Title: Physical multimorbidity and incident urinary incontinence among community-dwelling adults aged ≥50 years: findings from a prospective analysis of the Irish Longitudinal Study on Ageing

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Key Points:

- Those with 3 or 4 chronic conditions at baseline were almost two times more likely to develop urinary incontinence at two-year follow-up.
- Baseline multimorbidity and incident urinary incontinence was partly mediated by polypharmacy, sleep problems, and disability.
- Arthritis, heart disease, chronic lung disease, and eye disease at baseline were associated with significantly higher risk for development of urinary incontinence.

ABSTRACT

Background: There are no prospective studies on the association between multimorbidity and urinary incontinence (UI), while mediators in this association are unknown. Thus, we aimed to (i) investigate the longitudinal association between multimorbidity and UI in a large sample of Irish adults aged ≥50 years, and (ii) investigate to what extent physical activity, polypharmacy, cognitive function, sleep problems, handgrip strength, and disability mediate the association.

Methods: Data on 5946 adults aged ≥ 50 years old from the Irish Longitudinal Study on Aging (TILDA) were analyzed. The baseline survey was conducted between 2009-2011 and follow-up after two years was conducted. Information on self-reported occurrence of UI in the past 12 months, and lifetime diagnosis of 14 chronic conditions were obtained. Multivariable logistic regression and mediation analysis were conducted.

Results: After adjustment for potential confounders, compared to having no chronic conditions at baseline, having three (OR=1.79; 95%CI=1.30-2.48) and four or more (OR=1.86; 95%CI=1.32-2.60) chronic conditions were significantly associated with incident urinary incontinence. Mediation analysis showed that polypharmacy, sleep problems, and disability explained 22.7%, 17.8%, and 14.7% of the association between multimorbidity (i.e., two or more chronic conditions) and incident urinary incontinence, respectively.

Conclusion: A greater number of chronic conditions at baseline was associated with a higher risk for incident urinary incontinence at two-year follow-up among adults aged ≥50 years in Ireland. Considering the effects of different medications on urinary incontinence, and improving sleep quality and disability among people aged ≥50 years with multimorbidity may reduce the incidence of urinary incontinence.

INTRODUCTION

The International Continence Society (ICS) defines urinary incontinence as the complaint of involuntary loss of urine [1]. Other health bodies provide similar definitions. [2,3]. There are five common types of urinary incontinence including stress incontinence (complaint of involuntary loss of urine on effort or physical exertion including sporting activities, or on sneezing or coughing.), urgency incontinence (complaint of involuntary loss of urine associated with urgency), overflow incontinence (complaint of urinary incontinence in the symptomatic presence of an excessively (over) full bladder), impaired mobility urinary incontinence (complaint of inability to reach the toilet on time for voiding because of physical or medical disability), and mixed incontinence (complaints of both stress and urgency urinary incontinence) [1-3]. Importantly, urinary incontinence is highly prevalent particularly in middle-aged and older adults [4]. The prevalence of urinary incontinence reported in population-based studies of middle-aged and older adults ranges from 5% to 70% [4–7].

Such a high prevalence of urinary incontinence in the middle-aged and older population is of concern as urinary incontinence has been found to be associated with lower quality of life, higher level of mental health complications, higher risk of falls, and premature mortality [8-12]. Owing to the high prevalence of urinary incontinence in middle-aged and older adults and its detrimental outcomes, it is important to identify risk factors for urinary incontinence to inform targeted interventions.

Previous studies have shown that female sex, advanced age, low physical performance, impairment in activities of daily living, a high body mass index, alcohol consumption, and smoking are associated with increased risk for urinary incontinence [13–16]. However, one emerging but understudied risk factor for urinary incontinence is multimorbidity [17]. Multimorbidity is often defined as the simultaneous occurrence of ≥2 chronic diseases in one person and is highly prevalent in middle-aged and older adults [18].

Multimorbidity may increase risk for urinary incontinence via factors such as low physical activity, polypharmacy, cognitive impairment, sleep problems, low physical performance, and disability [14], [19–26].

To the best of our knowledge, to date, only two studies have investigated the association between multimorbidity and urinary incontinence. One study in a sample of 622 Brazilian females aged ≥50 years found that approximately two-thirds of females suffering from urinary incontinence reported multimorbidity [27]. Another study in a sample of 23089 individuals aged ≥15 years residing in Spain found that there was a significant and positive relationship between multimorbidity and urinary incontinence (odds ratio = 5.02, 95% confidence interval [CI] = 3.89 to 6.59) [17]. However, both of these studies were cross-sectional in nature and thus, it is not known whether multimorbidity precedes urinary incontinence or vice versa. Moreover, neither of these studies were able to identify mediators of the multimorbidity-urinary incontinence relationship. Identifying such mediators can provide insights into the mechanisms that link multimorbidity and urinary incontinence, and therefore help to inform targeted interventions. It should also be mentioned that there is a small body of literature showing that urgency urinary incontinence is associated with several comorbid conditions, but its association has not been investigated with multimorbidity per se. [28].

Given this background, the present study aims to (i) investigate the longitudinal association between multimorbidity at baseline and incident urinary incontinence at two-year follow-up in a large sample of Irish adults aged ≥50 years and (ii) investigate to what extent physical activity, polypharmacy, cognitive function, sleep problems, handgrip strength, and disability mediate the association.

METHODS

The survey

We analyzed data from two consecutive waves of the Irish Longitudinal Study on Ageing (TILDA) survey [29–31]. Full details of the survey, including its sampling methods, have been described in detail elsewhere. Briefly, this was a community-based survey of middle-aged and older adults residing in Ireland conducted by Trinity College Dublin. The first wave (Wave 1) or the baseline survey was conducted between October 2009 and February 2011, and the second wave (Wave 2) was undertaken between April 2012 and January 2013. The target sample consisted of all individuals living in private households aged 50 and over in Ireland. Clustered random sampling was used to obtain nationally representative samples. The first wave excluded institutionalized individuals, anyone with known dementia or anyone unable to personally provide written informed consent to participate due to severe cognitive impairment. Trained personnel conducted interviews with the use of Computer Assisted Personal Interviewing (CAPI). For sensitive questions (e.g., alcohol consumption), participants were asked to fill in a self-completion questionnaire (SCQ), which was returned after the interview. The response rate of Wave 1 was 62% and that of Wave 2 was 86%. Sampling weights were generated with respect to age, sex and educational attainment to the Quarterly National Household Survey 2010. Ethical approval for TILDA was obtained by the Faculty of Health Sciences Ethics Committee of Trinity College Dublin. Written informed consent was obtained from all participants.

Urinary incontinence (dependent variable)

Urinary incontinence was assessed by the question ‘During the last 12 months, have you lost any amount of urine beyond your control?’ with answer options ‘yes’ or ‘no’. The same question was asked at Wave 1 and 2.

Chronic physical conditions and multimorbidity (independent variables)

Chronic physical conditions were assessed at Wave 1 by the question "Has a doctor ever told you that you have any of the conditions on this card?" The total number of the following 14 conditions were summed: asthma, arthritis, cancer, chronic lung disease (chronic bronchitis or emphysema), cirrhosis, diabetes, eye disease (cataracts, glaucoma, age-related macular degeneration, or other eye disease), heart disease (angina, heart attack, congestive heart failure, heart murmur, abnormal heart rhythm, or other heart disease), high cholesterol, hypertension, osteoporosis, stomach ulcer, stroke, varicose ulcer. Multimorbidity was defined as having at least two chronic conditions, in line with previously used definitions [32]. The number of chronic conditions was also classified as 0, 1, 2, 3, and ≥4 conditions.

Mediators

The potential mediators in the association between multimorbidity and urinary incontinence were selected based on past literature and included physical activity, polypharmacy, cognitive function, sleep problems, handgrip strength, and disability [17]. Physical activity was measured with the International Physical Activity Questionnaire Short Form (IPAQ-SF). Based on the results of the IPAQ-SF, participants were classified as having low levels of physical activity if they did not meet the WHO physical activity guidelines (i.e., at least 150 min/week of moderate physical activity or 75 min/week of vigorous physical activity or 600 metabolic equivalents (Met) min of weekly moderate-to-vigorous physical activity) [33-34]. Polypharmacy was defined as taking ≥5 medications [35]. The scale used for cognitive impairment was the Mini-Mental State Examination (MMSE) which is a screening tool for the assessment of cognitive functioning [36]. A composite sleep score (range 0-7 with higher scores representing more sleep problems) was created based on three questions on the likelihood of dozing off or falling asleep during the day, frequency of trouble falling asleep,

and trouble with waking up too early and not being able to fall asleep again [37]. Weak handgrip strength was defined as <30 kg for men and <20 kg for women using the average value of the two handgrip measurements of the dominant hand [38]. Difficulties with six types of activities of daily living (ADL) (dressing, walking, bathing, eating, getting in or out of bed, and using the toilet) were assessed by asking participants to indicate whether they had difficulty performing these activities. ADL disability was defined as having difficulty with at least one of these ADLs. All these potential mediators were assessed at Wave 1.

Control variables

Control variables were selected based on past literature [17], and included sex, age, education, marital status (married/cohabiting, never married, separated/divorced/widowed), smoking (never, past, current), alcohol consumption (non-drinkers, light/moderate drinkers, heavy drinkers), and obesity [39]. Education was classified as: primary (some primary/not complete, primary or equivalent); secondary (intermediate/ junior/group certificate or equivalent, leaving certificate or equivalent); and tertiary (diploma/certificate, primary degree, postgraduate/higher degree). Obesity was defined as body mass index ≥30 kg/m^2 based on measured weight and height. The control variables were assessed at Wave 1.

Statistical analysis

The analysis was done with Stata version 14.2 (Stata Corp LP, College Station, Texas). A total of 8163 people aged ≥50 years participated at Wave 1 and of these individuals, 1023 individuals had urinary incontinence and 24 did not have information on urinary incontinence. These individuals were deleted from the analysis to obtain a sample that was free of urinary incontinence at baseline. This allowed us to analyze longitudinal associations focusing only on new onset of urinary incontinence at follow-up as the outcome, and this analytical method has

been used in previous TILDA publications [39]. Finally, after deleting 1098 people who did not participate in Wave 2 and further deleting 72 people who did not provide information on urinary incontinence at Wave 2, the final sample consisted of 5946 people (a flow chart of the participants is provided in Figure S1 of the Appendix). The difference in sample characteristics between those with and without multimorbidity (i.e., ≥2 chronic conditions) at baseline or urinary incontinence at follow-up was tested by Chi-squared tests and Student's *t*-tests for categorical and continuous variables, respectively. The association between individual chronic conditions or number of chronic conditions at baseline (exposures) and incident urinary incontinence at follow-up (outcome) was estimated by multivariable logistic regression. We also tested for interaction by sex in the association between number of chronic conditions and incident urinary incontinence by including an interaction term (sex X number of chronic conditions) in the model.

Next, in order to assess the degree to which the association between multimorbidity at baseline and incident urinary incontinence at follow-up can be explained by physical activity, polypharmacy, cognitive function, sleep problems, grip strength, and disability at baseline, we conducted mediation analysis using the *khb* (Karlson Holm Breen) command in Stata (Breen, Karlson, & Holm, 2013). This method can be applied in logistic regression models and decomposes the total effect (i.e., unadjusted for the mediator) of a variable into direct (i.e., the effect of multimorbidity on urinary incontinence adjusted for the mediator) and indirect effects (i.e., the mediational effect). Using this method, the percentage of the main association explained by the mediator can also be calculated (mediated percentage). The mediators were included individually in the models. All regression analyses including the mediation analysis were adjusted for sex, age, education, marital status, alcohol consumption, smoking, and obesity. The sample weighting and the complex study design including clustering within

households were taken into account to obtain nationally representative estimates using the Stata *svy* command. Model fit was tested by the Pearson X^2 goodness-of-fit test using the Stata command *gof* and this test suggested that final models were a good fit for the data. Results are expressed as odds ratios (ORs) and their 95% confidence intervals (95%CIs). A P-value <0.05 was considered to be statistically significant.

RESULTS

The final sample consisted of 5946 individuals [mean (SD) age 62.7 (8.8) years; 51.7% males] aged ≥50 years with no urinary incontinence at baseline. The prevalence of 1, 2, 3, and ≥4 chronic conditions were 27.7%, 23.2%, 14.1%, and 13.0%, respectively, while the prevalence of urinary incontinence at follow-up was 9.0%. For both multimorbidity and urinary incontinence, participants were more likely to be females, older, separated/divorced/widowed, non-drinkers, and have low physical activity, polypharmacy, low grip strength, disability, obesity and more sleep problems. In terms of individual chronic conditions, arthritis (OR=1.62; 95%CI=1.32-1.99), heart disease (OR=1.40; 95%CI=1.11-1.77), chronic lung disease (OR=2.17; 95%CI=1.47-3.19), and eye disease (OR=1.32; 95%CI=1.04-1.69) were significantly associated with higher risk for incident urinary incontinence (**Table 2**). The prevalence of incident urinary incontinence at follow-up increased linearly with increasing number of chronic conditions at baseline (**Figure 1**). For example, the prevalence of incident urinary incontinence among those with no chronic conditions at baseline was 5.9% but this increased to 14.4% among those with ≥4 chronic conditions. After adjustment for potential confounders, compared to having no chronic conditions at baseline, having 3 and ≥4 chronic conditions were significantly associated with incident urinary incontinence with the OR (95%CI) being 1.79 (95%CI=1.30-2.48) and 1.86 (95%CI=1.32-2.60), respectively (**Table 3**). There was no significant interaction by sex in this association. Mediation analysis showed that

polypharmacy, sleep problems, and disability explained 22.7%, 17.8%, and 14.7% of the association between multimorbidity at baseline and incident urinary incontinence, respectively (**Table 4**).

DISCUSSION

In this representative sample of 5946 Irish adults aged ≥50 years, it was found that those with 3 or 4 chronic conditions at baseline were almost two times more likely to develop urinary incontinence at two-year follow-up. The association between baseline multimorbidity (i.e., ≥2 chronic conditions) and incident urinary incontinence was partly mediated by polypharmacy (22.7%), sleep problems (17.8%), and disability (14.7%). In terms of individual chronic conditions, arthritis, heart disease, chronic lung disease, and eye disease at baseline were associated with significantly higher risk for development of urinary incontinence.

Findings from the present study both support and add to previous literature. They support previous literature through further confirming that an association exists between multimorbidity and urinary incontinence and add to this through showing that a longitudinal association exists where multimorbidity precedes urinary incontinence [27]. Moreover, the present study adds to the literature by demonstrating that polypharmacy, sleep problems, and disability explain 14.7% to 22.7% of the variation in the observed association.

There are several mechanisms that may explain the higher risk for urinary incontinence among those with multimorbidity. First, several individual chronic conditions have been shown to increase risk for urinary incontinence. For example, in our study, arthritis, heart disease, chronic lung disease, and eye disease were associated with particularly high risk for incident urinary incontinence. The higher risk in arthritis and eye disease may be explained by disability

associated incontinence whereby owing to the arthritis or eye disease, the individual is not able to reach the toilet before passing urine, and that of heart disease may be due to medications taken to treat the condition. For example, some medications used to treat heart failure increase frequency of daytime urination and nocturia, and these can in some cases result in incontinence [40-41]. In the case of lung disease, literature has suggested that there is an increase in stress urinary incontinence owing to coughing [42]. Interestingly, arterial disease is associated with a high risk of heart disease and eye disease. [43] Indeed, an association has been observed between vascular disease and an increased risk of urinary incontinence. [44] It is also important to note that many of these chronic conditions may lead to sleep problems, [45] and in turn, sleep problems may lead to urinary incontinence through their associations with obesity, metabolic dysregulation and systemic inflammation [46]. Thus, it is possible that the accumulation of individual chronic conditions and the associated symptoms including sleep problems or disability may further increase risk for urinary incontinence. Finally, the accumulation of white matter intensities in the central nervous system is associated with lower urinary tract symptoms, and thus may be another common pathway leading to urinary incontinence for many geriatric syndromes. [47]

Apart from this, in our study, we found that polypharmacy is a significant mediator. Polypharmacy is common in individuals with multimorbidity for having have to treat multiple conditions, and some medications are “urologically active” (e.g., diuretics, calcium channel blockers) and thus, such medication may increase one’s risk of urinary incontinence. Indeed, it has been suggested that patients with multimorbidity may benefit from discontinuation of drugs or a change to drugs less likely to affect the lower urinary tract [48].

However, mediators in the present study were only able to explain up to 22.7% of the variation in the association. Therefore, other mechanisms may also explain the remaining variation. For example, changes in age-related immune functions, hormonal changes, and increasing incidence of comorbid diseases may facilitate urinary tract infections that can result in urinary incontinence [49]. Moreover, multimorbidity may be directly associated with urinary incontinence owing to a multifactorial etiology behind urinary incontinence where cognitive, neurological, muscular, and urological systems must be robust to maintain continence [17].

The large representative sample of Irish adults and the longitudinal study design are clear strengths of the present study. However, findings must be interpreted in light of the study limitations. First, most of the study variables were self-reported introducing self-reporting and recall bias into the study findings. For example, it is possible that older adults in our study (particularly women) did not report having urinary incontinence as they may consider it as a normal consequence of ageing. Second, urinary incontinence per se was reported and not the different type of urinary incontinence or its severity. It is indeed possible that multimorbidity is differentially associated with different types of urinary incontinence. Moreover, our measure of urinary incontinence has not been validated. Future studies should investigate the longitudinal association between multimorbidity and different types of urinary incontinence. Third, baseline data on multimorbidity and other control or mediating variables were used for the analysis. Consequently, it is possible that some conditions or characteristics of the respondents changed between the two waves. Next, it is possible that some level of bias was introduced due to loss to follow-up. Finally, although the chronic conditions assessed in the TILDA were diverse, the association may have differed with the use of a different list of chronic conditions. Relatedly, the TILDA lacked data on some diseases (e.g., genito-urinary prolapse) which may be strongly linked with urinary incontinence.

In conclusion, in this large sample of Irish adults aged ≥50 years, multimorbidity at baseline was associated with increased risk for urinary incontinence onset at two-year follow-up. Considering that affected individuals often deny and hide urinary incontinence due to a sense of shame, health care providers should assess the presence of urinary incontinence when risk factors and multi-morbidities are present [50]. In fact, prompt and appropriate treatment could avoid the negative consequences of urinary incontinence such as anxiety, depression, deterioration in sexual life, and decrease in physical activity that are associated with poor quality of life in general. Considering the effects of different medications on urinary incontinence, and improving sleep quality and disability may reduce the incidence of urinary incontinence in people with multimorbidity.

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Researchers interested in using TILDA data may access the data for free from the following sites: Irish Social Science Data Archive (ISSDA) at University College Dublin http://www.ucd.ie/issda/data/tilda/; Interuniversity Consortium for Political and Social Research (ICPSR) at the University of Michigan [51].

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TABLES AND FIGURES

Table 1 Sample characteristics

			Multimorbidity			Urinary incontinence at follow-up		
Characteristics	Categories	Overall	No	Yes	P-value[a]	No	Yes	P-value[a]
Multimorbidity[b]	No	49.7				50.9	38.4	<0.001
	Yes	50.3				49.1	61.6	
Urinary incontinence	No	91.0	93.0	88.9	<0.001			
at follow-up	Yes	9.0	7.0	11.1				
Sex	Female	48.3	43.7	52.8	<0.001	46.3	68.3	<0.001
	Male	51.7	56.3	47.2		53.7	31.7	
Age (years)	Mean (SD)	62.7 (8.8)	60.1 (8.0)	65.2 (8.8)	<0.001	62.4 (8.7)	65.1 (9.2)	<0.001
Education	Primary	34.2	29.4	38.9	<0.001	33.8	37.9	0.145
	Secondary	45.7	49.2	42.3		45.9	43.6	
	Tertiary	20.1	21.4	18.8		20.3	18.5	
Marital status	Married cohabiting	70.6	73.8	67.4	<0.001	71.1	65.8	0.006
	Never married	9.7	10.2	9.2		9.8	8.9	
	Separated/Divorced/Widowed	19.7	16.0	23.3		19.1	25.3	
Alcohol consumption	Non-drinker	28.3	24.7	31.8	<0.001	27.8	33.2	0.008
	Light/moderate drinker	43.1	43.3	42.9		42.9	44.6	
	Heavy drinker	28.6	32.0	25.3		29.3	22.2	
Smoking	Never	43.7	45.3	42.2	<0.001	43.5	46.0	0.543
	Quit	38.0	34.3	41.6		38.1	37.0	
	Current	18.2	20.3	16.2		18.4	17.0	
Obesity	No	66.2	70.8	61.8	<0.001	66.9	59.5	0.003
	Yes	33.8	29.2	38.2		33.1	40.5	
Low physical activity	No	48.7	56.0	41.5	<0.001	49.7	38.4	<0.001
	Yes	51.3	44.0	58.5		50.3	61.6	
Polypharmacy	No	81.7	96.0	67.5	<0.001	82.5	73.2	<0.001

	Yes	18.3	4.0	32.5		17.5	26.8	
Cognitive function[c]	Mean (SD)	28.3 (2.0)	28.5 (1.9)	28.2 (2.1)	<0.001	28.3 (2.0)	28.2 (2.1)	0.148
Sleep problems[d]	Mean (SD)	2.1 (1.6)	1.8 (1.5)	2.3 (1.7)	<0.001	2.0 (1.6)	2.5 (1.7)	<0.001
Low grip strength	No	61.5	67.2	55.9	<0.001	62.7	49.5	<0.001
	Yes	38.5	32.8	44.1		37.3	50.5	
Disability	No	93.4	97.2	89.6	<0.001	94.0	87.1	<0.001
	Yes	6.6	2.8	10.4		6.0	12.0	

Abbreviation: SD Standard deviation
Sample is restricted to those who did not have urinary incontinence at baseline and who provided information on urinary incontinence at follow-up.
All variables were assessed at baseline with the exception of urinary incontinence at follow-up.
[a] P-value was estimated by Chi-squared tests and Student's *t*-tests for categorical and continuous variables, respectively.
[b] Multimorbidity was defined as two or more chronic conditions.
[c] Cognitive function was assessed with the Mini-Mental State Examination.
[d] Sleep problems was based on a scale ranging from 0 to 7 with higher scores representing more sleep problems.

Table 2 Prevalence of individual chronic conditions (baseline) and their associations with incident urinary incontinence at follow-up

		Urinary incontinence at follow-up		Logistic regression analysis[a]		
Chronic condition	%	No (%)[b]	Yes (%)[b]	OR	95%CI	P-value
Arthritis	24.7	23.3	38.7	1.62	[1.32,1.99]	<0.001
Asthma	8.2	8.0	10.6	1.24	[0.92,1.65]	0.153
Cancer	5.2	5.1	6.3	1.10	[0.75,1.60]	0.631
Heart disease	18.2	17.6	23.8	1.40	[1.11,1.77]	0.004
High cholesterol	37.7	37.6	39.2	0.99	[0.81,1.21]	0.918
Cirrhosis	0.5	0.5	0.9	1.86	[0.73,4.77]	0.194
Chronic lung disease	3.6	3.2	6.9	2.17	[1.47,3.19]	<0.001
Diabetes	7.2	7.1	8.6	1.22	[0.88,1.69]	0.230
Eye disease	13.4	21.7	14.2	1.32	[1.04,1.69]	0.025
Hypertension	35.7	35.2	40.3	1.03	[0.84,1.26]	0.790
Osteoporosis	8.7	8.2	14.0	1.25	[0.94,1.66]	0.133
Stomach ulcer	6.9	6.7	8.3	1.42	[0.99,2.03]	0.055
Stroke	1.4	1.3	2.0	1.33	[0.65,2.71]	0.440
Varicose ulcer	3.1	2.9	4.9	1.33	[0.85,2.08]	0.214

Abbreviation: OR Odds ratio; CI Confidence interval

Analysis is restricted to those who did not have urinary incontinence at baseline.

[a] Adjusted for sex, age, education, marital status, alcohol consumption, smoking, and obesity.

[b] Column percentage.

Table 3 Association between number of chronic conditions or covariates at baseline and incident urinary incontinence at follow-up

Characteristic	Categories	OR	95%CI	P-value
No. of chronic conditions	0	1.00		
	1	1.26	[0.93,1.72]	0.134
	2	1.22	[0.89,1.66]	0.210
	3	1.79	[1.30,2.48]	<0.001
	4+	1.86	[1.32,2.60]	<0.001
Sex	Female	1.00		
	Male	0.42	[0.34,0.51]	<0.001
Age (years)		1.02	[1.01,1.04]	<0.001
Education	Primary	1.00		
	Secondary	0.99	[0.78,1.25]	0.909
	Tertiary	1.00	[0.77,1.29]	0.974
Marital status	Married cohabiting	1.00		
	Never married	1.02	[0.73,1.42]	0.924
	Separated/Divorced/Widowed	1.04	[0.74,1.44]	0.832
Alcohol consumption	Non-drinker	1.00	[0.77,1.28]	0.973
	Light/moderate drinker	1.02	[0.79,1.32]	0.884
	Heavy drinker	1.06	[0.76,1.47]	0.739
Smoking	Never	1.00		
	Quit	1.04	[0.84,1.30]	0.715
	Current	1.11	[0.84,1.45]	0.462
Obesity	No	1.00		
	Yes	1.40	[1.13,1.74]	0.002

Abbreviation: OR Odds ratio; CI Confidence interval
Analysis is restricted to those who did not have urinary incontinence at baseline.
Model is mutually adjusted for all variables in the Table.

Table 4 Mediators in the association between multimorbidity at baseline and incident urinary incontinence at follow-up

Mediators	Effect	OR [95%CI]	P-value	% mediated
Physical activity	Total	1.32 [1.08,1.61]	0.007	NA
	Direct	1.29 [1.06,1.59]	0.013	
	Indirect	1.02 [1.00,1.04]	0.056	
Polypharmacy	Total	1.31 [1.07,1.60]	0.009	22.7
	Direct	1.23 [0.99,1.52]	0.057	
	Indirect	1.06 [1.00,1.13]	0.036	
Cognitive function	Total	1.17 [0.93,1.47]	0.188	NA
	Direct	1.17 [0.92,1.47]	0.194	
	Indirect	1.00 [0.99,1.01]	0.610	
Sleep problems	Total	1.32 [1.08,1.62]	0.006	17.8
	Direct	1.26 [1.03,1.54]	0.025	
	Indirect	1.05 [1.03,1.08]	<0.001	
Grip strength	Total	1.20 [0.95,1.53]	0.133	NA
	Direct	1.20 [0.94,1.53]	0.137	
	Indirect	1.00 [1.00,1.01]	0.559	
Disability	Total	1.31 [1.07,1.60]	0.009	14.7
	Direct	1.26 [1.03,1.54]	0.026	
	Indirect	1.04 [1.02,1.06]	0.001	

Abbreviation: OR Odds ratio; CI Confidence interval
Multimorbidity was defined as ≥2 chronic conditions.
Models are adjusted for sex, age, education, marital status, alcohol consumption, smoking, and obesity.
Mediators were assessed at baseline.
% mediated was only calculated when the indirect effect was significant (P<0.05).

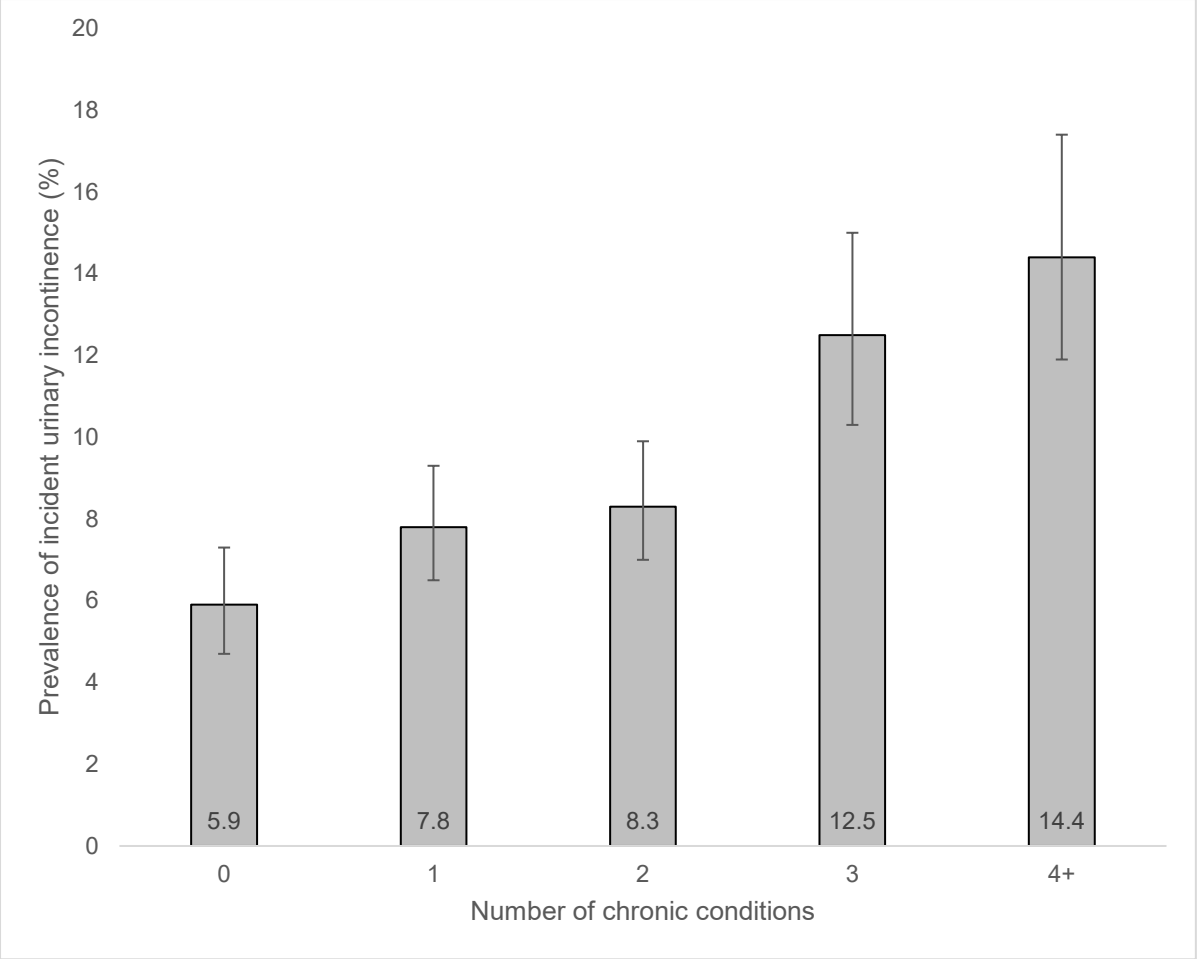

Figure 1 Prevalence of incident urinary continence at follow-up by number of chronic conditions at baseline

Restricted to those who did not have urinary incontinence at baseline.
Bars denote 95% confidence interval.

APPENDIX

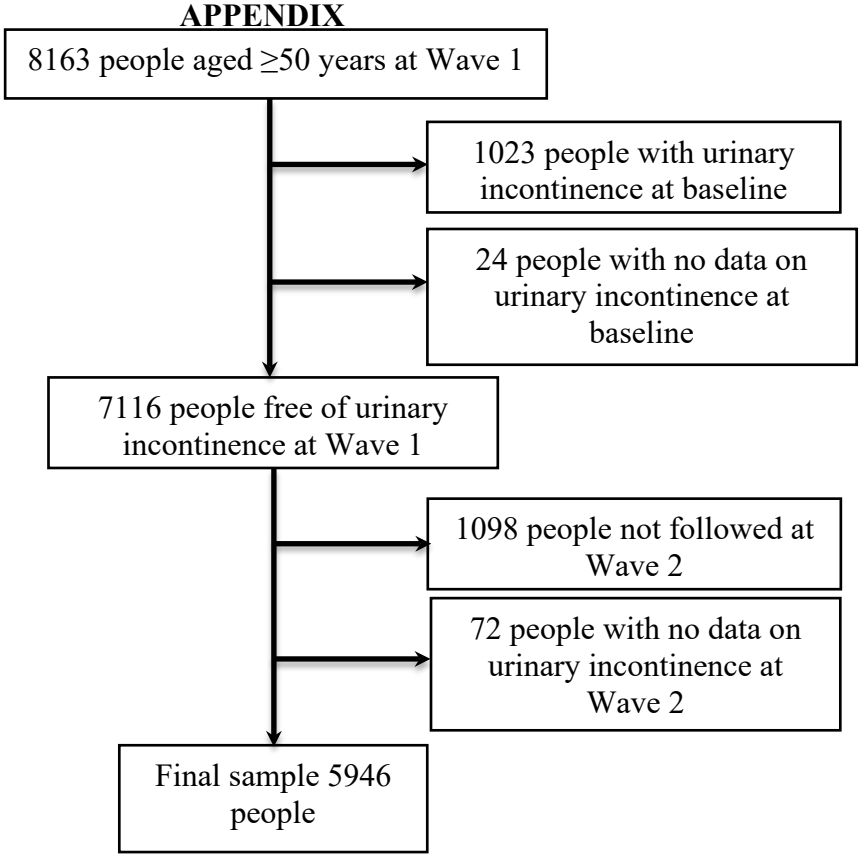

Figure S1 Flow chart of participants