease clusters exist within this large population and that these meaningful classes may encompass a range of specific physical activity behaviors.

Patients and Methods: Cross-sectional data was used from 3,386 patients, who were 55 years and up, were registered at one of nine primary healthcare facilities that participated in the SMILE cohort study and completed a lifestyle and a chronic illness questionnaire. A model for the association between multimorbidity and physical activity behavior was developed using latent class analysis.

Results: The best fit was a 4-class solution with: (1) a group with the lowest prevalence of cancer, rheumatoid arthritis, and cardiovascular disease and very active in walking, light and intensive household activities; (2) a relatively healthy group in which liver disease or cirrhosis and cycling, gardening, odd jobs and sports were prevalent; (3) a group with the lowest prevalence of migraine, inflammatory joint disease and lowest activity levels in all types of physical activities except for light household chores; and (4) a group with the highest prevalence of all chronic diseases except for liver disease or cirrhosis with moderate physical activity levels.

Conclusion: Multimorbidity did not seem to be the primary obstacle to engaging in physical activity. There was a difference between the classes in terms of the probability to engage in each form of activity, even though the pattern of physical activity behavior for all seven categories of activities appeared equivalent among classes.

Keywords: Comorbidity, Physical Activity, Chronic Disease, Quality of Care

Introduction

Multimorbidity, defined as any co-occurrence of two or more chronic medical or psychiatric conditions in the same individual [1], is becoming the clinical norm among middle aged and older adults [2,3]. Chronic conditions are expected to be exaggerated by physical inactivity [4,5]. Therefore, promotion of physical activity (PA) is suggested as being important in the secondary prevention of multimorbid chronic diseases [6]. In order to develop PA-promoting programs information is needed on the types of behaviors people with multimorbid conditions perform in order to tailor interventions to the behaviors in need of augmentation. Furthermore, a better understanding of which patients specifically need attention would facilitate more targeted approaches to raising and maintaining appropriate PA levels in patients with multiple chronic diseases.

On a population level, appropriate PA is often measured in terms of compliance with PA guideline recommendations. Patients with multimorbidity merely consist of older adults aged 55 and over. They should perform at least 30 minutes of moderate to intense PA (3 to 5 METs) at least five days per week. Muscle strengthening activities twice weekly and balance exercises are also recommended. However, to achieve behavioral change, research needs to focus on particular PA behaviors [7]. If the goal is to stimulate PA to improve the health of patients with multimorbidity, it may be useful to identify subgroups of individuals who could benefit from a common intervention based on their shared characteristics. One of the greatest obstacles in the ongoing development of PA interventions for patients with multimorbidity is the lack of data on common PA behaviors. In this study, we investigated the co-occurrence of chronic diseases in relation to patients' particular PA behaviors. So far, we are not aware of any study reporting on the association between multimorbidity and different physical activity types. In order to determine multimorbidity - physical activity behavior profiles, we performed latent class analysis in which we examined fifteen chronic disease variables and seven merely leisure-time PA variables simultaneously, i.e. walking, cycling, gardening activities, odd jobs, light household chores, intense household activities, and sports. The aim of the present study is to describe the types of PA performed in a representative, population-based Dutch sample of middle-aged to older adults with multimorbidity.

Method

Study Design and Setting

For the present cross-sectional study, we used data from the dynamic SMILE cohort study. The SMILE study was a joint initiative between Maastricht University and the Eindhoven Cooperation of Primary Health Care Centers, and included 32 general practitioners representing nine primary health care centers. Patients were asked questions about lifestyle and chronic diseases in self-administered, paper-based, annual questionnaires. The SMILE study has been approved by the medical ethics committee

of the Maastricht Academic Hospital (MEC 07-4-030) and detailed information about the study protocol was previously published [8]. To enhance transparency and reproducibility, this article has been written according to the Strengthening the Reporting of OBServational studies in Epidemiology (STROBE) checklist for cohort studies.

Participants

The current study used 2003 data from patients aged 55 years and up (n=3,386) because this time point included the largest population.

Measurement

Information on chronic diseases was measured using a self-reported chronic disease questionnaire [9]. The variables included fifteen self-reported chronic diseases (i.e. presence versus absence). Chronic respiratory disease, cardiovascular disease, severe bowel disease, liver disease or cirrhosis, severe kidney disease, diabetes mellitus, cancer, epilepsy, migraine, neurological disorders and stroke, inflammatory joint disease, rheumatoid arthritis, osteoarthritis of knees, hips and hands, severe back problems, and persistent injury from an accident occurring at home, in sports, school/work or traffic were the fifteen self-reported chronic diseases included in the analysis. Patients were asked to mark (thick "yes") for all diseases they currently have. We assumed that most patients followed this instruction and only indicated the presence of each disease without explicitly stating the absence (by thicking "no") of all other diseases listed [9]. At the end of the questionnaire, an open question was asked that allowed all patients to report diseases from which they currently suffered, but that were not included in the fifteen chronic diseases listed. All chronic diseases listed under this open question (n=1,077) were assigned to the existing categories of the questionnaire to maximize the usefulness of the available data. Two researchers (SD and IM) and a medical specialist (JT) independently assigned each disease to the categories.

The Short Questionnaire to Assess Health-enhancing Physical Activity (SQUASH) was used to measure physical activity behavior [10]. Types of leisure-time physical activity included walking, cycling, gardening, odd jobs, light and intense household activities, and sports. Patients were asked to mark participation versus lack of participation for seven types of merely leisure time PA, all of which were scored in binary. The SQUASH questionnaire asks participants about the number of days they were active per week, the average time per day they were active, and the intensity of the physical activity they performed. In the SQUASH questionnaire, PA is pre-structured into (a) commuting activities, (b) leisure-time activities, (c) household activities and (d) activities at work and school. A Metabolic Equivalent (MET value), defined as the ratio of the work metabolic rate to the resting metabolic rate according to the Ainsworth compendium for physical activity is assigned to each type of PA [11]. Activities

with a MET value between 1.6 and 2.9 were classified as intense; activities with a MET value between 3.0 and 5.9 were qualified as moderate-intense and physical activities with ≥ 6 METs were referred to as vigorous-intense[10,11]. Hobbies were excluded from this questionnaire because they often have low MET values (~2 MET), however hobbies that did have meaningful MET values were noted under sports. The data used for the present article did not include information about activities at work and school, because the population was 55 years and over and the majority of these patients were no longer working or going to school. By multiplying the frequency (days per week) and duration (minutes per day), the total number of minutes spent on each activity was calculated. Previous research showed the SQUASH questionnaire to be a reliable and sound questionnaire for measuring physical activity among the Dutch adult population [10].

Data Analysis

Latent class analysis (LCA) was used to identify qualitatively distinct subgroups within populations that frequently share certain outward characteristics. The assumption underlying LCA is that membership in unobserved groups (or classes) can be explained by patterns of scores across, for example, survey questions [12]. In this study, we have attempted to identify groups of related diseases and physical activity types (i.e., latent classes). LCA classified our study participants according to their distribution across all chronic diseases and PA behaviors, based on the mentioned survey questions. The following criteria were jointly considered: the relative goodness of fit estimates for Akaike's information criterion (AIC), the Bayesian information criterion (BIC), the adjusted Bayesian information criterion (SSA-BIC,) and the entropy value [13-15]. The optimal number of latent classes was determined by the model with the lowest AIC, the lowest BIC, the lowest SSA-BIC and the highest entropy value, respectively (Table 1) [16]. In addition to the model fit information provided

Table 1: Latent class models and relative goodness of fit indices.

Latent class model	-2 Log-likelihood	Number of parameters	AIC	BIC	SSA-BIC	Entropy
2 classes	50407.614	45	50497.614	50773.347	50630.361	0.681
3 classes	49725.626	68	49861.626	50278.289	50062.222	0.709
4 classes	49490.131	91	49672.131	50229.724	49940.575	0.763
5 classes	49277.266	114	49505.266	50203.790	49841.559	0.740

AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion; SSA-BIC: Sample-Size Adjusted BIC.

When comparing the four-class model with the five-class model an increase in the number of parameters from 91 to 114 was found and AIC, BIC and adjusted BIC values were slightly lower (AIC_{4class}: 49672.131 versus AIC_{5class}: 49505.266; BIC_{4class}: 50229.724 versus BIC_{5class}: 50203.790; SSA-BIC_{4class}: 49940.575 versus SSA-BIC_{5class}: 49841.559). Entropy results were highest for the four-class model; a higher value indicates a more precise assignment of individuals to latent classes. In addition to the model fit information provided by MPlus, we calculated the bootstrap -2 loglikelihood-ratio difference test and compared the model with k classes (in our case 5) to the model with (k-1) classes (in our

case, 5-1=4). The result of the -2 likelihood-ratio test showed a significant difference (p<0.005; -2 Log-likelihood ratio: 212.865; $\chi^2(df:23;0.995)$: 44.181).

When examining the two- to five-class models from a content perspective, we found that in the four- and five-class model, the distinction between classes for the musculoskeletal disorders became clearly visible (Figure 1). Data analysis revealed that the five-class model added little information to the four-class model: (1) the pattern across all seven physical activity types was comparable in the four and five class model; (2) the likelihood of

by MPlus, we calculated the bootstrap -2 loglikelihood-ratio difference test (AIC-2* number of free parameters). This test compares the model with K classes to a model with (K-1) classes. Because there are no criteria that are commonly accepted as the best for determining the number of classes, we also considered the latent class model's interpretability to determine the most optimal model. A series of latent class analyses with two to five classes per model were executed.

According to the response probabilities of all 22 variables for each individual (presence of 15 chronic diseases and performance on 7 specific physical activity types), individuals were allocated to the latent class for which they had the highest posterior probability. For each patient, the posterior probability of belonging to each latent class was calculated based on the model estimates. Subsequently, patients were allocated to the class for which this probability is the greatest. Item response probabilities were used to characterize latent classes in a similar way to factor loadings in factor analysis. LCA was performed using Mplus version 7 statistical software (Los Angeles, CA: Muthén and Muthén. Seventh Edition) [16].

Results

Participants

Of the in total 3,386 patients fifty-three percent were female and the average age was 68 (SD 8.3) years. The most prevalent chronic diseases were 'osteoarthritis of the knees, hips and hands' (23%), 'severe back problems, hernia, sciatica or osteoarthritis' (15%) and 'chronic bronchitis, emphysema and asthma' (10%).

Number of Classes

To obtain an overall picture of latent classes of chronic diseases and physical activity, we examined the two- to five class models. Statistically, the four-class and five-class solutions seemed to provide the best-fitting models (Table 1).

executing each type of activity differed among the classes was also comparable between both models; (3) the relatively healthy group showed the highest levels on ‘more intense’ physical activity types like cycling, gardening, intense household activities and sports (this was also comparable between both models) and (4) in both models light household activities were performed most. Summarized, the main results were the same, and only slight

differences were found in the probability of chronic diseases between the four and five class model. From a statistical point of view, the difference between AIC and SSA-BIC was hardly worth mentioning; the number of parameters increased, indicating an extra complex model, and the four-class model had even higher entropy. Ultimately, the four-class model was chosen for thorough investigation.

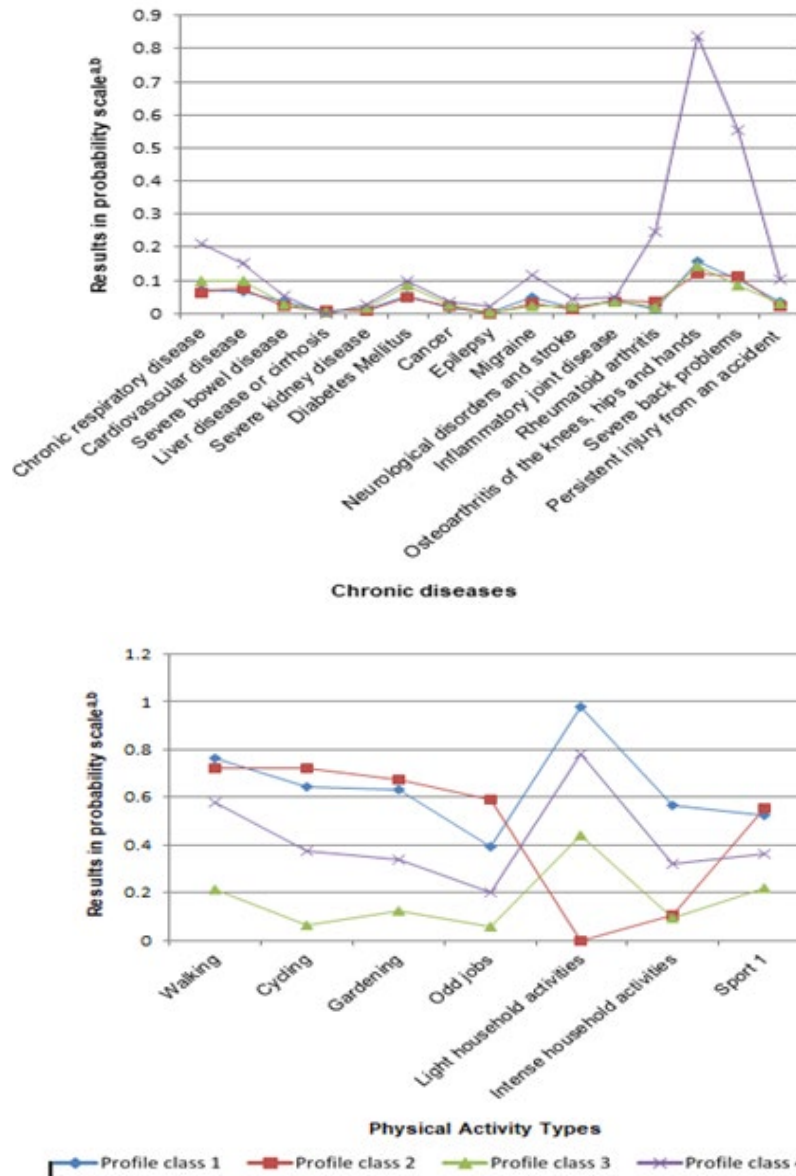


Figure 1: Chronic disease and physical activity type profiles for the four-class model.

^aThis legend applies to both graphs included in Figure 1. The graph was split to enhance visibility of class proportions caused by large differences in the scale of class probabilities (y-axis); ^bThe y-axis represents the probabilities of answering ‘yes’ to each item given that a person belongs to a certain latent class. So, if a person belongs to latent class 4, he or she has a 20.9% probability of saying ‘yes, I have chronic respiratory disease’ and thus a 79.1% chance of answering ‘no, I do not have chronic respiratory disease’.

By contrast, if a patient belongs to class 3, he or she has a 9.7% probability of saying ‘yes, I have chronic respiratory disease’.

Classification of Participants Based on Their Most Likely Latent Class Membership

For all 3,386 participants, MPlus estimated the probability that the person belonged to the first, second, third, or fourth class. For example, for patient 1, there was a 90% probability that the person

belonged to the first class, a 1% probability of belonging to the second class, 0% of belonging to the third class, and 8.9% of being a member of the fourth class. Thus, for patient 1 MPlus decided that he or she belonged to the first class since the probability associated with that class was the largest. Based on this rule, MPlus classified all 3,386 patients into one of four non-overlapping classes. The results showed that out of the 3,386 patients (100%), 1612 (47.6%) were members of latent class 1, 327 (9.7%) were part of latent class 2, 1081 (31.9%) belonged to latent class 3 and 366 (10.8%) were part of latent class 4.

Latent Class Profiles

The proportion of participants assigned to each of the four latent classes and the probabilities for each chronic disease and physical activity type by latent class are presented in Table 2. The probabilities listed for each chronic disease and physical activity type are parameter estimates and can be interpreted as the percentage of patients within the given latent class who reported having the relevant chronic disease or performing the physical activity type in question. For example, consider the question, “Do you have chronic respiratory disease?”. The probability of answering “yes” to this question was 7.0% for the first class, 6.4% for the second class, 9.7% for the third class, and 20.9% for the fourth class. Consequently, the chance of answering ‘no’ to this question was 93% for the first class, 93.6% for the second class, 90.3% for the third class and 79.1% for the fourth class. The same applied to physical activity behavior, since it was also measured in as a binary variable. The probability reflects the percentage of participants within the given latent class who performed the given physical activity type. For example, the chance of walking was 76.6% for the patients in class 1. Conversely, 23.4% of the patients in class 1 did not walk. Looking at the pattern of estimated percentages for all fifteen chronic disease variables and seven physical activity types is needed in order to characterize each class. A graph of chronic diseases and physical activity type probabilities for all four latent classes is presented in Figure 1.

Latent Class 1

Latent 1 class consisted of patients with the lowest chance of cardiovascular disease, cancer, and rheumatoid arthritis combined with the highest probabilities for walking and light and intensive household activities compared to the three other latent classes. Most patients were classified as members of latent class 1 (n=1612) and the probabilities for cardiovascular disease, cancer, and rheumatoid arthritis were 6.8%, 1.8% and 1.2%, respectively. The chance of having one of these three diseases was lower in latent class 1 compared with the total population of 3,386 patients (where these values were 8.8%, 2.3%, and 4.4%, respectively). With respect to the physical activity types, the probabilities for walking, light household chores, and intense household activities were 76.6%, 98.0% and 56.7%, respectively. Compared to the overall population, the probabilities for walking, light and intensive household chores were 20.2%, 28.6%, and 22.3% higher, respectively.

Latent Class 2

Compared to the other three latent classes, class two was generally the healthiest group, with the highest probabilities for liver disease or cirrhosis, cycling, gardening, odd jobs and sports. The probabilities for chronic respiratory disease (6.4%), severe bowel disease (2.0%), severe kidney disease (0.6%), diabetes mellitus (4.7%), epilepsy (0%), neurological disorders and stroke (1.4%), osteoarthritis of the knees, hips and hands (12.1%), and persistent injury from an accident (2.3%) were the lowest compared to the other four classes. In latent class 2, the probability for liver disease or cirrhosis was 0.9%, and this figure exceeded not only the probabilities of the other three classes but also those of the total population of 3,386 patients (0.5%). The probabilities for cycling, gardening, odd jobs, and sports were also the highest of all four classes and higher than those in the total population. In latent class 2, which consisted of 327 patients, the chance for cycling was 72.2%, for gardening 67.6%, for odd jobs 59.0%, and for sports 55.5%, while these values were 44.4%, 43.9%, 28.3%, and 41.2%, respectively, for the overall population of 3,386 patients.

Latent Class 3

Latent class 3 consisted of patients with the lowest probability for migraine, inflammatory joint disease and all physical activity types except light household activities. Of the 1081 patients belonging to class 4, the probabilities for migraine and inflammatory joint disease were lowest at 2.3% and 3.4%, respectively. Out of 3,386 patients, more patients (4.7% and 8.9%, respectively) reported having migraines and struggling with inflammatory joint disease. had and were lower than that of the overall population that reported engaging in these six physical activity types. Walking (21.2%), cycling (6.4%), gardening (12.2%), odd jobs (5.8%), intensive household activities (9.2%), and sports (22.2%) in this class were the lowest compared to the other classes as well as the overall population that reported engaging in these six types of physical activity.

Latent Class 4

Latent class 4 was designated as having the highest probability for all chronic diseases except liver disease or cirrhosis, as well as moderate physical activity levels. All chronic disease probabilities were higher than the other three latent classes, as well as the proportion of patients in the overall population who reported having one of these 14 chronic diseases. The probabilities for the 366 patients assigned to latent class 4 were 20.9% for chronic respiratory disease, 15.2% for cardiovascular disease, 5.1% for severe bowel disease, 2.5% for severe kidney disease, 10.0% for diabetes mellitus, 3.6% for cancer, 2.2% for epilepsy, 11.7% for migraine, 4.3% for neurological disorders and stroke, 47.3% for inflammatory joint disease, 24.5% for rheumatoid arthritis, 83.7% for osteoarthritis of the knees, hips and hands, 55.3% for severe back problems, and 10.1% for persistent injury from an accident. The probabilities for all types of physical activity were moderate compared to the other three classes. The probability of being able to walk and perform light household activities was higher compared to the proportion of the overall population that reported

performing these physical activity types (58.1% versus 56.4% activity types, the probability was lower compared to the overall and 78.0% versus 69.4%, respectively). For all other physical population.

The four latent classes were labelled as follows:

Class 1	Group with the lowest prevalence of cardiovascular disease, cancer and rheumatoid arthritis and very active in walking, light and intense household activities
Class 2	Relatively healthy group with a high prevalence of liver disease or cirrhosis, active in cycling, gardening, odd jobs and sports
Class 3	Group with the lowest prevalence of migraine, inflammatory joint disease and lowest activity levels in all types of physical activities except for light household chores
Class 4	Group with the highest prevalence of all chronic diseases except for liver disease or cirrhosis with moderate physical activity levels

Table 2: Latent class specific probabilities for all chronic diseases and physical activity types.

Variable	Total population (N=3,386)N (%)	Latent class 1 (n=1612)	Latent class 2 (n=327)	Latent class 3 (n=1081)	Latent class 4 (n=366)
Chronic diseases					
Chronic respiratory disease	321 (9.5)	0.070	0.064	0.097	0.209 ^a
Cardiovascular disease	299 (8.8)	0.068	0.077	0.098	0.152 ^a
Severe bowel disease	112 (3.3)	0.034	0.020	0.028	0.051 ^a
Liver disease or cirrhosis	16 (0.5)	0.006	0.009 ^a	0.003	0.000
Severe kidney disease	48 (1.4)	0.011	0.006	0.017	0.025 ^a
Diabetes Mellitus	230 (6.8)	0.052	0.047	0.085	0.100 ^a
Cancer	77 (2.3)	0.018	0.022	0.025	0.036 ^a
Epilepsy	20 (0.6)	0.004	0.000	0.004	0.022 ^a
Migraine	158 (4.7)	0.048	0.030	0.023	0.117 ^a
Neurological disorders and stroke	70 (2.1)	0.017	0.014	0.020	0.043 ^a
Inflammatory joint disease	302 (8.9)	0.038	0.037	0.034	0.473 ^a
Rheumatoid arthritis	150 (4.4)	0.012	0.034	0.019	0.245 ^a
Osteoarthritis of the knees, hips and hands	780 (23.0)	0.157	0.121	0.141	0.837 ^a
Severe back problems	517 (15.3)	0.104	0.111	0.085	0.553 ^a
Persistent injury from an accident	132 (3.9)	0.033	0.023	0.029	0.101 ^a
Physical activity types					
Walking	1910 (56.4)	0.766 ^a	0.722	0.212	0.581
Cycling	1503 (44.4)	0.664	0.722 ^a	0.064	0.374
Gardening	1487 (43.9)	0.633	0.676 ^a	0.122	0.337
Odd jobs	957 (28.3)	0.395	0.590 ^a	0.058	0.200
Light household activities	2351 (69.4)	0.980 ^a	0.000	0.440	0.780
Intense household activities	1165 (34.4)	0.567 ^a	0.108	0.092	0.319
Sport 1	1394 (41.2)	0.525	0.555 ^a	0.222	0.361

^aHighest probability for the indicator variable across the four latent classes.

Discussion

A Statement of The Principal Findings

Latent class analysis (LCA) was executed to establish a multimorbidity-physical activity behavior model. Four latent classes were identified. The first group had the lowest prevalence of cancer, rheumatoid arthritis, and cardiovascular disease and engaged the most in walking and household activities. The second group was the healthiest and had the highest prevalence of liver disease or cirrhosis and engaged in cycling, gardening, odd jobs, and sports. The third group had the lowest prevalence of migraine, inflammatory joint disease and performed all types of physical activities except light household chores. The fourth group had the highest prevalence of all chronic diseases except for liver disease or cirrhosis and had moderate activity levels.

Strengths and Weaknesses of The Study

The strengths of our study included the use of LCA incorporating both chronic diseases and physical activity types simultaneously to obtain in-depth information about the association between multimorbidity and physical activity; the availability of information on different types of leisure time physical activity; the rigorous statistical analyses performed; and the large sample size. The main weakness was that the presence of chronic diseases was determined using a self-reported questionnaire. Despite the fact that chronic disease information was also recorded in an electronic medical record, we were unable to access this data due to a lack of informed consent. Nonetheless, previous research on the SMILE cohort found more than 80% correspondence between self-reported data and electronic medical record data for most of the fifteen chronic diseases. This finding lends support to the current study's use of self-reports [17]. The self-reported questionnaire also did not provide information about the severity of each chronic disease, which could be seen as a limitation. Aside from that, despite the fact that participants were explicitly informed that none of the information reported in the questionnaires would be sent to their health care providers, social desirability may have influenced self-reported physical activity data.

Strengths and Weaknesses in Relation to Other Studies, Discussing Important Differences in Results

Although the use of LCA to establish multimorbidity clusters is becoming more common, this kind of analysis has rarely been used in the field of multimorbidity research [18,19]. The current study was the first to include both chronic disease variables and physical activity variables simultaneously in one latent class model. Moreover, to the best of our knowledge, we were also the first to assess physical activity behavior in relation to multimorbidity across seven different types of physical activity. As a result, we cannot compare our findings to previous research. Instead, we did additional analyses to check the robustness of our findings. To begin, we ran a sensitivity analysis on the sports variable. In response to an open item in the SQUASH questionnaire, patients could choose to report up to four sports activities. For each sports activity, they were asked to indicate how many days per week they performed the activity and how much time they spent on average

doing each sport. Our findings were consistent with other studies in that most older adults only participate in one sport [20]. Since, less than 10% reported doing more than two sports on a regular basis, we performed the LCA twice: first, we included all four sports variables in the model; second, we only included the first sports activity listed in our model. The findings revealed comparable latent classes. Nonetheless, we choose to include only the primary (first) sports activity in our final model in order to 1) improve stability among the four latent classes and 2) to acknowledge and accurately reflect in the classes identified that the majority of older adults participate in only one sports activity on a regular basis.

Second, the LCA was repeated three times. All three models included the fifteen chronic disease variables, but we varied the measurement types for the seven physical activity types (binary, ordinal, and continuous). The results showed identical latent classes. We chose to present the binary physical activity measurement for simplicity and clarity because the results were similar.

Possible Explanations and Implications for Clinicians and Policymakers Based on This Study

First, our finding suggest that chronic diseases may not be the primary impediment to physical activity, as the highest probability of most chronic diseases was associated with moderate likelihoods of physical inactivity. Previous research on the motives and barriers to physical activity among older adults with limitations showed that nearly half of those with severe or moderate limitations reported disease management and health maintenance as a reason for being physically active [20]. We hypothesize that a higher probability of chronic diseases and/or multimorbidity is related to a higher probability of obtaining physical activity advice and, thus, a higher level of perceived necessity for disease management, including physical activity. We expect that chronically ill patients will visit health care professionals more frequently, thereby raising the probability of receiving physical activity advice or even a physical therapy prescription. Second, physical activity behavior patterns for all seven types of physical activity seemed comparable among the four latent classes. The size of the probability of executing each type of activity, however, differed among classes. The second class, and thus the relatively healthy group, appeared to be associated with the highest levels of leisure time physical activity (e.g., cycling, gardening, odd jobs and sports), in spite of having the highest chance of liver disease or cirrhosis. This seems to confirm findings from previous research that showed that healthy individuals had the highest physical activity [5,21]. Previous investigations have shown that skeletal muscle contraction alleviates symptoms of liver disease, lowers pain, reduces inflammation, improves oxygen delivery to the liver, which enhances liver function and seems to delay severe muscle wasting, which is common in advanced liver disease [19,22]. Thus, directly noticeable benefits of physical activity might explain the enhanced leisure time physical activity in patients with liver disease. However, only 16 (0.5%) of our total population of 3,386 patients reported having liver disease, implying that a higher likelihood of leisure time activity levels

may be due to this group's better health rather than in increased risk of liver disease. The probability of performing light household chores was lowest in this latent class, while the probability of engaging in more physically challenging activities, as odd jobs or gardening, were the highest when compared to the other three classes. It is unclear why the healthiest patients participate in household activities so infrequently. Overall, the probability of performing household chores was highest in the group with the least cardiovascular disease, cancer and rheumatoid arthritis. As Dutch people nowadays need to stay at home as long as possible as they get older, the likelihood of doing house hold activities was expected to be high in this group. On the other hand, this finding may reflect that, particularly for those who are most likely to have the most severe chronic diseases, doing household activities may make them feel more independent [22].

The findings of this study suggest that policymakers should encourage increased physical activity levels among older individuals with a low probability of chronic diseases and/or multimorbidity (prevention of onset). Simultaneously, health care providers should clearly emphasize the benefits of physical activity in patients who are most likely to suffer from chronic diseases (prevention of worsening). Our results suggest that patients, as those with liver disease or cirrhosis, are more likely to engage in leisure-time physical activity, particularly sports, because the benefits are directly noticeable in certain groups. If future research confirms this hypothesis, it may be even more important to emphasize that patients with high risk of other chronic diseases may benefit from engaging in physical activity, even if the benefits are not immediately apparent.

Unanswered Questions and Future Research

The present study was the first to integrate multimorbidity and physical activity in a latent class analysis to establish a model of their relationship. Nonetheless, the design was cross-sectional, and therefore more research is needed to determine whether the multimorbidity-physical activity behavior model suggests temporality and, thus, a causal relationship. In addition, to enhance interpretability and accuracy, we propose including other indicators associated with multimorbidity and/or physical activity, such as age, gender, and living environment of participants; and extending the maybe latent class analysis is better than the abbreviation LCA? toward structural equation models for measuring variability and change, e.g., latent change and latent growth curve models.

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Competing Interest's Statement

All authors declare that they have not received any support from any organization for the submitted work; that they have no financial relationship in the last three years with any organizations that might have an interest in the submitted work; and that they have not maintained any other relationships or participated in other activities that could appear to have influenced the submitted work.

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Author Contributions

Substantial contributions to the realization or design of the article or the acquisition, analysis, or interpretation of study data were made by SD, IM, RV, JS, MvA, JT (Prof.dr. JAW Teijink, Catharina Hospital, Eindhoven, The Netherlands) and RdB. SD and IM wrote the manuscript, and IM, RV, JS, MvA, JT and RdB examined it for important intellectual content and gave their final approval for the definitive version to be published. Each author agreed to bear responsibility for all aspects of the work to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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