

**What is the impact of physical activity and physical function on the development of
Multimorbidity in older adults over time? A population based cohort study.**

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Abstract

Background

Multimorbidity is recognised internationally as having a serious impact on health outcomes. It is associated with reduced quality of life, increased healthcare utilisation and future functional decline. Physical activity is associated with good health and psychological well-being. The aim of this study was to identify the impact of physical activity and physical function on the development and worsening of multimorbidity over time.

Methods

Using The Irish Longitudinal Study on Ageing (TILDA), we analysed 4,823 participants ≥ 50 years with and without multimorbidity. Multimorbidity was defined as the presence of ≥ 2 chronic conditions. Development of multimorbidity was measured as the accrual of additional conditions over a two year period. Physical activity and physical function were measured using the International Physical Activity Questionnaire (IPAQ), gait speed (m/sec) and grip strength (kg).

Results

Sixteen groups of chronic conditions were included in analyses. 53.7% of included participants had multimorbidity at baseline and 71.7% at follow up. 638/2092 (30.4%) participants without multimorbidity and 1005/2415 (41.6%) with existing multimorbidity

developed new condition/s. Gait speed (RR=0.67, CI:0.49-0.90), grip strength (RR=0.98, CI:0.97-0.99) and age (compared to 50-59 years, 60-69: RR=1.30, CI:1.11-1.52; ≥ 70 : RR=1.35, CI:1.03 – 1.77) were significantly associated with development of multimorbidity and accrual of additional conditions.

Conclusion

These results show that physical function is associated with the development and worsening of multimorbidity over time. They support the recent National Institute for Health & Care Excellence (NICE) Guidance on multimorbidity that suggests that patients with multimorbidity and reduced gait speed should be identified and targeted for interventions to improve health outcomes.

Keywords: Multiple Chronic Conditions; Gait Speed; Grip strength; Longitudinal Study

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Background

Average life expectancy is rising worldwide with increasing numbers of people living with multiple chronic medical conditions. Multimorbidity, commonly defined as the co-occurrence of two or more chronic medical conditions in an individual [1], affects up to one quarter of primary care populations [2, 3]. Higher prevalence is associated with socioeconomic deprivation and ageing [2]. It is associated with reduced quality of life, increased healthcare utilisation and an increased risk of mental health difficulties [1, 2, 4]. Complex multimorbidity, defined as three or more chronic conditions affecting three or more body systems can be especially challenging with higher healthcare utilization and polypharmacy [5]. Management of multimorbidity is a major challenge for health systems globally. It has been reported that one third of all consultations in general practice in the United Kingdom are for patients with more than one chronic condition [6].

The World Health Organization estimates that approximately 3.2 million deaths each year are attributable to insufficient physical inactivity [7]. Older adults who are more physically active have lower rates of cardiovascular disease, cancer and all-cause mortality along with improved cognition and reduced risk of falling [7]. Physical activity prevents or reduces functional decline [8, 9]. The existing literature examining the association between multimorbidity and physical activity has demonstrated mixed results with two studies findings an association [10, 11] and two reporting no link [12, 13]. However, these studies were all cross-sectional in design and did not assess the trends in multimorbidity over time.

One previous longitudinal study investigated the prevalence of multimorbidity over time by levels of physical activity and identified an inverse dose-response relationship in that the odds of multimorbidity were lower in those who were physically active compared to those who were physically inactive [14]. This study included refreshment samples at different time-points which may have affected estimates and the only outcome measure used was a study specific self-reported measure of physical activity.

Poor physical functioning is also linked to adverse health outcomes [15] and is addressed by the WHO's International Classification of Functioning, Disability and Health (ICF) [16]. Grip strength and gait speed assessments are reliable measures of physical function [17]. Grip strength has been reported to predict accelerated dependency in activities of daily living and cognitive decline in older people [18]. Gait speed has been described as the sixth vital sign and labelled as a principal indicator of health and is an inexpensive, reliable measure of physical function [19].

We previously conducted a systematic review which demonstrated that multimorbidity is associated with poorer function and with future functional decline. The review indicated that there is greater functional decline in patients with higher numbers of conditions and greater disease severity [20]. It is not known whether the effect also occurs in the opposite direction i.e. do poor levels of physical activity and function lead to the development of multimorbidity? Determining the impact of levels of physical activity and physical function on multimorbidity development will inform healthcare providers and aid the design of appropriate interventions that can improve health outcomes and reduce health care costs.

The primary aim of this study was to assess the impact of physical activity and function on the development of multimorbidity over a two year period in an older population without multimorbidity at baseline. Secondary aims were to assess the impact of physical activity and

function on the worsening of multimorbidity over a two year period in a population of older adults with established multimorbidity and in those with complex multimorbidity at baseline.

Methods

Study design

We completed secondary analysis of a longitudinal cohort study. The strengthening the reporting of observational studies in epidemiology (STROBE) guidelines were utilised in the conduct and reporting of this study [21].

Data source and study population

The Irish Longitudinal Study on Ageing (TILDA) is a population based cohort study assessing health, economic and social aspects of ageing in the Republic of Ireland. TILDA is a nationally representative study of 8,175 community-dwelling residents aged 50 years and older [22]. This study is an analysis of the first (2010) and second (2012) waves of TILDA. At Wave 1 participants completed a computer-assisted personal interview in their own home and subsequently were invited to attend a health centre for a comprehensive health assessment. Ethical approval for TILDA was obtained from the Trinity College Dublin Research Ethics Committee.

Included conditions

Thirty individual chronic conditions were included in analyses. The thirty chronic conditions were chosen by TILDA as of their public health significance and their prevalence in those > 50 years [23]. These conditions were consolidated to sixteen chronic conditions or groups of conditions: cardiac conditions; cerebrovascular disease; hypertension; diabetes; high

cholesterol; chronic respiratory disease; liver disease; eye disease; cognitive impairment; arthritis; osteoporosis; cancer; Parkinson's disease; emotional /psychological condition; stomach ulcers; varicose veins (Appendix A).

Multimorbidity was defined as two or more chronic conditions in the one individual. The study participants were grouped into two categories: no multimorbidity (zero or one condition) n=2,235 and established multimorbidity (two or more conditions) n=2,588 at Wave 1. These groups of participants were followed to Wave 2. Development of multimorbidity and worsening of multimorbidity was measured by accrual of new condition/s between Wave 1 and Wave 2. In addition, we completed a sub-group analysis, following participants with complex multimorbidity (≥ 3 chronic conditions) n=2415 at baseline to Wave 2.

Measures of physical activity and function

Levels of physical activity and function were assessed using three validated outcome measures: the International Physical Activity Questionnaire (IPAQ), gait speed and grip strength [22, 24]. The IPAQ is a self-reported measure and gait speed and grip strength are performance-based assessments. Only study participants with complete data recorded on all three measures were included (Figure 1).

Physical activity was measured using the short form of the IPAQ [25]. Each participant was classified as having High, Moderate or Low activity levels based on agreed criteria [26].

Grip strength was measured using a grip dynamometer, two measures of handgrip strength were taken from the dominant hand and the mean of these readings was calculated. Gait speed was measured using the GAITRite portable electronic walkway system [24].

Participants performed two walks at their usual pace along a 4.88m (16ft) walkway. They

started and finished walking 2.5m before and 2m after the walkway to allow for acceleration and deceleration. The two walks were combined and the average gait speed was calculated.

Statistical analysis

A modified Poisson regression analysis with robust error variances was used to determine the relationship between levels of physical activity and function with both the development of multimorbidity and worsening of multimorbidity. Binary outcomes in cohort studies are commonly analysed using a logistic regression model to obtain odds ratios. However, in order to estimate and report relative risks and confidence intervals, we used a modified Poisson regression analysis with robust error variances.

Confounders and covariates

Age and sex were included in the models as covariates. To make analysis comparable to other similar studies age was categorised in ten year age bands; 50-59 years; 60-69 years; ≥ 70 years [2, 13]. Additional confounders included in the analysis were education level, body mass index (BMI) and smoking (smoker, non-smoker). Participants deemed as underweight (0.5%), were merged with the normal category for BMI. The presence of state financial support for healthcare was used as a proxy for socioeconomic status. Measurement for each of the variables has been described previously [22, 24, 26].

Results are presented as adjusted relative risks (RR) with associated 95% confidence intervals (CI). P -values ≤ 0.05 were deemed significant. All analyses were conducted using Stata Version 13.0 (Stata Statistical Software: Release 13. College Station, TX: StataCorpLP).

Results

Characteristics of the sample

Included participants (n=4823) are presented in Figure 1. The characteristics of the study population are displayed in Table 1. At Wave 1, 2235 (46.3%) participants did not have multimorbidity and 2588 (53.7%) had multimorbidity. The two groups were significantly different in all categories at baseline (Table 1). We completed a test of gender interaction and there was no significant difference between male and females and thus no evidence to warrant stratifying the data by gender. Those with multimorbidity were older than those without multimorbidity and the majority in both groups were non-smokers and overweight or obese. The most common conditions in study participants were high cholesterol (41.3%), high blood pressure (33.6%) and arthritis (26.3%), while the prevalence of other conditions such as cardiac conditions, diabetes, respiratory disease, eye disease and osteoporosis varied from 6.1% to 16.7%. These results are in keeping with previous research which demonstrated high blood pressure, arthritis and cardiovascular disease to be the most prevalent conditions in a cohort aged 65 years or older [27].

Development of multimorbidity

Of the 2235 participants with no multimorbidity at baseline, 2092 (93.6%) were followed up two years later. By Wave 2, 638 (30.4%) had developed multimorbidity. Multivariate analysis demonstrated that age (compared to 50-59 years, 60-69 years: RR=1.30, 95% CI: 1.11-1.52; ≥ 70 years: RR=1.35, 95% CI: 1.03 – 1.77), obesity (compared to normal and underweight: RR=1.26, 95% CI: 1.05-1.51), gait speed (RR=0.67, 95% CI: 0.49-0.90) and grip strength (RR=0.98, 95% CI: 0.97-0.99) were significantly associated with the development of multimorbidity. There was no evidence of an association between IPAQ and the development of multimorbidity (Table 2). With every one kilogramme increase in grip

strength, the risk of developing multimorbidity decreases. Similarly, each metre per second increase in gait speed decreases the risk of developing multimorbidity (Table 2).

Worsening of multimorbidity

Of the 2588 participants with multimorbidity at baseline, 2415 (93.3%) were followed up two years later. Of these, 1005 (41.6%) had developed worsened multimorbidity in Wave 2. Age (compared to 50-59 years, 60-69 years: RR=1.20, 95% CI: 1.07-1.34; ≥ 70 years: RR=1.18, 95% CI: 1.01-1.37), access to government funded primary healthcare (RR=1.20, 95% CI: 1.07-1.34), grip strength (RR=0.990, 95% CI: 0.982-0.998), and gait speed (RR=0.61, 95% CI: 0.50-0.82), were all significantly associated with worsening of multimorbidity. For every one kilogramme increase in grip strength the incidence of worsening multimorbidity decreases. For each metre per second increase in gait speed, the risk of worsening multimorbidity also decreases. There was no significant association between the IPAQ and the worsening of multimorbidity (Table 2).

Complex multimorbidity

1488 participants presented with complex multimorbidity at baseline (Appendix B), 1391 of these participants were followed up in Wave 2. 600 of the 1391 participants (43.1%) with complex multimorbidity had developed a new condition/s. Gait speed (RR=0.59; 95% CI: 0.43-0.82), and age (compared to 50-59 years, 60-69 years: RR=1.18, 95% CI: 1.02-1.36; ≥ 70 years: RR=1.20, 95% CI: 1.10-1.44), were significantly associated with the development of new conditions but grip strength was not (Appendix C).

Discussion

This study presents a longitudinal analysis of multimorbidity in a nationally-representative, population based sample of older adults. Over a two year follow up period, 30.4% developed

multimorbidity and 41.6% with multimorbidity experienced worsening multimorbidity. Gait speed, grip strength and increasing age were significantly associated both with the development of multimorbidity and the worsening of existing multimorbidity with evidence of a dose-response relationship.

Grip strength is a predictor of cognitive decline, disability and contributes to increasing dependency in old age [18]. Our study highlighted that the stronger one's grip strength the less likely new chronic conditions will develop within two years. Gait speed assessment is also a valuable tool in the clinical assessment of frailty and lower gait speed is associated with reduced strength, power, coordination and balance [19, 28]. Our results support the recent NICE Multimorbidity Guidance, which recommends using gait speed as an assessment measure to identify those patients who require prioritised/targeted care [29]. NICE is the National Institute for Health Care and Excellence based in the United Kingdom. They provide evidence based national guidance to all stakeholders with the aim to improve health and social care. While our study highlighted the clinical relevance of reduced gait speed, we did not identify a specific cut-point at which the risk of multimorbidity increased. Further research in this area is needed.

Dhalwanai et al. (2016) demonstrated an inverse dose-response association between levels of physical activity and multimorbidity using frequency of vigorous, moderate and mild physical activity [14]. They highlighted the potential that the existence of multimorbidity may limit physical activity, which could also have happened in our cohort. The Dhalwhani study had a similar definition of multimorbidity but only included 16 chronic conditions compared to 30 in our study. In addition the only outcome measure used was a study specific self-report measure which was shown to have moderate correlation with accelerometer data. In our study, there was no evidence that the self-reported outcome measure, the IPAQ, was associated with development or worsening of multimorbidity. It has been acknowledged in

the literature that over-reporting amounts of physical activity when completing the IPAQ is common, with older adults having difficulty completing it accurately [30]. The IPAQ is recommended for population level research, however is not intended to replace instruments which can be more responsive to changes in individual activity level such as gait speed. Comparisons with the previous cross-sectional studies (10, 11, 12, 13) is difficult due to different measures of physical activity, differences in study population and definitions of multimorbidity used. Accelerometer measurements would provide added value, however, gait speed and grip strength assessments are cost-effective and easily accessible measurements used in clinical practice.

In keeping with the evidence that obesity has negative impacts on health outcomes, individuals in our study with obesity were more likely to develop multimorbidity compared to those of normal weight though obesity was not associated with worsening of multimorbidity over time. The results regarding socioeconomic status were mixed. This may relate to the higher prevalence of socioeconomic deprivation in those with established multimorbidity at baseline. These results may also relate to the measure used as it does not identify the most socioeconomically deprived groups within the cohort as income thresholds for access to government funded healthcare increases with age. Existing evidence highlights that, patients with higher levels of socioeconomic deprivation develop multimorbidity significantly earlier in life than their more affluent counterparts [2]. Dhalwanai et al. included socioeconomic status and BMI as confounders but did not comment whether either impacted on the presence of multimorbidity over time [14].

Strengths and Limitations

TILDA is a nationally representative population based cohort study using validated measures and health assessments carried out by trained research nurses using standardised protocols

[24]. We included thirty different conditions in our analysis encompassing a broad range of conditions including mental health conditions which are commonly omitted in other studies.

A potential limitation of this study may relate to participant characteristics. The outcome measures used to measure physical activity and function dictated that TILDA participants who did not attend the health centre assessment were excluded. It has been demonstrated that those who were frail or disabled or more elderly were less inclined to attend the health centre for assessment and thus presents a potential source of bias [22]. As with other longitudinal studies of ageing, all participants were required to provide written informed consent to participate in the study at Wave 1, this will have resulted in the exclusion of individuals with severe cognitive impairment. We also need to acknowledge those who were lost to follow up, though this was minimal with 6.6% (n=148) participants with no multimorbidity and 7.2% (n=173) participants with multimorbidity not available for analysis two years later. A further limitation is that the definition of multimorbidity used does not take into account disease severity. However, we did use the most commonly reported definition i.e. ≥ 2 chronic conditions and we also conducted analyses examining complex multimorbidity (≥ 3 chronic conditions) with complex multimorbid patients having higher care needs [5]. The use of self-reported diagnoses in the analysis may be an additional limitation. However, evidence has demonstrated moderate to good agreement between self-reported and physician reported chronic conditions among multimorbid patients [31]. A final limitation was the use of State financial support as a proxy for socioeconomic status. While state financial support is an accurate proxy for socioeconomic status in Irish people under the age of 70, over this age different income thresholds apply and there is nearly universal coverage for this age group. However the majority of our cohort (80.3%) were < 70 years.

Conclusion

With an ageing population, the management of chronic medical conditions is at the forefront of healthcare planning and policy. Our results have implications for clinical practice in that assessment of physical function and appropriate intervention may prevent an inevitable cascade towards poorer health outcomes. Future research should focus on the development of interventions which prioritise physical function for this patient group to prevent the poorer health outcomes and increased healthcare costs associated with multimorbidity.

Key points

- Gait speed, grip strength and increasing age were shown to be significantly associated with the development of multimorbidity and the worsening of existing multimorbidity.
- Faster gait speed and stronger grip strength were found to be associated with a reduced risk of developing new conditions.
- Poor levels of physical function, as measured by grip strength and gait speed lead to the worsening of multimorbidity over time.
- These results support the NICE Multimorbidity Guidance (2016), which recommends using gait speed as an assessment measure to identify those patients who require prioritised/targeted care.

Conflicts of Interest

The authors declare that they have no competing interests.

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CM is a Visiting Researcher at TILDA.

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Table 1: Baseline characteristics of study participants

		<u>No multimorbidity</u> 0/1 condition n= 2235 (46.3%)	<u>Multimorbidity</u> 2/more conditions n= 2588 (53.7%)	p-value
Age	50-59 60-69 70 +	1282 (57.4%) 697 (31.2%) 252 (11.3%)	893 (34.5%) 995 (35.4%) 696 (26.9%)	<0.001 (c)
Sex	Male Female	1115 (49.9%) 1120 (50.1%)	1106 (42.7%) 1482 (57.3%)	<0.001 (c)
Education	Primary/ none Secondary Third/ higher	401 (17.9%) 1003 (44.9%) 830 (37.1%)	653 (25.2%) 1008 (38.9%) 926 (35.8%)	<0.001 (c)
Body Mass Index (kg/m ²)	Underweight (< 18.5) Normal (18.5 -25) Overweight (25.1 -30) Obese (≥30.1)	12 (0.5%) 566 (25.3%) 1021 (45.7%) 634 (28.4%)	9 (0.3%) 518 (20.0%) 1097 (42.4%) 963 (37.2%)	<0.001 (c)
Smoking Status	Non-smoker Smoker	1865 (83.5%) 370 (16.5%)	2244 (86.7%) 344 (13.3%)	0.001 (c)
State support	No medical/General Practitioner card Medical/General Practitioner card	1628 (78.8%) 605 (27.1%)	1338 (51.7%) 1249 (48.3%)	<0.001 (c)
International Physical Activity Questionnaire (IPAQ)	Low exercise Moderate exercise High exercise	539 (24.1%) 761 (34.1%) 935 (41.8%)	782 (30.2%) 994 (38.4%) 812 (31.4%)	<0.001 (c)

Grip Strength (kg)	Mean (SD)	Mean (SD)	
50-59	28.5 (9.9)	26.8 (9.8)	
60-69	27.0 (8.9)	24.8 (8.8)	
70+	24.6 (8.6)	21.9 (8.3)	
Total	27.6 (9.5)	24.7 (9.2)	<0.001 (t)
Gait Speed (m/second)	Mean (SD)	Mean (SD)	
50-59	1.4 (0.2)	1.4 (0.2)	
60-69	1.4 (0.2)	1.3 (0.2)	
70+	1.3 (0.2)	1.2 (0.2)	
Total	1.4 (0.2)	1.3 (0.2)	<0.001 (t)

Note. Confounder variables missing <0.2% data in all cases; c= chi-squared test; t= t-test

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Table 2: Multivariable Poisson regression model for A) development of multimorbidity in those with no multimorbidity at baseline and B) worsening multimorbidity in those with multimorbidity at baseline, over a two year period in adults aged 50 years and over (TILDA wave 1 &2)

	<u>No multimorbidity</u>	p-value	<u>Multimorbidity</u>	p-value
	Relative risks and 95% confidence intervals of those with no multimorbidity at baseline		Relative risks and 95% confidence intervals of those with multimorbidity at baseline	
<u>Age</u>				
50-59	1.00		1.00	
60-69	1.30 (1.11-1.52)	0.001	1.20 (1.07-1.34)	0.002
70 +	1.35 (1.03-1.77)	0.027	1.18 (1.01-1.37)	0.039
<u>Sex</u>				
Male	1.00		1.00	
Female	1.05 (0.86-1.27)	0.649	0.95(0.83-1.09)	0.468
<u>Education</u>				
Secondary	1.00		1.00	
Primary/ none	1.10 (0.93-1.30)	0.279	0.94 (0.84-1.06)	0.314
Third/ higher	0.96 (0.83-1.11)	0.582	1.02 (0.91-1.14)	0.760
<u>Body Mass Index</u>				
Normal: 18.5 -25 & underweight:< 18.5	1.00		1.00	
Overweight:25.1 -30	1.09 (0.92-1.28)	0.319	0.96 (0.85-1.09)	0.542
Obese: ≥ 30.1	1.26 (1.05-1.51)	0.011	0.96 (0.84-1.10)	0.572
<u>Smoking</u>				

Non-smoker Smoker	1.00 1.08 (0.91-1.29)	0.361	1.00 1.06 (0.92-1.22)	0.457
<u>State Support</u> No medical/General Practitioner card Medical/ General Practitioner card	1.00 1.13 (0.97-1.31)	0.130	1.00 1.20(1.07-1.34)	0.002
<u>International Physical Activity Questionnaire (IPAQ)</u> Low exercise Moderate High exercise	1.00 1.00 (0.85-1.19) 1.04 (0.88-1.23)	0.969 0.640	1.00 0.94 (0.85-1.06) 0.92 (0.81-1.04)	0.309 0.168
<u>Grip Strength (kg)</u>	0.98 (0.97-0.99)	0.002	0.990 (0.982-0.998)	0.014
<u>Gait Speed (m/second)</u>	0.67 (0.49-0.90)	0.046	0.61 (0.50-0.82)	<0.001

Figure 1. Study Participants Flow Chart

