

Physical activity and 4-year changes in body weight in 52,498 non-obese people: The Lifelines Cohort

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Abstract

Objectives: We investigated associations between leisure-time physical activity (LTPA) at different intensities (moderate and vigorous or moderate-to-vigorous) and prospective weight gain in non-obese people. We also examined whether these associations were independent of other lifestyle factors and changes in muscle mass and whether they were age-dependent and changed over a person's life course.

Methods: The data were extracted from the Lifelines cohort study (N=52,498; 43.5% men) and excluded obese individuals ($BMI > 30 \text{ kg/m}^2$). We used the validated SQUASH questionnaire to estimate moderate-to-vigorous (MVPA; MET ≥ 4), moderate (MPA; MET between 4 and 6.5) and vigorous PA (VPA; MET ≥ 6.5). Body weight was objectively measured, and changes were standardized to a 4-year period. Separate analyses, adjusted for age, educational level, diet, smoking, alcohol consumption and changes in creatinine excretion (a marker of muscle mass), were performed for men and women.

Results: The average weight gain was $+0.45 \pm 0.03$ kg in women. Relative to each reference groups (No-MVPA, No-MPA and No-VPA), MVPA (Beta (95%CI): -0.34 kg (-0.56;-0.13)), MPA (-0.32 kg (-0.54;-0.10)) and VPA (-0.30 kg (-0.43;-0.18)) were associated with less gain in body weight in women after adjusting for potential confounders, described above. These associations were dose-dependent when physically active individuals were divided in tertiles. Beta-coefficients (95%CI) for the lowest, middle, and highest MVPA tertiles relative to the 'No-MVPA' were, respectively, -0.24 (-0.47;-0.02), -0.31 (-0.53;-0.08), and -0.38 (-0.61;-0.16) kg. The average weight gain in men was $+0.13 \pm 0.03$ kg, and only VPA, not MPA was associated with less body weight gain. Beta-coefficients (95%CI) for the VPA tertiles relative to the 'No-VPA' group were, respectively, -0.25 (-0.42;-0.09), -0.19 (-0.38;-0.01) and -0.20 (-0.38;-0.02) kg. However, after adjusting for potential confounders, the association was no longer significant in men. The potential benefits of leisure-time PA were age-stratified and mainly observed in younger adults (men: <35 years; women: <55 years). Moreover, occupational MVPA was not associated with favourable changes in body weight in males and females.

Conclusion: Higher leisure-time MVPA, MPA, and VPA were associated with less weight gain in women <55 years. In younger men (<35 years), only VPA was associated with less weight gain.

Introduction

Obesity contributes to the development of a number of chronic diseases, such as type 2 diabetes, cardiovascular diseases, and certain cancers.[1] Obesity rates among adults nearly trebled between 1975 and 2016 [2], and the epidemic proportions of obesity and obesity-related diseases continue to pose major health problems, globally. The global rate of type 2 diabetes among adults rose from 4.7% in 1980 to 8.5% in 2014.[1] while one-third of all deaths worldwide are attributed to cardiovascular diseases.[3] With obesity acknowledged as the underlying cause of these health concerns, attention has shifted to the primordial prevention of obesity in non-obese people, necessitating the development and improvement of strategies for preventing weight gain[4][5]. Genetic, socio-economic, and environmental factors generally

account for body weight gain[6][7][8]. These factors influence energy balance-related behaviours that determine energy intake and expenditure. The primordial prevention of excessive calorie intake and of low levels of energy expenditure (i.e., low physical activity) constitute the main strategy for reducing the risk of weight gain[7][9].

Previous studies have mainly focused on the benefits of increased physical activity (PA) as a strategy for promoting body weight loss and for preventing the regaining of body weight in obese individuals.[10] They have shown that individuals who become more active lose more body weight. Several large-scale studies have found that PA plays a role in the prevention of body weight gain.[11][12][13] By contrast, other studies have found no association between baseline PA and changes in body weight during follow-up assessments.[14][15][16][17] In some studies that mostly included small sample sizes, this association was only observed in subgroups, for example, in normal weight, female, or younger adults. [18][19] Therefore, large-scale population-based studies that test the benefits of PA across groups differentiated by age and sex are required. Moreover, little is known about how the intensity and type of daily-life PA impact on its association with prospective changes in body weight. Clinical guidelines on physical activity recommended that people should do at least 150 minutes of moderate-intensity, or 75 minutes of vigorous intensity PA a week.[20] Although clinical guidelines recommend that physical activities should be conducted at moderate-to-vigorous and not at light intensity levels, most previous studies focused on total PA, including light PA.[14][15][18][21][19] Moreover, there are still unanswered questions as to whether vigorous PA is necessary for achieving a health benefit. As reported in the literature, VPA has more impact on VO_2^{max} and fitness level and induces more release of growth hormone and catecholamines, suggesting that benefits of physical activity differ according to intensity level, such that vigorous PA may affect muscle mass more, and also increase basal metabolic rate more, than moderate and light PA[22][23]. However, not all individuals are able or willing to perform vigorous PA, and this may not even be necessary if a moderate intensity level is in fact effective. Furthermore, it is not clear whether all types of activities can contribute to the recommended amount of daily PA as there is emerging evidence that occupational moderate-to-vigorous PA (MVPA) may not have the same level of health benefits as do physical activities conducted at leisure-time. [24] [25] [26][27] "As mentioned above, since it is not clear in previous studies whether the effects of MVPA prevent weight gain depending on whether it is more moderate or vigorous intensity activities, the primary objective of our study is to determine whether the association of MVPA on body weight gain are more dependent on moderate and vigorous physical activities. In case that the association of MVPA depends on its intensity, we explored how it relates to the types of activities reported by the participants." We also examined whether these associations are independent of other lifestyle factors, such as diet, smoking and alcohol use, and changes in creatinine excretion, which is a marker of muscle mass. Furthermore, we examined whether the associations were age-dependent and differed over the life course within a large cohort deemed representative of the general population.

Methods

Data source and study population

Lifelines is a multidisciplinary prospective population-based cohort and biobank of more than 167,000 people living in the North of the Netherlands.[21] It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioral, physical, and psychological factors that contribute to the health and disease of the general population, with a special focus on multi-morbidity and complex genetics. The study is conducted according to the Helsinki Declaration, and it was approved by the medical ethical committee of the University Medical Center Groningen in the Netherlands. All participants provided their written informed consent.[28]

In this study, the analyses were based on the data at baseline and at 4-year follow-up. We included non-obese ($\text{BMI} < 30 \text{ kg/m}^2$) adult (> 18 years) subjects of Western European origin. The first exclusion was any missing and/or implausible data related to the main determinant and outcome: assessment of physical activity and the measurements of body weight. Further exclusions were related to minimize bias from changes in physical activity or body weight: excessive or unwanted weight loss, pregnancy, type 2 diabetes, thyroid diseases, irritable bowel syndrome, transplantation, cancer, heart failure, stroke, stent or bypass and pacemaker. In all, 52,498 participants were included in the current analyses (**Figure S1**).

Assessment of physical activity

Physical activity was assessed using the Short QUESSENHEIMER ASSESS Health-enhancing (SQUASH) physical activity, a validated questionnaire, which estimates habitual physical activities with reference to a normal week in the past month.[29] The SQUASH questionnaire allows for the categorization of minutes of PA according to levels of intensity, namely light, moderate, and vigorous. Furthermore, another reason for having chosen this questionnaire in this study is that the SQUASH allows to measure PA minutes through intensity level and through different types of daily-life PA at the same time. The SQUASH is pre-structured into four domains: commuting, leisure time, household, and occupational activities. Questions consisted of three main queries: days per week, average time per day, and intensity. Each activity in minutes per week was calculated by multiplying frequency (days/week) by duration (min/day). Then, the activities were assigned to a certain level of effort, or intensity, indicated by the MET value of the activity[29][30] MET values were assigned to activities with the help of Ainsworth's Compendium of Physical Activities.[31]

In this study, leisure-time (including commuting) moderate-to-vigorous PA (MVPA; MET ≥ 4.0), moderate PA (MPA; MET between 4 and 6.5) and vigorous PA (VPA; MET ≥ 6.5) categories were used as the main measures of physical activity. These intervals are applied according to the guidelines for Dutch physical activity.[32] Participants were divided into distinct categories based on the amount of MVPA, MPA and VPA. Individuals who performed no physical activity at MVPA, MPA and VPA, respectively were classified as 'No-MVPA', 'No-MPA' and 'No-VPA' (T0). The other participants (MVPA>0 min/week, MPA>0 min/week and VPA>0 min/week) were divided into distinct tertiles of MVPA, MPA and VPA ranging from low (tertile

1, T1), middle (tertile 2, T2) to high (tertile 3, T3). Thus, T0, T1, T2 and T3 were considered as 'inactive', 'a little bit active', 'active', and 'very active' respectively.

Additionally, activity minutes per week for specific types of daily-life physical activity (walking, cycling, sports and odd jobs) at moderate or vigorous intensity were categorized into two levels: No-MPA and MPA>0 minutes per week, or No-VPA and VPA>0 minutes per week.

Body weight measurement

Participants' body weights (in kg) were measured by well-trained assistants who are permanent staff members using a standardized protocol.[28] At a follow-up session conducted after 4 years, their body weights were measured to the nearest 0.1 kg using the same baseline protocol. Changes between baseline and follow-up measurements were standardized to a 4-year period.

Other baseline measurements

Body height, waist circumference and blood pressure were measured by trained assistants at baseline, and BMI (kg/m^2) was calculated. Blood samples were collected in the fasting state and analyzed on the day of collection at the Department of Laboratory Medicine of the University Medical Center Groningen, the Netherlands (**Supplementary method 1**).[28]

The supplementary methods section (**Supplementary method 2**) provides definitions for the covariates. In brief, education levels were categorized as low, medium, and high. Current smoking status was categorized as non-smokers and smokers. Daily caloric and alcohol intakes were calculated using the Food Frequency Questionnaire and presented as kilocalories per day (kcal/day) and grammes of alcohol per day (g/day). Diet quality was assessed using the Lifelines Diet Score, which is described in greater detail elsewhere.[33] Creatinine excretion was calculated as the mean value derived from two urine samples collected over a 24-hour period [34]. The method applied for analysing the urine samples is described in detail elsewhere.[28]

Statistical analysis

The study characteristics were expressed as means with a standard deviation for normally distributed variables or as medians with interquartile range (25th to 75th percentile) for non-normally distributed variables and numbers with percentages in case of categorical data. The differences between groups were compared using 1-way analysis of variance tests or Kruskal-Wallis tests for continuous variables. The frequency distributions of categorical variables were analyzed using the Pearson Chi-Square test. Furthermore, estimated changes in body weight were estimated according to the level of physical activity (MVPA and VPA) using age and education adjusted ANOVA. Outcomes were presented as mean of kilogram body weight with standard error.

Linear regression analysis was performed to evaluate the association between PA and changes in body weight. First, we investigated MVPA, MPA and VPA dichotomously (No-PA and PA>0). In the main

analysis, dummy exposure variables were created to compare each tertile of MVPA, MPA and VPA (T1-3) with the reference group (No-MVPA, No-MPA and No-VPA). Outcomes were presented as unstandardized beta-coefficients with 95% confidence intervals (95%CI). In the regression analyses, the basic model was adjusted for age and education level. In model 1, we added diet (LLDS for diet quality and daily caloric intake for diet quantity), current smoking (yes/no) and alcohol consumption (g/day) as potential lifestyle confounders to the basic model. Model 2 was adjusted for changes in creatinine excretion, a marker of muscle mass, in addition to adjustments in model 1. All the regression analyses were repeated stratified by age categories (<35, 35-55, and >55 years). Furthermore, the role of specific types of daily-life physical activities was investigated by repeating the analyses with the physical activity determinant divided into its underlying components (e.g. occupational PA, walking, cycling, sports etc.).

All statistical analyses were performed using IBM SPSS V.22.0 (Chicago, IL) and GraphPad Prism V.4.03 (San Diego, CA). A two-sided statistical significance was set at $p<0.05$ for all tests.

Results

Female participants were more likely to maintain healthy lifestyles. Fewer women were smokers or consumed alcohol, and their diet scores were healthier than those of men (**Table 1**). Of the participants, 13.3% of males ($n = 3,035$) and 8.8% of females ($n = 2,519$) did not perform any activities at a moderate-to-vigorous level (No-MVPA). The numbers of smokers and of participants with lower education levels were higher in the No-MVPA group compared with those in the MVPA groups. Furthermore, higher concentrations of total cholesterol and triglycerides and a lower concentration of HDL-C as well as lower diet scores were noted for this group. **Table S1** shows the participants' characteristics stratified by age. Men's PA levels (min/week), and especially VPA were significantly higher than those of women. The age- and education-adjusted MVPA mean values for men and women in min/week were, respectively, 288.0 ± 1.9 and 279.4 ± 1.7 , and those for VPA were 133.4 ± 4.2 and 88.8 ± 1.1 , respectively. **Figure S2** shows the levels of specific types of MVPA.

Table 1. General characteristics of the study population by leisure-time MVPA level in males and females

Characteristics	Total	According to MVPA level			
		T0	T1	T2	T3
Men					
MVPA min/week	288.0 ± 1.9*	0	3-160	162-360	361-4015
Number (%)	22,827 (43.5)	3035 (13.3)	6597 (28.9)	6888 (30.2)	6307 (27.6)
Age (years)	45 (36-52)	45 (37-51)	44 (37-51)	45 (36-51)	46 (35-56)
Education:					
Lower (%), n	24.7 (5,630)	36.4 (1,195)	24.2 (1,597)	21.3 (1,465)	23.2 (1,463)
Middle (%), n	38.5 (8,784)	42.0 (1,275)	40.4 (2,668)	36.7 (2,525)	36.7 (2,316)
Higher (%), n	36.9 (8,413)	21.6 (655)	35.3 (2,332)	42.1 (2,898)	40.1 (2,528)
Current smoking, (%), n	20.6 (4,695)	30.3 (1,192)	21.5 (1,349)	17.8 (1,112)	16.4 (1,057)
Alcohol use, (gr/day)	6.9 (2.7-15.5)	6.6 (2.2-15.8)	6.8 (2.7-14.9)	6.9 (3.1-15.6)	7.6 (2.8-15.8)
Lifelines Diet score	22.7 ± 5.63	21.3 ± 5.56	22.5 ± 5.48	23.3 ± 5.59	23.5 ± 5.67
Energy intake (kcal/day)	2406.7±621.1	2426.7±641.0	2405.9±610.4	2363.7±595.6	2443.1±644.9
Body weight (kg)	84.7 ± 9.95	85.1 ± 10.3	85.0 ± 9.93	84.8 ± 9.85	84.2 ± 9.89
BMI (kg/m ²)	25.2 ± 2.5	25.6 ± 2.5	25.3 ± 2.5	25.2 ± 2.4	25.1 ± 2.4
Waist circumference (cm)	92.2 ± 8.2	94.0± 8.2	92.9 ± 8.1	92.0 ± 8.0	90.7± 8.1
Systolic BP (mmHg)	129.0 ± 13.2	130.1 ± 13.3	129.2 ± 13.2	128.6 ± 12.9	128.5 ± 13.3
Diastolic BP (mm Hg)	76.0 ± 9.1	77.1 ± 9.0	76.3 ± 9.1	75.9 ± 9.0	75.5 ± 9.2
Total cholesterol (mmol/L)	5.18 ± 0.98	5.27 ± 0.99	5.20 ± 0.98	5.15 ± 0.96	5.14 ± 0.98
HDL-cholesterol	1.35 ± 0.31	1.28 ± 0.31	1.32 ± 0.30	1.36 ± 0.31	1.41 ± 0.33
Triglycerides (mmol/L)	1.09 (0.8-1.5)	1.21 (0.86-1.8)	1.14 (0.82-1.6)	1.08 (0.8-1.5)	1.02 (0.8-1.4)
Plasma glucose (mmol/L)	5.01 ± 0.46	5.08 ± 0.46	5.03 ± 0.46	5.01 ± 0.46	4.98 ± 0.45
Women					
MVPA min/week	279.4 ± 1.7*	0	3-150	151-330	331-3440
Number (%)	29,671 (56.5)	2599 (8.8)	9200 (31.0)	8979 (30.3)	8893 (30.0)
Age (years)	45 (38-52)	45 (38-50)	44 (37-50)	45 (38-52)	47 (39-57)
Education:					
Lower (%), n	26.7 (7,924)	33.3 (865)	25.1 (2,308)	24.5 (2,203)	28.7 (2,548)
Middle (%), n	46.1 (12,333)	41.4 (1,076)	42.6 (3,918)	41.3 (3,711)	40.8 (3,628)
Higher (%), n	31.7 (9,414)	25.3 (658)	32.3 (2,974)	34.1 (3,065)	30.6 (2,717)
Current smoking, (%), n	17.5 (5,206)	29.8 (1,132)	19.0 (1,672)	15.0 (1,410)	13.0 (1,008)
Alcohol use, (gr/day)	2.9 (0.7-7.2)	2.5 (0.3-7.1)	2.7 (0.6-6.9)	3.1 (0.8-7.2)	3.4 (0.8-8.8)
Lifelines Diet score	25.4 ± 6.00	23.6 ± 6.07	24.7 ± 5.84	25.7 ± 5.83	26.5 ± 6.11
Energy intake (kcal/day)	1861.6±456.2	1796.7±461.0	1873.1±451.1	1863.4±443.9	1867.0±470.0
Body weight (kg)	69.8 ± 8.96	70.1 ± 9.30	70.2 ± 9.14	69.7 ± 8.85	69.3 ± 8.69
BMI (kg/m ²)	24.2 ± 2.8	24.5 ± 2.8	24.3 ± 2.8	24.2 ± 2.7	24.0 ± 2.7
Waist circumference (cm)	83.1 ± 8.8	84.5 ± 9.0	83.7 ± 8.9	83.0 ± 8.8	82.2 ± 8.6
Systolic BP (mmHg)	120.7 ± 14.6	122.3 ± 14.9	120.2 ± 14.2	120.5 ± 14.7	120.9 ± 14.8
Diastolic BP (mm Hg)	71.4 ± 8.6	72.3 ± 9.0	71.2 ± 8.5	71.4 ± 8.6	71.3 ± 8.7
Total cholesterol (mmol/L)	5.08 ± 0.99	5.09 ± 0.97	5.01 ± 0.98	5.08 ± 0.98	5.16 ± 1.03
HDL-cholesterol	1.68 ± 0.39	1.62 ± 0.39	1.64 ± 0.38	1.69 ± 0.38	1.74 ± 0.41
Triglycerides (mmol/L)	0.83 (0.6-1.1)	0.89 (0.67-1.2)	0.84 (0.63-1.1)	0.82 (0.6-1.1)	0.81 (0.6-1.1)
Plasma glucose (mmol/L)	4.76 ± 0.44	4.77 ± 0.43	4.75 ± 0.43	4.76 ± 0.44	4.76 ± 0.45

Data are presented as mean ± SD or median (25th to 75th percentile) and number (percentages, %). Abbreviations: BMI=body mass index, BP=blood pressure, HDL-C=high-density lipoprotein cholesterol, HbA1c=hemoglobin-A1c, MVPA=moderate-to-vigorous physical activity, VPA=vigorous physical activity, T=tertile.

*age- and education- adjusted mean ± standardized error.

After 4 years, the body weights of male and female participants had increased on average by 0.13 ± 0.03 kg and 0.45 ± 0.03 kg, respectively. Changes in body weight, estimated with an age- and education-adjusted ANOVA and visualized according to PA levels, were significantly higher in inactive women

belonging to the No-MVPA, and No-VPA categories compared with these changes in groups with higher MVPA and VPA. It was observed in men only for the association between VPA and changes in body weight estimated with an age- and education-adjusted ANOVA (**Figure 1**). On average, all groups of the female participants gained body weight, but this increase in body weight was attenuated with increasing MVPA and VPA levels (T1–T3). Increases in the body weights of participants, stratified by age, were mostly observed in younger men (18–35 years) and young and middle-aged women (18–54 years) (**Figure S3**). **Figure S4** sheds light on whether these changes may have been more or less related to body fat or lean mass through its depiction of changes in body weight and creatinine excretion. Taking PA levels into consideration, the results of our analysis indicated that very active young men demonstrated lower levels of change in their body weights but higher levels of change in their creatinine excretion compared with the inactive group. To incorporate this finding within subsequent regression analyses, we adjusted for changes in creatinine excretion when considering changes in body weight.

In regression analyses, higher leisure-time MVPA, MPA and VPA were associated with less gain in body weight in women. Beta coefficients (95%CI) for the MVPA>0, MPA>0 and VPA>0 relative to each reference groups (No-MVPA, No-MPA and No-VPA) were, respectively -0.34 (-0.56;-0.13), -0.32 (-0.54;-0.10) and -0.30 (-0.43;-0.18) kg. These associations were dose-dependent when PA was categorized in four groups (**Table 2, Table S3**). The beta-coefficients attenuated by 10-20% but remained significant after adjusting for potential confounders, including muscle mass. An in-depth investigation of the roles of the confounders indicated that the diet-based confounding effect was stronger than the confounding effects of smoking and alcohol consumption (**Table S2**). In men, higher VPA, but not higher MPA or MVPA, was associated with less body weight gain. However, after adjusting for potential confounders, the association was no longer significant (**Table 2, Table S3**).

Table 2. Leisure-time physical activity and 4-year changes in body weight

Physical activity	Unstandardized beta coefficients kg body weight					
	Basic model		Model 1		Model 2	
	B (95%CI)	P-value	B (95%CI)	P-value	B (95%CI)	P-value
Men						
MVPA-T0	0 (Reference)	-	0 (Reference)	-	0 (Reference)	-
MVPA-T1	-0.14 (-0.35; 0.07)	0.19	-0.05 (-0.26; 0.16)	0.61	-0.03 (-0.25; 0.19)	0.78
MVPA-T2	-0.03(-0.24; 0.18)	0.81	0.10 (-0.11; 0.31)	0.35	0.12 (-0.10; 0.33)	0.30
MVPA-T3	0.02 (-0.19; 0.24)	0.82	0.19 (-0.03; 0.40)	0.09	0.20 (-0.02; 0.42)	0.08
VPA-T0	0 (Reference)	-	0 (Reference)	-	0 (Reference)	-
VPA-T1	-0.25 (-0.42; -0.09)	0.03	-0.20 (-0.37;-0.03)	0.02	-0.20 (-0.37;-0.02)	0.03
VPA-T2	-0.19 (-0.38; -0.01)	0.04	-0.11 (-0.30; 0.07)	0.24	-0.09 (-0.28; 0.11)	0.39
VPA-T3	-0.20 (-0.38; -0.02)	0.03	-0.09 (-0.27; 0.09)	0.34	-0.10 (-0.28; 0.09)	0.32
Women						
MVPA-T0	0 (Reference)	-	0 (Reference)	-	0 (Reference)	-
MVPA-T1	-0.32 (-0.55; -0.10)	0.005	-0.24 (-0.47; -0.02)	0.036	-0.25 (-0.48; -0.02)	0.037
MVPA-T2	-0.42 (-0.65; -0.20)	0.000	-0.31 (-0.53; -0.08)	0.008	-0.35 (-0.59; -0.12)	0.003
MVPA-T3	-0.53 (-0.75; -0.30)	0.000	-0.38 (-0.61; -0.16)	0.001	-0.42 (-0.65; -0.18)	0.001
VPA-T0	0 (Reference)	-	0 (Reference)	-	0 (Reference)	-
VPA-T1	-0.27 (-0.44; -0.10)	0.002	-0.22 (-0.39; -0.05)	0.011	-0.24 (-0.42; -0.07)	0.007
VPA-T2	-0.35 (-0.51; -0.18)	0.000	-0.30 (-0.46; -0.13)	0.001	-0.33 (-0.51; -0.16)	0.000
VPA-T3	-0.38 (-0.55; -0.21)	0.000	-0.32 (-0.49; -0.15)	0.000	-0.33 (-0.51; -0.15)	0.000

Regression analysis. Data on MPA is shown in Supplementary material, Table S3. Determinants are dummy exposure variables for physical activities for comparison between the reference group (No-MVPA, and No-VPA, T0) and tertiles of MVPA and VPA (T1-3). Data are expressed as unstandardized beta coefficient with 95% confidence interval (95% CI). MVPA=moderate-to-vigorous physical activity, VPA=vigorous physical activity, MPA=moderate physical activity. T=tertile.

Basic model=age and education.

Model 1 = Basic model + diet, smoking and alcohol use.

Model 2 = Model 1 + 24-hour urinary creatinine excretion.

Stratification of the participants by age revealed significant associations mainly in younger adults (**Figure 2**). For men below 35 years and for women below 55 years, leisure-time VPA was dose-dependently associated with less gain in body weight after fully adjusting for confounding factors.

We conducted additional analyses aimed at elucidating the role of individual daily-life activities within the physical activity domain (**Table S5**). These analyses were performed for men below 35 years and women below 55 of age years because significant associations of LTPA and changes in body weight were observed for individuals in these age groups. Our findings, based on analyses with dichotomized PA (No-MPA and MPA > 0 or No-VPA and VPA > 0) indicated that higher levels of moderate (cycling) and vigorous (cycling and sports) PA were associated with less weight gain in women after fully adjusting for confounding factors. For men, only higher levels of VPA (cycling and sports) were associated with less weight gain (**Table S5**). In further additional analysis, hen occupational MVPA>0 was compared to No-MVPA in occupational activities, showing no clear association between occupational MVPA and changes in body weight. The crude association was significant and positive for men but ceased to be significant after adjusting for age, education, diet, smoking, and alcohol use. In women, the association was positive but non-significant. According to occupational MVPA tertiles, we also did not find a dose-response relationship for occupational PA ($\beta=0.208 [-0.041-0.457]$ for occupational PA tertile-1; $\beta=0.250 [-0.008-0.508]$ for occupational PA tertile-2; $\beta=0.203 [-0.059-0.466]$ for occupational PA tertile-3).

Discussion

In this large-scale, population-based study, a higher leisure-time MVPA was found to be dose-dependently related to less weight gain in women. Moreover, these associations were stronger and independent of other potential confounders in women under the age of 55 years. Furthermore, the potentially favourable effects of PA for women applied to both moderate and vigorous physical activities like cycling and sports. Among male participants, strenuous physical activities, such as vigorous cycling and sports, were predominantly related to lower weight gain but only in younger (< 35 years) men after adjusting for other lifestyle factors. There was no clear association between occupational MVPA and changes in body weight among both men and women.

Several previous prospective studies found an inverse association between PA and changes in body weight.[11][12][13][35][36] However this association has not been confirmed in other studies.[14][15][16]

[17] Moreover, this association was found to be restricted to specific groups in some studies.[18][19] For instance, a large-scale, multi-country EPIC study ($n = 288,498$) found an association between PA and 5-year changes in body weight only in younger women (<50 years) and those of normal weight.[18] In our large-scale, population-based study, the benefits of LTPA differed among men and women relative to the PA intensity level. Moreover, the associations between PA and changes in body weight differed according to the PA domain (non-occupational or occupational), in addition to being age-dependent. These core findings are discussed in more detail below.

Clinical guidelines on PA levels state that physical activities at the moderate-to-vigorous level, but not at the light level, are essential for maintaining a healthy body weight.[37] However, most previous studies focused on total PA, including light PA, and did not test for or report on different PA intensity levels.[14] [15][18][21][19] The few studies that tested intensity levels suggest that physical activities at higher intensity levels are more effective than those at lower intensity levels in weight management.[17][38] For instance, in their study of a 6.2-year prospective follow-up assessment, Williams et al. found that weight loss from running exceeded that from walking.[38] Furthermore, there is some debate about intensity, duration and load. In theory, a longer bout of MPA would lead to the same energy expenditure as a shorter bout of VPA. However, a review study concluded that even if the PA requires the same amount of energy, so same energy expenditure but at moderate or vigorous load, there were different effects, suggesting a greater cardioprotective benefits from VPA than MPA[39]. Furthermore, recent studies have shown that the benefits of vigorous PA are more than moderate PA in relation to cardiometabolic health[40][41]. Of course, in this observational study, we cannot replicate these findings or provide you with explanatory mechanisms. Instead, we study the effects of MPA and VPA in free-living situations, as how they associate with weight gain in daily practice. So, the interpretation is then, that people who practice more VPA, are less prone to gain weight. The value is in quantifying this association, describing relevant gender differences, and attributing this relation to the type of activity in a large population of participants.

A question that we aimed to address in our study was whether a vigorous level of PA better predicts future changes in body weight. This was found to be the case in men (<35 years) for whom only vigorous activities were related to weight changes. However, in women, both moderate (cycling) and vigorous (cycling and sports) activities were related to body weight changes. However, the benefits of total daily-life MVPA were mostly explained by MPA in women. By contrast, only VPA, and not MPA, or a combination of moderate and vigorous PA, was associated with less weight gain in men. The considerably lower changes in the body weights of men compared with those of women during the follow-up assessment may be indicative of a statistical power issue that could partly account for this difference. Another explanation could be that male participants' reporting of VPA was more accurate than their reporting of MPA or other physical activities in the questionnaire.[42] Accordingly, more longitudinal studies are needed to establish the effects of different PA intensities for men to prevent body weight gain. For women, not only VPA but also MPA can be considered as an option for avoiding body weight gain.

Obesity is mainly caused by a long-term energy imbalance, any increase in PA, irrespective of the type of daily-life activities, which can be work-related, may support an active lifestyle. However, along with other

researchers, we found that occupational MVPA has no association with weight gain.[25][26][43][44] Evidently, there is a possibility of (residual) confounding by socio-economic status, type of work, transportation to/from work, or energy intake associated with work-related cultures and habits. In line with the findings of the above-mentioned studies, our results did not change after adjusting for factors relating to diet and socio-economic status. Furthermore, increased muscle mass observed during the follow-up assessment may have occurred because of higher MVPA in the occupational domain. However, the results remained unchanged after we adjusted for changes in creatinine excretion. Nevertheless, it should be noted that some studies have found that occupational PA could be beneficial in the prevention of weight gain.[45][46][47][48][49] Among these studies, only one longitudinal Chinese study tested the association of occupational PA with changes in body weight, reporting an inverse association.[47] However, the definition of occupational PA in this study differed from that used in other studies, as it included a wide range of work-related activities such as unpaid home-based jobs (e.g., working on a farm or vegetable garden). Two more Chinese studies found an inverse association between occupational PA and body weight.[48][49] These inconsistent findings may be partly explained by cultural differences. They indicate a need for future studies to test the effects of specific types of occupational PA on changes in body weight, attending especially to cultural differences within a broader context.

In this study, the association of physical activity with changes in body weight was mainly observed in younger adults. This association may be related to the observation that life-time weight gain mostly occurred during this period (**Figure S3**). In line with our findings, another study found that the transition from normal weight to obesity was mostly observed around the ages of 28–33 and 31–36 years.[36] The findings of this and other studies suggest that a high level of activity during those ages can prevent overweight or obesity.[11][36] This finding raises the question of whether the mechanisms for the prevention of weight gain differ from those for the resolution of overweight requiring weight loss. In this Lifelines study we look at weight gain over time. Now here it seems that physical activity alone, independent of caloric intake, can be related to less weight gain over time. In a sense, this is logical because the increased energy expenditure is avoiding a positive energy balance. The reason we bring this forward is because the usefulness of physical activity alone in body weight control has been doubted. This is based on studies showing that increasing physical activity alone is not effective for weight loss. [10] Thus, we conclude that it may be worthwhile to explore the hypothesis that the process of weight loss is not simply the reverse of the process of weight gain, as with weight loss, there are many hormones counteracting negative energy balance.[50] In the case of prevention of weight gain, these hormones do not play a role, and under these circumstances we believe that physical activity alone can play an important role in the prevention of weight gain and ultimately the prevention of overweight and obesity. In contrast to the aim of achieving weight loss, that is based on negative energy balance, it seems from our results, that physical activity alone can benefit the prevention of weight gain. Thus, more studies should explore the role of increased PA in the prevention of weight gain, rather than focusing on PA as a strategy for reversing overweight and obesity. Furthermore, a number of studies have reported that a very active lifestyle at younger adult ages may entail the benefit of obesity prevention at later ages.[9][12][30] Moreover, a higher BMI in early adult life is a predictor of cardiovascular diseases in later life.[51] Thus, a

conclusion that merits emphasis is that increasing PA at younger ages may be an important primordial obesity prevention strategy while simultaneously preventing non-communicable diseases in later adult life.

It should be noted that our outcome measure focused on changes in overall body weight and not specifically on body fat mass. Changes in body weight, especially in younger adults, could reflect changes in muscle mass. Indeed, in our descriptive analyses, we observed that whereas active younger men evidenced smaller changes in body weight compared with less active younger men, the latter showed greater changes in creatinine excretion compared with the former (**Figure S4**). Consequently, we adjusted for creatinine excretion in all of the analyses. We found that the association between PA and changes in body weight was independent of changes in muscle mass over time. These results are supported by those of previous studies that used direct measures of body composition, indicating smaller changes in body fat in very active younger adults and greater gains in body fat in inactive young adults. [11][52] Although 24-hour urinary creatinine excretion may not be a precise marker for the absolute level of muscle mass, changes in creatinine excretion have been found to be a more sensitive measure for changes in body composition compared with DEXA.[53] Therefore, we concluded that increased PA can be an effective strategy for preventing body weight gain independently of muscle mass.

The main strength of our study is its large sample size obtained from the general population, which enabled us to estimate the dose-dependency of different PA intensities with changes in body weight for sex- and age-differentiated groups with sufficient statistical power. A second strength of the study relates to the objective measurements of body weight that were taken during the baseline and follow-up phases. Although we excluded many participants who are obese or with several diseases it helps to minimize cause-effect bias relating to changes in PA or body weight caused by poor health. However, it also can be a limitation such as reduction of representativity of the population. Another limitation is that PA was reported only at the baseline stage. A few studies have concluded that a single measure of PA weakly predicts future changes in body weight [14][54], which may be related to a bidirectional association of PA and obesity.[17][55] The inclusion of more obese individuals in the analyses could attenuate the association between baseline PA and body weight at the follow-up assessment because obese individuals are mostly inactive while simultaneously making conscious efforts to prevent weight gain through diet. In our study, we included only non-obese individuals with the aim of reducing such information bias. Another limitation relates to our assessment of PA that was based on self-reporting and therefore subject to recall bias. However, the SQUASH questionnaire has been validated within the general population, demonstrating a Spearman correlation coefficient for reproducibility of 0.58.[29] Furthermore, the SQUASH questionnaire was not specifically validated for the different types of leisure time activity. Furthermore, although PA quantification may have been subject to reporting bias, the qualitative information about the types and domain of MVPA proved valuable.

Conclusions

A higher level of leisure-time MVPA is associated with less gain in body weight in women. The potentially favourable effects of MVPA for women applied to both moderate and vigorous physical activities. The associations were found to be dose-dependent, suggesting that more MVPA is more beneficial. Furthermore, the associations were strongest in younger and middle-aged women (<55 years) and were independent of diet, smoking, alcohol use, and 4-year changes in creatinine excretion, considered a marker of muscle mass. For men, only vigorous LTPA was associated with less weight gain in younger adults (<35 years). By contrast, a higher level of occupational MVPA was not conclusively associated with changes in body weight.

Abbreviations

BMI: Body mass index; CI: Confidence interval;

Declarations

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None.

Authors' contributions

All authors drafted the concept and design. OB performed the analysis, and drafted the manuscript. PV prepared the dataset for the current study. EC edited the drafts. PV, DK and GN commented on the drafts. OB and EC produced the final manuscript. All authors approved the final manuscript.

Availability of data and materials

The Lifelines Cohort does not enable public data sharing. The cohort's data is only available to researchers who, upon approval of a submitted research proposal, have signed a Data/Material Transfer Agreement.

Ethics approval and consent to participate

The study was approved by the medical ethical review committee of the University Medical Center Groningen, the Netherlands. All participants provided their written informed consent.

Consent for publication

Not applicable

Competing interests

The authors declare no conflict of interest.

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Figures

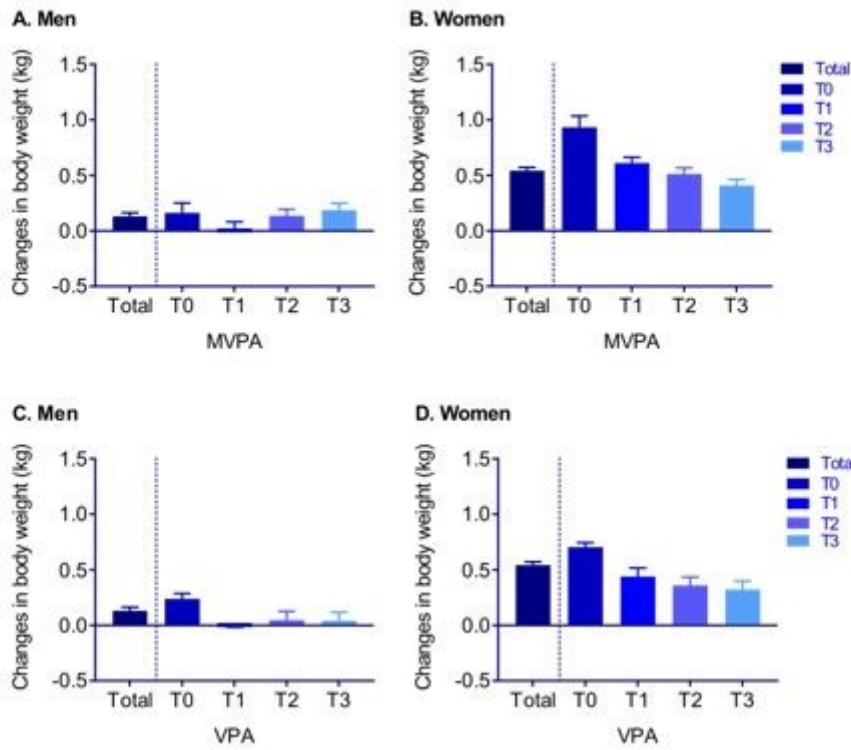


Figure 1

Estimated changes in body weight (kg) adjusted for age and education level, stratified by levels of moderate-to-vigorous (A and B) and vigorous (C and D) physical activity. Measured body weight change adjusted with ANOVA. MVPA=moderate-to-vigorous physical activity, VPA=vigorous physical activity, T=tertile. Non-occupational MVPA and VPA were used in the analysis.

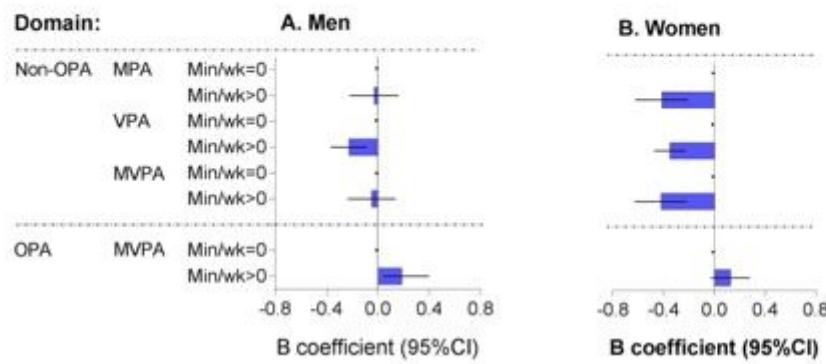


Figure 2

Domain- and intensity-specific associations of physical activity and 4-year changes in body weight.

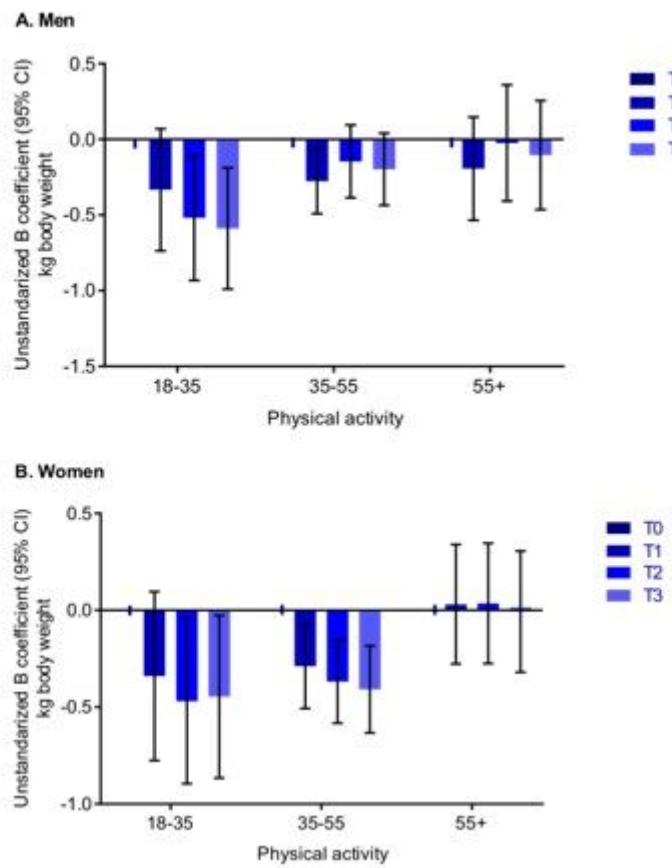


Figure 3

Association between vigorous physical activity and changes in body weight, stratified by age in men (A) and women (B). Regression analysis. Data are expressed as unstandardized beta coefficient (presented as bar) with 95% confidence interval (95% CI, presented as arrow). Physical activity was shown as vigorous physical activity categories (T0-T3). T=tertile. Analysis was adjusted for age, education, diet score, energy intake, smoking and alcohol use.

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