Multimorbidity and Leisure-Time Physical Activity Over The Life Course: A Population-Based Birth Cohort Study.

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Abstract

Background: We aimed to test which life course model best described the association between leisure-time physical activity (LTPA) and multimorbidity at age 55. We analyzed data from birth to age 55 using the database from the 1958 National Child Development Survey.

Methods: Multimorbidity was considered as the presence of more than one chronic condition. LTPA was measured through questionnaires from 1965 (age 7) to 2013 (age 55), which were applied in eight different occasions. We compared the fit of a series of nested adjusted logistic regression models (representing either the critical, accumulation or sensitive period models) with a fully saturated model. Data were reported as odds ratio (OR) and 95% confidence interval (CI).

Results: From the initial sample of 17,415 cohort members, 9,134 were interviewed in the latest sweep (49.2%). Men were more physically active than women at ages 11, 16, and 23 ($p<0.001$). LTPA every day in the week was more frequent in women than men in ages 33, 42, and 50 ($p<0.001$). The sensitive analysis revealed that LTPA during adolescence (OR: 0.72; 95% CI: 0.57, 0.92) and late adult life (OR: 0.71; 95%CI: 0.55, 0.91) have a stronger effect on the risk for multimorbidity at age 55 considering all other life stages in the model. Also, adolescence showed a critical independent effect on the risk for multimorbidity (OR: 0.74; 95%CI: 0.59, 0.92). No difference was found between those models.

Conclusions: These data support the notion of a protective physical activity “legacy” at early ages of childhood against multimorbidity at older ages. We highlight the need for LTPA promotion through intervention tailored especially on schooling and older ages in order to reduce the burden of multimorbidity.

Introduction

Multimorbidity, defined as the co-occurrence of two or more chronic conditions in the same individual[1], affects adults from all age groups, and its burden increases with aging[2]. It is associated with diminished quality of life of both individuals and their families[3]. Likewise, multimorbidity has been shown to a higher frequency of hospitalizations[4, 5], which are usually followed by decreased functional capacity, cognitive function, and increased use of prescribed medications[6]. One important clinical aspect of multimorbidity is its multifactorial nature. The chronic conditions that are affecting the same individual simultaneously are related to an impairment on different organic systems, which may lead to higher risk of disability and mortality[7–9]. Also, the burden of multimorbidity for the patient is increased when primary care systems fail to appropriately address the needs of these patients[9, 10].

Moreover, multimorbidity has increased the risk of all-cause mortality in a dose-response effect[11] regardless of age, gender, and economic stratus[12]. Therefore, investigations about how lifestyle factors through life course could be associated with multimorbidity in older ages should be encouraged. Physical activity should be considered an alternative that deserves attention and investment, given its benefits on prevention and treatment of several noncommunicable chronic diseases[13].

It is understood that leisure-time physical activity (LTPA) in older age could promote healthy ageing[14]. Nevertheless, it is unknown how LTPA in early ages could prevent multimorbidity in later life stages. Also, determine how many physically active life stages are necessary in order to prevent multimorbidity in older ages, are still undefined in literature. Our hypothesis is that people who were physically active in early life stages would have lower risk for multimorbidity than those with low physical activity practice.

Thus, the present study aimed to assess whether there is an association of LTPA at different stages of life with multimorbidity at age 55 and evaluate its cumulative effect during the early life stages on multimorbidity in middle-to-older adults.

Methods

Study design

We analyzed data from the 1958 National Child Development Survey (NCDS). The dataset is freely available upon request at the UK Data Service[15] (https://www.ukdataservice.ac.uk/deposit-data/). Full description of sampling design and methods can be found elsewhere[16]. Briefly, this birth cohort collected data from approximately 94% (N=17,415) of all births between 3rd and 9th March 1958 in England, Wale, and Scotland. Sociodemographic and behavioral information from both parents besides data regarding to pregnancy and the child were assessed. Further, any child born in the Great Britain in that specific week were identified by school registers and added to cohort sample during second through fourth sweeps (1965, 1969, and 1974). Flow diagram about sample composition is shown in Figure S1 (supplementary material).

Fifty-five years after baseline assessments, this cohort remains largely representative of the sample that it was drawn. In the latest sweep (2013) 9,137 participants were interviewed and cumulative deaths through cohort summed 1,548 (response rate: 61.3%) [16]. After baseline measurements, new sweeps occurred in 1965 (cohort age: 7 years), 1969 (11 years), 1974 (16 years), 1981 (23 years), 1991 (33 years), 2000 (42 years), 2002 (44 years), 2004 (46 years), 2008 (50 years), and the latest in 2013 (55 years). The 2002 and 2004 sweeps were not included in the present analysis due to methodological distinctions compared to the others (i.e. self-reported and telephone-based interview, respectively). The next sweep was programed to occur in 2020 and 2021; however, fieldwork was paused in light of COVID-19.

Outcome

We considered multimorbidity as the co-occurrence of more than one of the following morbidities at age 55: obesity, hypertension, diabetes, depression, asthma, cancer, visual and hearing impairment. Then, based on this classification, a dichotomic variable was created.

Exposure

LTPA was assessed from 1965 to 2013. Data collected in 2002 (age 44 sweep) and 2004 (age 46 sweep) regarding to LTPA were not used in this study because they were assessed by different interview methods (self-reported and telephone-based interview, respectively), which may decrease significantly both reliability and comparability of measurements[17]. All included LTPA data were assessed by face-to-face interview-administered paper-based questionnaire. Table S1 (electronic supplemental material) describes how it was measured in each sweep and how we operationalized it for this study. Briefly, participants were classified as physically active when performed physical activity regularly (age 7, 11, and 16) and at least once per week (from age 23 to the latest), as in previous work[18].

Confounding variables

All multivariate analyses were adjusted for the following variables: gender, marital status, education level, income, country of birth, ethnicity, body mass index (BMI), smoking, alcohol intake, hours of sleep, and LTPA. We considered sex, country of birth, and ethnicity collected at birth sweep. We used LTPA as a possible confounder in analysis where the main exposure was a time-specific sweep and it was adjusted for previous and future LTPA practice. All remaining used variables were assessed in the latest sweep (2013).

Statistical analysis

Descriptive analysis is reported as absolute and relative frequencies. Difference between groups was verified using chi-square tests. To evaluate the PA effect during earlier life, we stratified the variable in childhood (age 7 and 11 sweeps), teenage (age 16 sweep), young (age 23 sweep), middle (age 33 sweep), and middle-to-old age (age 50 and 55 sweeps) adults.

Logistic regression was performed as crude analysis (model 1) and using hierarchical model adjusting for gender, marital status, education level, income, country of birth, ethnicity (model 2), as well as BMI, smoking, alcohol intake, and hours of sleep. For regression analyses, PA was categorized as reported in Table S1: inactive and active.

Then, a structured modeling approach developed by Mishra et al.[19] was used to select the most appropriate life course model for multimorbidity at age 55. Four different hypothesized life course model were examined: saturated, critical, sensitive, and accumulation. Saturated model included all possible exposure combinations and interactions and describes all possible trajectories of LTPA throughout life course (childhood, teenage, young, middle, and middle-to-older adults).

Accumulation model was tested in two versions. First, a strict model (continuous) was assessed by adding the number of times an individual reported being physically active across their life course to form an overall score, which was then used as the exposure. This model assumes that the effect of physical activity at each period is the same. Second, a relaxed model (categorical) was examined in which all time periods are contributing to multimorbidity at age 55 but not necessarily in an equal way.

Critical period model assumes that only physical activity in a certain age influences multimorbidity at age 55 regardless of any other time period. Similarly, sensitive model was tested to allow the examination of the varied effect of LTPA across the life course, which can be modelled by simultaneously including all physical activity variables in the model. Finally, a null model was tested with only our outcome at the model[19].

To identify the most appropriate life course model to explain multimorbidity at age 55, likelihood ratio test was conducted comparing each life course model to the saturated model. When nested life course models (critical period, sensitive period, and accumulation) provided similar fit to the fully saturated model ($p>0.05$), the one with the lowest Akaike's information criterion (AIC) was selected. When more than one model presented p-value higher than 0.05 and there is not a large difference in p-values, the simpler model was selected[19].

To minimize data loss, missing data were imputed using multiple imputation chained equations as recommended by the NCDS user guide[20]. We ran imputation models with all variables from our logistic models across 20 imputed datasets. When imputed results were similar to those obtained using observed values, the latest was presented. All statistical analyzes were carried out using STATA 13.1 software[21]. A p value of <0.05 was accepted as statistically significant.

Results

From the initial sample of 17,415 cohort members, 9,137 (49.2%) were interviewed in the latest sweep. Most individuals were born in England (83.5%), female (51.5%), and white (97.8%) (Table 1). At age 55, 27.4% had at least a university or equivalent degree, while 69.9% were married or lived with a partner. Although more men were overweight or obese (71.3%; $p < 0.001$), alcohol intake were higher among women ($p < 0.001$).

Table 1
Sociodemographic, behavioral, and clinical characteristics of the sample. N = 9,137. United Kingdom, 2013.

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
Sample, N				-
0	17,415 (100.0)	9,004 (52.5)	8,410 (47.5)	
7yr	15,425 (92.3)	7,915 (51.3)	7,506 (48.7)	
11yr	15,333 (91.6)	7,894 (51.4)	7,449 (48.6)	
16yr	14,650 (86.8)	7,544 (51.5)	7,106 (48.5)	
23yr	12,533 (75.3)	6,264 (50.0)	6,269 (50,0)	
33yr	11,465 (70.9)	5,632 (49.1)	5,833 (50.9)	
42yr	11,416 (71.0)	5,624 (49.3)	5,792 (50.7)	
50yr	9,787 (61.9)	4,819 (49.2)	4,968 (50.8)	
55yr	9,137 (58.5)	4,433 (48.5)	4,704 (51.5)	
Country of Birth				0.771
England	7,625 (83.5)	3,695 (83.4)	3,930 (83.6)	
Wales	482 (5.3)	236 (5.3)	246 (5.2)	
Scotland	826 (9.0)	396 (8.9)	430 (9.1)	
Not in Great Britain	204 (2.2)	106 (2.4)	98 (2.1)	
Ethnicity, %				**0.010**
White	8,948 (97.9)	4,344 (98.0)	4,604 (97.9)	
Mixed	27 (0.3)	11 (0.2)	16 (0.3)	

* At age 55. BMI: Body mass index; Numbers in bold indicates statistical significance ($p < 0.05$).

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
Indian	33 (0.4)	11 (0.2)	22 (0.5)	
Pakistani/Bangladeshi	12 (0.1)	10 (0.3)	2 (0.1)	
Black	54 (0.6)	20 (0.5)	34 (0.7)	
Other	63 (0.7)	37 (0.8)	26 (0.5)	
Educational level*, %				**< 0.001**
No academic qualification	1,478 (16.5)	798 (18.4)	680 (14.7)	
CSE 2–5 or equivalent	1,285 (14.3)	668 (15.4)	617 (13.4)	
O Level or equivalent	3,021 (33.8)	1,373 (31.6)	1,648 (35.7)	
A level or equivalent	789 (8.8)	382 (8.8)	407 (8.8)	
University degree or equivalent	1,998 (22.3)	910 (21.0)	1,088 (23.6)	
Higher degree	381 (4.3)	207 (4.8)	174 (3.8)	
Marital status*, %				**< 0.001**
Married/living with partner	6,549 (71.7)	3.260 (73.6)	3.289 (69.9)	
Widowed	214 (2.3)	51 (1.2)	163 (3.5)	
Divorced/separated	1,459 (16.0)	619 (14.0)	840 (17.9)	
Single	908 (10.0)	498 (11.2)	410 (8.7)	
Income* (£$), %				**< 0.001**
1st quintile (poorest)	1,293 (20.0)	680 (20.3)	613 (19.7)	
2nd quintile	1,317 (20.4)	555 (16.6)	762 (24.5)	
3rd quintile	1,338 (20.7)	655 (19.5)	683 (22.0)	
4th quintile	1,226 (19.0)	699 (20.9)	527 (16.9)	
5th quintile (wealthiest)	1,287 (19.9)	761 (22.7)	526 (16.9)	

* At age 55. BMI: Body mass index; Numbers in bold indicates statistical significance ($p < 0.05$).

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
BMI*, %				**< 0.001**
Normal	3,041 (35.9)	1.212 (28.7)	1.829 (42.9)	
Overweight	3,438 (40.5)	1.985 (47.1)	1.453 (34.1)	
Obese	2,004 (23.6)	1.022 (24.2)	982 (23.0)	
Number of units of alcohol in last 7 days*, %				**< 0.001**
1	1,633 (18.1)	970 (22.2)	663 (14.3)	
2	2,806 (31.1)	1,495 (34.2)	1,311 (28.2)	
3	1,372 (15.2)	705 (16.1)	667 (14.3)	
4–6	2,411 (26.7)	918 (21.0)	1.493 (32.1)	
7–8	800 (8.9)	282 (6.5)	518 (11.1)	
Smoking*, %				0.071
Smoke cigarettes every day	1,256 (13.9)	607 (13.9)	649 (14.0)	
Smokes occasionally/not everyday	297 (3.3)	141 (3.2)	156 (3.3)	
Ex-smoker	2,879 (31.9)	1.451 (33.2)	1.428 (30.7)	
Never smoked cigarettes	4,590 (50.9)	2.170 (49.7)	2.420 (52.0)	
General health perception*				0.071
Excellent	1,217 (13.5)	599 (13.7)	618 (13.3)	
Very good	3,095 (34.2)	1,531 (35.0)	1,564 (33.5)	
Good	2,915 (32.3)	1,410 (32.2)	1,505 (32.3)	
Fair	1,266 (14.0)	605 (13.8)	661 (14.2)	

* At age 55. BMI: Body mass index; Numbers in bold indicates statistical significance ($p < 0.05$).

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
Poor	546 (6.0)	234 (5.3)	312 (6.7)	
* At age 55. BMI: Body mass index; Numbers in bold indicates statistical significance ($p < 0.05$).				

Our analysis did not detect difference in LTPA between gender ($p = 0.087$), however, men reported higher work-related physical activity than women ($p < 0.001$). In addition, 80% of sample self-rated their health as good to excellent with no detectable difference between gender ($p = 0.071$).

Men were more physically active than women in age 11, 16, and 23 ($p < 0.001$; Table 2). The proportion of women who engage in in PA all days in the week was higher in age 33, 42, and 50. ($p < 0.001$).

Table 2
Leisure-time physical activity practice from age 7 to 55 among adults aged 55 years. N = 9,137. United Kingdom, 2008.

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
Childhood (7 year)	N = 8,010 (87.7)			0.247
Inactive	321 (4.0)	148 (3.8)	173 (4.2)	
Normally active	6,613 (82.6)	3,187 (82.2)	3,426 (82.9)	
Over active	1,076 (13.4)	544 (14.0)	532 (12.9)	
Childhood (11 year)	N = 7,715 (84.4)			**< 0.001**
Hardly ever	866 (11.2)	332 (8.9)	534 (13.4)	
Sometimes	3,332 (43.2)	1,381 (37.0)	1,951 (49.0)	
Most days	3,517 (45.6)	2,017 (54.1)	1,500 (37.6)	
Teenager (16 year)				
Outdoor activities	N = 6,739 (73.7)			**< 0.001**
No chance/Hardly ever	1,795 (26.6)	460 (14.0)	1,335 (38.6)	
Sometimes	2,431 (36.1)	1,061 (32.4)	1,370 (39.6)	
Often	2,513 (37.3)	1,757 (53.6)	756 (21.8)	
Indoor activities	N = 6,618 (72.4)			**< 0.001**
No chance/Hardly ever	2,821 (42.6)	1,150 (36.1)	1,671 (48.6)	
Sometimes	2,136 (32.3)	1,052 (33.1)	1,084 (31.6)	
Often	1,661 (25.1)	979 (30.8)	682 (19.8)	
Adult				
Young (23 year)	N = 7,807 (85.4)			**< 0.001**
No sport last 4 weeks	3,919 (50.2)	1,439 (38.4)	2,480 (61.1)	
Once last 4 weeks	529 (6.8)	272 (7.3)	257 (6.3)	
2–3 times last 4 weeks	764 (9.8)	410 (10.9)	354 (8.7)	
1–2 times a week	1,495 (19.1)	833 (22.2)	662 (16.3)	
3–4 times per week	607 (7.8)	442 (11.8)	165 (4.1)	

Numbers in bold indicates statistical significance ($p < 0.05$).

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
5 or more times per week	493 (6.3)	352 (9.4)	141 (3.5)	
Young (33 year)	N = 7,918 (86.7)			**< 0.001**
No exercise	1,648 (20.8)	764 (20.3)	884 (21.3)	
Less often	227 (2.9)	122 (3.2)	105 (2.5)	
2–3 times a month	508 (6.4)	261 (6.9)	247 (6.0)	
once a week	1,808 (22.8)	824 (21.8)	984 (23.7)	
2–3 days a week	1,752 (22.1)	915 (24.3)	837 (20.2)	
4–5 days a week	519 (6.6)	298 (7.9)	221 (5.4)	
Every day	1,456 (18.4)	589 (15.6)	867 (20.9)	
Middle (42 year)	N = 8,433 (92.3)			**< 0.001**
No exercise	2,058 (24.4)	914 (22.6)	1,144 (26.1)	
Less often	210 (2.5)	102 (2.5)	108 (2.5)	
2–3 times a month	536 (6.4)	304 (7.5)	232 (5.3)	
Once a week	1,587 (18.8)	832 (20.6)	755 (17.2)	
2–3 days a week	1,847 (21.9)	904 (22.3)	943 (21.5)	
4–5 days a week	805 (9.5)	407 (10.1)	398 (9.0)	
Every day	1,390 (16.5)	581 (14.4)	809 (18.4)	
Older (50 year)	N = 8,362 (91.5)			**< 0.001**
None	1,849 (22.1)	858 (21.1)	991 (23.1)	
3 times per month or less	633 (7.5)	328 (8.1)	305 (7.1)	
Once a week	1,269 (15.2)	678 (16.7)	591 (13.7)	
2–3 days a week	1,899 (22.7)	981 (24.2)	918 (21.3)	
4–5 days a week	900 (10.8)	430 (10.6)	470 (10.9)	
Every day	1,812 (21.7)	786 (19.3)	1,026 (23.9)	
Older (55 year)	N = 9011 (98.6)			0.087

Numbers in bold indicates statistical significance ($p < 0.05$).

	Total, n (%)	Sex, n (%)		p value
		Male	Female	
Never	943 (10.5)	452 (10.4)	491 (10.6)	
Less than once per month	1,111 (12.3)	570 (13.1)	541 (11.6)	
At least once per month	1,227 (13.6)	565 (12.9)	662 (14.2)	
At least once per week	5,730 (63.6)	2,776 (63.6)	2,954 (63.6)	
Numbers in bold indicates statistical significance ($p < 0.05$).				

Table 3 exhibits results from log-likelihood ratio test to examine which life course model best described the association between LTPA through life course and multimorbidity. We compared the fit of a series of nested logistic models (critical, accumulation or sensitive period models) with a fully saturated model. Accumulation models and critical periods of LTPA during childhood and adulthood provided an inferior fit compared to saturated model ($p < 0.001$). However, critical period model for physical activity during adolescence provided adequate fit of data ($p > 0.99$). Also, sensitive model provided a fit not worse than saturated model ($p > 0.99$) with no clear difference between critical period in adolescence and sensitive model based on p-value, log-likelihood, and AIC.

Table 3
Likelihood-ratio test to estimate the best model of physical activity throughout life course and the risk of multimorbidity at age 55. National Child Development Study. United Kingdom (1958–2008). N = 8435.

	LL	AIC	p-value [a]
No effect	-4,909.4	9,820.7	< 0.001
Critical period			
Childhood	-1,331.8	2,711.6	< 0.001
Adolescence	**-1,018,9**	**2,093.8**	**> 0.99**
Young-adult	-1,453.9	2,957.8	< 0.001
Middle-aged adults	-1,466.5	2,981.0	< 0.001
Middle-to-older adults	-1,462.8	2,971.7	< 0.001
Accumulation			
Categorical	-1,108.8	2.257.6	> 0.99
Continuous	-1,110.0	2.252.0	> 0.99
Sensitive period	**-1,018.9**	**2.093.8**	**> 0.99**
Saturated model	-1,169.2	2,429.2	[b]

LL: log-likelihood; AIC Akaike information criterion.

[a] Compared to saturated model (all possible exposure combinations and interactions describes all possible trajectories of physical activity throughout life course);

[b] p value not applicable.

As shown in Table 4, LTPA during adolescence was associated with lower odds for multimorbidity at age 55 (OR: 0.74; 95%CI: 0.59; 0.92) independently of LTPA performed in other stages of life. Besides a slightly higher protective effect of LTPA in adolescence from the sensitive model (OR: 0.72; 95CI: 0.57; 0.92), being physically active at late adult life (ages 50 and 55) also promoted a protective effect against multimorbidity (OR:0.71; 95%CI: 0.55; 0.91).

Table 4
Odds ratio and 95% confidence interval (CI) for multimorbidity at age 55 by different life course models.

	Model 1			Model 2			Model 3		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Saturation model									
0,0,0,0,0	1.58	0.40; 6.18	0.510	1.69	0.38; 7.60	0.493	0.86	0.15; 4.97	0.868
0,0,0,1,0	5.53	0.92; 33.39	0.062	4.72	0.75; 29.69	0.098	5.83	0.95; 35.63	0.056
0,0,1,0,0	7.38	0.66; 81.90	0.104						
0,0,1,0,1	1.23	0.25; 6.15	0.801	1.79	0.35; 9.03	0.482	2.47	0.54; 11.37	0.244
0,0,1,1,0	1.48	0.28; 7.67	0.643	0.89	0.13; 6.17	0.909	0.49	0.09; 2.74	0.420
0,0,1,1,1	1.64	0.70; 3.84	0.254	2.05	0.78; 5.42	0.147	2.61	0.87; 7.79	0.086
0,1,1,0,0	1.85	0.17; 2.48	0.618						
0,1,1,0,1	3.69	0.74; 18.45	0.112	6.64	1.31; 33.69	**0.022**	8.35	1.61; 43.16	**0.011**
0,1,1,1,1	0.79	0.22; 2.78	0.715	0.65	0.14; 3.06	0.591	0.77	0.24; 2.49	0.669
1,0,0,0,0	2.55	1.74; 3.73	**< 0.001**	2.27	1.46; 3.53	**< 0.001**	1.73	1.05; 2.85	**0.033**
1,0,0,0,1	1.45	0.96; 2.20	0.079	1.77	1.11; 2.84	**0.017**	1.97	1.17; 3.31	**0.010**
1,0,0,1,0	2.41	1.50; 3.88	**< 0.001**	2.33	1.33; 4.08	**0.003**	2.08	1.04; 4.18	**0.039**

Numbers in bold indicates statistical significance ($p < 0.05$).

Each number position (“0” for inactive or “1” for active) for the saturation model represents, respectively, 5 lifetime stages: childhood, teenage, and young, middle, and middle-to-older adults

Model 1: Unadjusted

Model 2: Adjusted for sex, education, income, marital status, country of birth, ethnicity.

Model 3: Model 2 + body mass index, smoking, alcohol, and hours of sleep at age 50.

	Model 1			Model 2			Model 3		
1,0,0,1,1	1.29	0.87; 1.92	0.201	1.34	0.84; 2.13	0.213	1.05	0.61; 1.82	0.861
1,0,1,0,0	1.53	1.05; 2.24	**0.027**	1.77	1.12; 2.78	**0.014**	1.24	0.73; 2.13	0.429
1,0,1,0,1	0.96	0.67; 1.38	0.817	1.05	0.68; 1.62	0.819	1.25	0.79; 1.98	0.333
1,0,1,1,0	1.76	1.24; 2.50	**0.002**	2.22	1.47; 3.37	**< 0.001**	2.22	1.41; 3.50	**0.001**
1,0,1,1,1	1.14	0.90; 1.45	0.266	1.19	0.90; 1.59	0.220	1.20	0.87; 1.65	0.258
1,1,0,0,0	2.29	1.33; 3.96	**0.003**	1.49	0.75; 2.93	0.250	1.34	0.61; 2.95	0.473
1,1,0,0,1	1.53	0.85; 2.76	0.158	1.49	0.74; 3.00	0.259	1.12	0.52; 2.42	0.775
1,1,0,1,0	1.85	0.85; 4.01	0.123	4.22	1.66; 10.71	**0.002**	3.30	1.01; 10.74	**0.048**
1,1,0,1,1	0.99	0.57; 1.71	0.975	0.81	0.41; 1.58	0.533	0.74	0.31; 1.78	0.507
1,1,1,0,0	1.98	1.28; 3.07	**0.002**	1.87	1.14; 3.09	**0.014**	1.43	0.74; 2.78	0.292
1,1,1,0,1	0.97	0.66; 1.44	0.888	1.02	0.64; 1.60	0.939	0.81	0.50; 1.31	0.393
1,1,1,1,0	1.23	0.83; 1.83	0.305	1.24	0.79; 1.96	0.352	1.00	0.61; 1.65	0.997
Critical period									
Childhood	0.95	0.85; 1.06	0.329	0.92	0.80; 1.04	0.188	0.89	0.74; 1.07	0.228
Adolescence	0.82	0.73; 0.92	0.001	0.82	0.72; 0.94	0.005	**0.74**	**0.59; 0.92**	**0.004**

Numbers in bold indicates statistical significance ($p < 0.05$).

Each number position (“0” for inactive or “1” for active) for the saturation model represents, respectively, 5 lifetime stages: childhood, teenage, and young, middle, and middle-to-older adults

Model 1: Unadjusted

Model 2: Adjusted for sex, education, income, marital status, country of birth, ethnicity.

Model 3: Model 2 + body mass index, smoking, alcohol, and hours of sleep at age 50.

	Model 1			Model 2			Model 3		
Young-adult	0.70	0.62; 0.79	< 0.001	0.77	0.66; 0.89	0.001	**0.77**	**0.63; 0.94**	**0.013**
Middle-aged adults	0.76	0.68; 0.84	< 0.001	0.87	0.77; 0.98	0.028	0.91	0.75; 1.10	0.309
Middle-to-older adults	0.61	0.54; 0.67	< 0.001	0.67	0.59; 0.75	< 0.001	**0.74**	**0.61; 0.90**	**0.003**
Accumulation									
Categorical									
None	Ref			Ref			Ref		
One	2.05	0.92; 4.59	0.080	1.77	0.72; 4.39	0.215	1.27	0.46; 3.47	0.643
Two	0.75	0.52; 1.09	0.132	0.77	0.50; 1.19	0.247	0.70	0.43; 1.16	0.167
Three	0.66	0.47; 0.94	0.020	0.76	0.51; 1.13	0.177	0.77	0.49; 1.23	0.285
Four	0.54	0.39; 0.76	< 0.001	0.61	0.41; 0.90	0.014	**0.61**	**0.38; 0.95**	**0.030**
Five	0.51	0.36; 0.73	< 0.001	0.51	0.34; 0.78	0.002	**0.48**	**0.30; 0.78**	**0.003**
Continuous	0.84	0.79; 0.90	< 0.001	0.94	0.77; 0.90	< 0.001	0.86	**0.78; 0.94**	**0.001**
Sensitive period									
Childhood	1.00	0.86; 1.17	0.962	0.96	0.80; 1.16	0.683	0.95	0.76; 1.18	0.626
Adolescence	0.89	0.76; 1.05	0.161	0.81	0.67; 0.99	0.041	**0.72**	**0.57; 0.92**	**0.008**
Young-adult	0.77	0.64; 0.93	0.007	0.85	0.68; 1.06	0.140	0.91	0.70; 1.18	0.475

Numbers in bold indicates statistical significance ($p < 0.05$).

Each number position (“0” for inactive or “1” for active) for the saturation model represents, respectively, 5 lifetime stages: childhood, teenage, and young, middle, and middle-to-older adults

Model 1: Unadjusted

Model 2: Adjusted for sex, education, income, marital status, country of birth, ethnicity.

Model 3: Model 2 + body mass index, smoking, alcohol, and hours of sleep at age 50.

	Model 1			Model 2			Model 3		
Middle-aged adults	0.97	0.82; 1.15	0.719	0.98	0.80; 1.20	0.829	0.93	0.73; 1.19	0.581
Middle-to-older adults	0.63	0.53; 0.75	< 0.001	0.62	0.51; 0.76	< 0.001	**0.71**	**0.55; 0.91**	**0.007**
Numbers in bold indicates statistical significance ($p < 0.05$).									
Each number position (“0” for inactive or “1” for active) for the saturation model represents, respectively, 5 lifetime stages: childhood, teenage, and young, middle, and middle-to-older adults									
Model 1: Unadjusted									
Model 2: Adjusted for sex, education, income, marital status, country of birth, ethnicity.									
Model 3: Model 2 + body mass index, smoking, alcohol, and hours of sleep at age 50.									

Discussion

Our findings confirmed our hypothesis that engage in LTPA through life would reduce the risk for multimorbidity in older ages. Both sensitive and critical periods provided the best model to describe the association between LTPA through life course and multimorbidity. We revealed that being physically active at adolescence and late adult life reduced in about 28% and 29% the odds of multimorbidity at age 55, even when controlled for PA at all other analyzed ages. Similarly, engage in LTPA early in life was revealed as a critical period for decreasing the odds of multimorbidity at age 55.

Adolescence is an important life period where healthy lifestyle promotion (e.g. LTPA) could reduce the risk for some conditions such as obesity[22, 23], diabetes[24], and cognitive impairment[25] in older ages. Nevertheless, physical inactivity is predominant among children and adolescents aged between 6 and 15 years[26–28]. This scenario seems to be associated with additional health-related events over the next decades, turning out also to be related to the prevalence of multimorbidity[11]. Given the burden on healthcare systems, that are already poised by elevated prevalence of those conditions[2], it is important to consider physical activity as a continued lifetime strategy for disease prevention instead of a solely rehabilitative method at advanced ages.

In a retrospective study conducted by Fernandes and Zanesco[24], physical activity at childhood (7 to 10 years) and adolescence (11 to 17 years) were related to a decreased risk for arterial hypertension and diabetes in adulthood (18 or more years). In our study, we observed that LTPA at adolescence was associated with odds reduction for multimorbidity at age 55 in all adjusted models. The fact that this association was sustained in model 3 (adjusted for BMI, smoking, alcohol intake, and hours of sleep at late adult life) show the importance of adolescence as a critical period for reducing the risk of multimorbidity in later life. Taken together, these previous findings support the notion of a protective physical activity “legacy” at early ages of childhood against multimorbidity at older ages. As this

population is on school ages, the development of multicomponent school-based interventions promoting healthy lifestyle should be encouraged in order to reduce the likelihood of being affected by multimorbidity[29]. This scenario could also result in an increased quality of life and decreased the burden of multimorbidity in healthcare systems[30, 31].

Physical activity engagement in practice adulthood have been associated with reduced risk for chronic diseases and all-cause mortality[13]. Based on data from the English Longitudinal Study of Aging, Hamer et al.[14] reported that from a sample of older adults aged 50 or more, those who were physically inactive at baseline and became active at older ages had higher odds to have a healthier aging compared to those who remained inactive. Similarly, we reported that LTPA at late adult life (ages 50 and 55) had a significant protective effect against multimorbidity at age 55. Although the World Health Organization[32] recommends 150 minutes per week of moderate-to-vigorous physical activity, some studies have showed that lower levels could led to reduced risk for chronic diseases and all-cause mortality. In this regard, Ekelund et al.[33, 34] revealed that lower doses of moderate-to vigorous physical activity (i.e., 24 minutes per day) could contribute for risk reduction of premature mortality, with a dose-response pattern in adulthood (20 years or more).

Dregan et al [25] reported that LTPA sustained through life periods improved cognitive function in older adults. Another study[14] showed that becoming physically active at age 50 was associated with lower risk for depression symptoms, cognitive impairment, and functional disability at older ages (8-year follow-up). Even though our results corroborate previous findings, cumulative models did not provide a sufficient explanation of the effect of LTPA during life course in multimorbidity. However, we highlight that, whenever feasible, LTPA must be promoted in all age groups especially among those groups with higher prevalence of physical inactivity (children, adolescents, and older adults)[26, 35, 36]. Intervention tailored from those groups are necessary in order to prevent in the future a scenario with even higher prevalence of multimorbidity and its burden on healthcare system[37–40].

Some limitations on this present study must be acknowledged. First, LTPA was measured by questionnaires. In order to reduce the bias from that measurement, we chose to use in our study only those sweeps with face-to-face interview administrated questionnaire. The 1958 National Child Development Survey is one of the oldest national-based cohort study, so although the level of LTPA was not examined by devices-based measurements, the information from those sweeps are reliable, comparable, and relevant. Second, our results must be interpreted with caution, since other important factors through life course may contribute to multimorbidity at the fifth decade of life. Third, although loss to follow-up may be interpreted as a source of selection bias, the NCDS cohort remains largely representative of the sample that it was drawn with a response rate of 61.3%[41]. Furthermore, we used multiple imputation to avoid further reductions in the sample due to missing information[20].

In conclusion, we identified LTPA during adolescence as a critical period associated with reduced risk for multimorbidity at late adult life. Similar protective status was found in sensitive model for PA during the same period and in later stages of life (ages 50 and 55). Although analysis of factors associated with

outcome along lifetime is complex and should be carefully interpreted, our results support the need for LTPA promotion through intervention tailored especially on schooling age and older ages to reduce the burden of multimorbidity.

Abbreviations

LTPA: leisure-time physical activity; NCDS: National Child Development Study.

Declarations

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Authors' contributions: NF, JSL, DU, and AJR conceived the concept and design of the study. NF and JSL wrote the first draft and underwent substantial revision based on the inputs from all other authors. All the authors have read and approved the manuscript.

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Availability of data and materials: The datasets analyzed during the current study are available on registration at the Data Archive at the University of Essex: https://beta.ukdataservice.ac.uk/datacatalogue/studies/study?id=5560

Competing interests: Authors have no competing interest associated with this paper. Daniel Umpierre is on the editorial board of BMC Public Health.

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Ethics approval and consent to participate: Multicentre Research Ethics Committee (MREC) approval was sought for NCDS follow-ups from 2000 on, and for the Biomedical Survey. The 1958 and 1965 follow-ups

pre-dated the establishment of ethics committees; the 1969, 1974, 1981 and 1991 follow-ups came before the establishment of the MREC system. Internal ethical reviews were undertaken for these waves. Participants in later waves were required to sign informed consent, and ethical approval was obtained from South East and London Multicentre Research Ethics Committee. (Shepherd, P.M. An Introduction to the Background to the Study and Methods of Data Collection in The National Child Development Study. Social Statistics Research Unit. London City University 1985). NCDS sought informed parental consent for the 7-year (1965), 11-year (1969) and 16-year (1974) surveys.

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