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### **The association between multimorbidity and mobility disability-free life expectancy in adults aged 85 years and over**

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1 **MANUSCRIPT TITLE PAGE**

2 **Title**

3 The association between multimorbidity and mobility disability-free life expectancy in adults aged 85 years  
4 and over: A modelling study in the Newcastle 85+ cohort

5  
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29 **Abstract**

30 **Background**

31 Mobility disability is predictive of further functional decline and can itself compromise older people's  
32 capacity (and preference) to live independently. The world's population is also ageing, and multimorbidity is  
33 the norm in those aged  $\geq 85$ . What is unclear in this age group, is the influence of multimorbidity on a)  
34 transitions in mobility disability and b) mobility disability-free life expectancy.

35 **Methods and findings**

36 Using multi-state modelling in an inception cohort of 714 85-year-olds followed over a ten-year period (aged  
37 85 in 2006 to 95 in 2016), we investigated the association between increasing numbers of long-term  
38 conditions and (1) mobility disability incidence, (2) recovery from mobility disability and (3) death, and then  
39 explored how this shaped the remaining life expectancy free from mobility disability at age 85. Models were  
40 adjusted for age, sex, disease group count, BMI and education. We defined mobility disability based on  
41 participants self-reported ability to get around the house, go up and down stairs/steps and walk at least 400  
42 yards; participants were defined as having mobility disability if, for one or more these activities, they had any  
43 difficulty with them or could not perform them. Data were drawn from the Newcastle 85+ Study: a  
44 longitudinal population-based cohort study that recruited community-dwelling and institutionalised  
45 individuals from Newcastle upon Tyne and North Tyneside general practices.

46 We observed that each additional disease was associated with a 16% increased risk of incident mobility  
47 disability (HR 1.16, 95% CI: 1.07-1.25,  $p < 0.001$ ), a 26% decrease in the chance of recovery from this state  
48 (HR 0.74, 95% CI: 0.63-0.86,  $p < 0.001$ ), and a 12% increased risk of death with mobility disability (HR: 1.12,  
49 95% CI: 1.07-1.17,  $p < 0.001$ ). This translated to reductions in mobility disability-free life expectancy with  
50 increasing numbers of long-term conditions. However, residual and unmeasured confounding cannot be  
51 excluded from these analyses, and there may be unobserved transitions to/from mobility disability between  
52 interviews and prior to death.

53 **Conclusions**

54 We suggest two implications from this work. (1) Our findings support calls for a greater focus on the  
55 prevention of multimorbidity as populations age. (2) As more time spent with mobility disability could  
56 potentially lead to greater care needs, maintaining independence with increasing age should also be a key  
57 focus for health/social care and reablement services.

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61 **Author summary**

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63 **Why was this study done?**

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- 65 • Multimorbidity is the norm in growing older populations.
  - 66 • Mobility disability also has profound consequences for health, wellbeing and independent living.
  - 67 • However, there is a dearth of research exploring the relationship between multimorbidity and mobility disability in those aged  $\geq 85$ , even though attention is now more focussed on the quality of remaining
  - 68 life expectancy.

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70 **What did the researchers do and find?**

- 71
- 72 • In an inception cohort of 85-year-olds followed over 10 years (age 85-95), we explored the association between multimorbidity and transitions in mobility disability, and then examined how this was associated with mobility disability-free life expectancy.
  - 73
  - 74 • We found that there is no threshold beyond which multimorbidity becomes disabling in those aged  $\geq 85$ , rather each additional disease is associated with a 16% increased risk of incident mobility
  - 75 disability.
  - 76
  - 77 • This translates to reductions in mobility disability-free life-expectancy with increasing numbers of
  - 78 long-term conditions.

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80 **What do these findings mean?**

- 81
- 82 • Our findings suggest that, in those aged  $\geq 85$ , multimorbidity is an important determinant of mobility disability, and the number of years spent living with it.
  - 83 • As mobility disability can lead to greater care needs, preventing multimorbidity and maintaining
  - 84 independence including from earlier in the life course could be beneficial.

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## 92 **Introduction**

93 The World Health Organisation prioritises the preservation of functional ability to enable older people to carry  
94 on doing the things in life to which they attribute value [1], like the shopping and the housework, the ability to  
95 go outdoors and meet other people [2]. This priority complements the UK Ageing Society Grand Challenge  
96 which aims to ‘ensure that people can enjoy at least 5 extra healthy, independent years of life by 2035, while  
97 narrowing the gap between the experience of the richest and poorest’ [3]. The significance of these goals  
98 reflects the profound impact that loss of functional ability can have on quality of life, its power to reinforce  
99 further functional decline, the complex bi-directional interplay with diseases, the increased risk for medical  
100 and social care, and its association with mortality [4].

101 Functional ability is generally measured through activities that we do every day to maintain independence,  
102 such as walking, washing and eating. Losing the capacity to carry out such tasks leads to disability and when  
103 this happens an underlying hierarchical property of the disability process is revealed [5]. Disability onset  
104 usually occurs first with mobility (e.g. walking and using steps); mobility disability then predicts the incidence  
105 of disability with tasks essential to living (e.g. meal preparation, housework) and the ability to care for oneself  
106 (e.g. dressing and using the bathroom) [5,6]. Mobility disability therefore represents the gateway to further  
107 functional decline, and can itself compromise older people’s ability to self-care and their capacity (and  
108 preference) to live independently [7]. However the factors that drive the incidence of mobility disability are  
109 less well described, despite it also being the optimal point for interventions to slow down functional decline  
110 and/or regain independence [8].

111 For those aged  $\geq 85$  years, who are the fastest growing age group in many high-income countries [9], the  
112 identification of disease-based factors that increase the risk of mobility disability is clouded by their chronic  
113 co-occurrence i.e., multimorbidity [10]. In addition, we do not know how, as the number of multiple long-  
114 term conditions increase, this impacts mobility disability incidence, or recovery from mobility disability, or  
115 the amount of remaining life expectancy a person aged 85 may expect to spend free of mobility disability.  
116 Furthermore, the age at which diseases occur, and their type, are modified by factors related to lifestyle and  
117 sociodemographics [11].

118 Through multi-state modelling in an inception cohort of 85-year-olds followed over ten years (age 85 to 95  
119 years), we aimed to examine the association between increasing numbers of long-term conditions and (i)  
120 mobility disability incidence, (ii) recovery from mobility disability and (iii) death, and (iv) then explore how  
121 this shapes mobility disability-free life expectancy (mobDFLE), the remaining life expectancy free from  
122 mobility disability at age 85.

## 123 **Methods**

124 This study is reported as per the Strengthening the Reporting of Observational Studies in Epidemiology  
125 (STROBE) guideline (S1 Appendix).

## 126 **Participants**

127 The Newcastle 85+ Study is a population-based longitudinal study of community-dwelling and  
128 institutionalised individuals who were born in 1921, aged 85 in 2006, and permanently registered with one of  
129 53 participating general practices in Newcastle or North Tyneside [12]. When the study began (2006),  
130 participants were broadly representative of 85-year-olds in England and Wales in terms of sex, care home  
131 residence and whether living alone, but participants with end stage terminal illness were excluded (n=11) [13].  
132 Data were gathered by two methods: i) multidimensional health assessment by a trained research nurse in the  
133 participant's place of residence, inclusive of care homes, at baseline (wave 1), 18 months (wave 2), 36 months  
134 (wave 3), 60 months (wave 4) and 120 months (wave 5), and ii) review of general practice medical records at  
135 baseline, waves 3, 4 and 5 [14]. Participants received the same assessment at baseline and follow-up to look  
136 for changes in mobility disability items. Full details of the study design, participant recruitment and  
137 representativeness are reported elsewhere [12-14]. Further details, including study questionnaires and the GP  
138 record review proforma can be found on the Newcastle 85+ Study website <https://research.ncl.ac.uk/85plus/>,  
139 whilst study retention can be found in S2 Appendix. Of the 849 people who were eligible for analyses at  
140 baseline (S2 Appendix), we constructed a measure of mobility disability on 845 individuals (524 females and  
141 321 males), of whom, 714 (424 females and 290 males) had complete data for all confounding variables used  
142 in the analysis. Over the five waves of data collection, participants were lost to follow-up for health reasons,  
143 non-health reasons and death [15].

## 144 **Ethical approval**

145 The Newcastle 85+ Study was approved by the Newcastle and North Tyneside Local Research Committee  
146 One (Ref: 06/Q0905/2). Written informed consent was obtained from participants, and where people lacked  
147 capacity to consent—for example, because of dementia—an opinion was sought from a relative or carer (a  
148 “consultee”) [13].

## 149 **Definition of mobility disability**

150 Using items predominantly from the Groningen Activity Restriction Scale [16] as previously described  
151 [17,18], a binary variable for mobility disability was constructed based on participants self-reported ability to  
152 get around the house, go up and down stairs/steps and walk at least 400 yards [17,18]. Participants were  
153 defined as having mobility disability if, for one or more these activities, they had any difficulty with them  
154 (responding yes to ‘I have some difficulty doing this by myself’, or ‘I can only do this by myself if I use an aid  
155 or appliance’) or could not perform them (responding yes to ‘I am unable to do this by myself, I need someone  
156 else's help’). Data were gathered from questionnaires from the multidimensional health assessment.

## 157 **Definition of multiple long-term conditions**

158 Disease group count was created by scoring nine chronic diseases as either present (1) or absent (0), based on  
159 review of general practice medical records by trained research nurses (arthritis, diabetes, hypertension, cardiac  
160 disease, chronic obstructive pulmonary disease, other respiratory disease, stroke, other cerebrovascular

161 disease, and cancer in the past 5 years excluding non-melanoma skin cancer). Some conditions were grouped  
162 into a category (e.g. all arthritic diseases) whilst others were retained as single entities (e.g. hypertension).  
163 Full details of disease status construction can be found in S3 Appendix.

#### 164 **Other variables**

165 Age, sex, years in education and body mass index (BMI), calculated as kg weight/m<sup>2</sup> height and categorized  
166 as <18.5 (underweight), 18.5-24.99 (healthy weight), 25-29.99 (overweight) and ≥30 (obese) [19], were also  
167 included in the model building strategy. These data were obtained from general practice record review (age,  
168 sex) and a multidimensional health assessment comprising questionnaires (years in education) and  
169 measurement tests (BMI). The following sociodemographic variables, derived from multidimensional health  
170 assessment questionnaire data, were used to characterise the sample: housing (standard/sheltered/care home);  
171 living arrangements (alone/not alone); marital status (never married/married/divorced/separated or widowed)  
172 and socioeconomic position (<25th, 25th-75th and >75th centile Index of Multiple Deprivation) [20].

#### 173 **Statistical analysis**

174 The sociodemographic and health characteristics of the baseline cohort were examined through descriptive  
175 statistics. To model transitions to and from mobility disability, and to death in the inception cohort of 85-  
176 year-olds followed over ten years (age 85 to 95 years), we fitted a Markov multi-state transition model with  
177 three states - mobility disability-free, mobility disability and death (Figure 1) – using a Gompertz model and  
178 the ‘msm’ package [21]. Recovery (transitioning from mobility disability to mobility disability free) was  
179 defined as no longer having difficulty with any of the three mobility disability items. Survival time was  
180 calculated from the date of baseline interview to date of death or censoring at 120 months (10 years from  
181 baseline or after final interview if a participant had taken part in the 10-year follow-up). Age was used as a  
182 time-dependent co-variate under the Gompertz model to allow piecewise-constant approximation of the  
183 dependency on age [22]. Models were adjusted in stages as follows: age and disease group count (model 1),  
184 age, sex and disease group count (model 2); age, sex, disease group count and BMI (model 3); age, sex,  
185 disease group count, BMI and education (model 4). Using model 4 estimates, we implemented the ELECT  
186 library (estimating life expectancies for continuous time) to estimate state specific life expectancy, with 500  
187 replications of the points estimates to approximate uncertainty [22]. Briefly, ELECT uses established  
188 methodology to calculate state specific life expectancies using numerical methods and the transition  
189 probabilities defined by the state space (the possible states and transitions) of a fitted multistate model [22,23].  
190 For our estimates, we held education at mean years and BMI at normal weight, and for each disease group  
191 count, we calculated the remaining life expectancy with and without mobility disability in the male and female  
192 participants at age 85. All covariates (excepting fixed variables – sex and years in education) were treated as  
193 time-varying to account for their values potentially changing over time (for example, due to incident disease  
194 with respect to multiple long-term conditions).

195

196 We did not have a prospective analysis plan; our analysis was decided when our research question was  
197 formed, but we made two changes to it after peer review: 1) Upon investigating a wide confidence interval  
198 raised by one reviewer, we detected a small error in our analytical code which we rectified. 2) We reanalysed  
199 our data with the ELECT library to estimate life expectancy, as in response to comments from reviewers and  
200 wider reading, we learnt that our previous approximation using mean sojourn times was not suitable [22].  
201 Analyses were performed using R version 4.0.2.

202

### 203 **Figure 1: Markov multistate transition model for mobility disability-death in the Newcastle 85+ Study**

204

205 <sup>a</sup> Censored = 23; <sup>b</sup> Censored = 53

206 Note: numbers represent the number of transitions between states, not the number of people that moved. For  
207 example, there were 83 transitions, classed as recovery, from the mobility disability to mobility disability-free  
208 state, whilst there were 316 transitions for remaining mobility disability free between the Newcastle 85+  
209 Study waves, and 860 transitions for remaining with mobility disability between the study waves.

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## 212 **Results**

### 213 **Participant characteristics**

214 Of the 845 baseline participants (aged 85), most were female (62.01%, 524/845), educated for approximately  
215 9 years (mean: 9.91, standard deviation: 1.86), lived in standard housing (76.6%, 647/845), lived alone  
216 (60.9%, 462/759), were widowed (58.9%, 495/841) and had multiple long-term conditions (mean disease  
217 group count: 3.22, standard deviation: 1.85). Approximately half of the participants belonged to the 25<sup>th</sup>-75<sup>th</sup>  
218 centile Index of Multiple Deprivation (50.3%, 425/845), were of healthy weight (51.2%, 368/719) and had  
219 mobility disability (56.3%, 476/845) (Table 1). The characteristics of the baseline participants according to the  
220 number of disease groups are shown in S4 Appendix.

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**Table 1: Baseline sociodemographic and health characteristics of Newcastle 85+ participants**

	<b>% of total (n)</b>
<b>Sex</b>	100 (845)
Male	37.99 (321)
Female	62.01 (524)
<b>Education (years) (mean (SD))</b>	9.91 (1.86)
<b>Housing</b>	
Standard	76.57 (647)
Sheltered	13.37 (113)
Care home	10.06 (85)
<b>Living alone</b>	60.87 (462)
<b>Marital status</b>	
Never married	8.20 (69)
Married	30.20 (254)
Divorced/separated	2.73 (23)
Widowed	58.86 (495)
<b>Deprivation (IMD)</b>	
<25 <sup>th</sup> centile	25.21 (213)
25 <sup>th</sup> -75 <sup>th</sup> centile	50.29 (425)
>75 <sup>th</sup> centile	24.50 (207)
<b>BMI (kg/m<sup>2</sup>)</b>	
<18.5: underweight	6.54 (47)
18.5-24.99: healthy weight	51.18 (368)
25-29.99: overweight	32.82 (236)
>30: overweight and obese	9.46 (68)
<b>Mobility disability</b>	56.33 (476)
<b>Disease group count (mean (SD))</b>	3.22 (1.85)

SD = standard deviation; IMD = Index of Multiple Deprivation; BMI = body mass index  
Where numbers do not add up to 845 data are missing

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241 **Mobility disability prevalence over 10 years (from age 85-95)**

242 The prevalence of mobility disability broadly increased in the female participants through to age 95 but  
243 plateaued in the male participants from 88 years of age (36 months) (Figure 2).

244

245 **Figure 2: Prevalence of self-reported mobility disability in male and female participants from age 85-95**

246 Note: ages represent mean ages

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249 **Associations between sociodemographic/health factors and transitions between mobility disability states**  
250 **and death over 10 years**

251 For each additional disease, the risk of incident mobility disability was increased by 16% (HR 1.16, 95% CI:  
252 1.07-1.25,  $p < 0.001$ ), the chance of recovery was reduced by 26% (HR 0.74, 95% CI: 0.63-0.86,  $p < 0.001$ ),  
253 and the risk of death with mobility disability was increased by 12% (HR 1.12, 95% CI: 1.07-1.17,  $p < 0.001$ ).  
254 Female participants had a higher risk of incident mobility disability than the male participants (HR: 1.64, 95%  
255 CI: 1.25-2.14,  $p < 0.001$ ), and a lower risk of death with mobility disability (HR: 0.61, 0.52-0.72,  $p < 0.001$ ).  
256 For every annual increase in age, the risk of death with mobility disability increased by 8% (HR: 1.08, 95%  
257 CI: 1.05-1.11,  $p < 0.001$ ). Those overweight (BMI 25-29.99 kg/m<sup>2</sup>) were more likely to develop incident  
258 mobility disability than people of a healthy weight (HR: 1.51, 95% CI: 1.14-2.02,  $p < 0.05$ ) (Table 2, Model 4,  
259 adjusted for disease group count, age, sex, BMI and years in education).

260

**Table 2: Hazard ratios (HR) and 95% confidence intervals (95% CI) for transitions between mobility disability states and death**

	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>
	<b>HR (95% CI), p-value</b>	<b>HR (95% CI), p-value</b>	<b>HR (95% CI), p-value</b>	<b>HR (95% CI), p-value</b>
<b>Incident mobility disability</b>				
Disease group count	1.12 (1.04-1.22), p<0.01	1.14 (1.06-1.24), p<0.01	1.16 (1.07-1.25), p<0.001	1.16 (1.07-1.25), p<0.001
Age	1.01 (0.95-1.08), p=0.77	1.01 (0.95-1.08), p=0.17	1.02 (0.96-1.09), p=0.55	1.02 (0.96-1.09), p=0.55
Sex <sup>a</sup>	-	1.52 (1.18-1.95), p<0.01	1.67 (1.28-2.18), p<0.001	1.64 (1.25-2.14), p<0.001
BMI (kg/m <sup>2</sup> )				
<18.5: underweight	-	-	0.97 (0.60-1.57), p=0.91	0.98 (0.60-1.60), p=0.94
18.5-24.99: healthy weight	-	-	Reference	Reference
25-29.99: overweight	-	-	1.51 (1.14-1.99), p<0.05	1.51 (1.14-2.02), p<0.05
>30: overweight and obese	-	-	1.47 (0.86-2.50), p=0.16	1.47 (0.86-2.52), p=0.16
Education (years)	-	-	-	0.97 (0.82-1.14), p=0.73
<b>Recovery from mobility disability</b>				
Disease group count	0.74 (0.64-0.86), p<0.001	0.75 (0.64-0.86), p<0.001	0.74 (0.64-0.86), p<0.001	0.74 (0.63-0.86), p<0.001
Age	0.87 (0.75-1.01), p=0.07	0.86 (0.75-1.00), p=0.04	0.87 (0.75-1.01), p=0.07	0.87 (0.75-1.01), p=0.07
Sex <sup>a</sup>	-	1.10 (0.67-1.80), p=0.72	1.13 (0.69-1.86), p=0.64	1.12 (0.68-1.85), p=0.67
BMI (kg/m <sup>2</sup> )				
<18.5: underweight	-	-	0.58 (0.22-1.55), p=0.28	0.57 (0.22-1.53), p=0.26
18.5-24.99: healthy weight	-	-	Reference	Reference
25-29.99: overweight	-	-	1.51 (0.90-2.53), p=0.12	1.55 (0.92-2.61), p=0.10
>30: overweight and obese	-	-	1.05 (0.40-2.75), p=0.93	1.02 (0.38-2.71), p=0.97
Education (years)	-	-	-	0.80 (0.56-1.13), p=0.21

<b>Death with mobility disability</b>				
Disease group count	1.10 (1.06-1.15), p<0.001	1.11 (1.06-1.15), p<0.001	1.11 (1.07-1.16), p<0.001	1.12 (1.07-1.17), p<0.001
Age	1.07 (1.04-1.10), p<0.001	1.07 (1.04-1.10), p<0.001	1.07 (1.04-1.10), p<0.001	1.08 (1.05-1.11), p<0.001
Sex <sup>a</sup>	-	0.61 (0.52-0.71), p<0.001	0.61 (0.52-0.72), p<0.001	0.61 (0.52-0.72), p<0.001
BMI (kg/m <sup>2</sup> )				
<18.5: underweight	-	-	1.11 (0.85-1.44), p=0.45	1.14 (0.88-1.49), p=0.33
18.5-24.99: healthy weight	-	-	Reference	Reference
25-29.99: overweight	-	-	0.80 (0.67-0.96), p<0.05	0.81 (0.68-0.96), p<0.05
>30: overweight and obese	-	-	0.77 (0.59-1.01), p=0.06	0.79 (0.60-1.04), p=0.09
Education (years)	-	-	-	0.96 (0.87-1.07), p=0.45
<b>Death without mobility disability</b>				
Disease group count	1.04 (0.71-1.52), p=0.85	0.99 (0.69-1.42), p=0.96	0.87 (0.62-1.24), p=0.44	0.87 (0.62-1.23), p=0.43
Age	0.71 (0.45-1.11), p=0.13	0.68 (0.43-1.06), p=0.09	0.59 (0.32-1.10), p=0.09	0.60 (0.33-1.08), p=0.09
Sex <sup>a</sup>	-	0.67 (0.22-2.03), p=0.49	0.41 (0.13-1.31), p=0.13	0.42 (0.14-1.29), p=0.13
BMI (kg/m <sup>2</sup> )				
<18.5: underweight	-	-	1.29 (0.20-8.49), p=0.80	1.27 (0.20-8.06), p=0.81
18.5-24.99: healthy weight	-	-	Reference	Reference
25-29.99: overweight	-	-	0.42 (0.10-1.73), p=0.24	0.41 (0.09-1.81), p=0.25
>30: overweight and obese	-	-	0.74 (0.08-7.13), p=0.80	0.73 (0.08-6.58), p=0.79
Education (years)	-	-	-	0.86 (0.41-1.82), p=0.70

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<sup>a</sup> Male participants were the reference category

263

HR = hazard ratio; CI = confidence interval; BMI = body mass index.

264

Note: Model 1 is adjusted for disease group count and age; Model 2 is adjusted for disease group count, age and sex; Model 3 is adjusted for disease group count, age, sex and BMI; Model 4 is adjusted for disease group count, age, sex, BMI and years in education

265

266 **Association between multiple long-term conditions and mobility disability-free life expectancy in male**  
267 **and female participants at age 85 over 10 years**

268 In this study, increasing numbers of multiple long-term conditions were associated with a decrease in life  
269 expectancy (Figure 3) and an increase in the proportion of remaining time spent with mobility-disability  
270 (Figure 4).

271 At age 85, males without disease have a remaining life expectancy of 7.1 years, 4.0 years of which are spent  
272 with mobility disability and 3.1 without mobility disability. Males with 1 diagnosed disease can expect to live  
273 0.8 years less than males without disease (with their 6.3 years of remaining life comprising 3.9 years with and  
274 2.4 years without mobility disability). Further increases in multiple long-term conditions followed a similar  
275 pattern, with fewer years of remaining life spent mobility disability-free as the number of diseases  
276 increased. 85-year-old males with nine diagnosed diseases can, for example, expect to live 4.5 years less than  
277 males without disease (spending 2.1 of their remaining 2.6 years with mobility disability, and only 0.5 years  
278 without mobility disability, on average) (Figure 3). Confidence intervals for remaining life expectancy with  
279 and without mobility disability at each disease count can be found in Table 3.

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**Table 3: Point estimates with 95% confidence intervals for remaining life-expectancy (in years) spent with and without mobility disability for each disease group count, in male and female participants at age 85**

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Number of Disease Groups	Males			Females		
	mobDFLE <sup>a</sup>	mobDLE <sup>b</sup>	TLE <sup>c</sup>	mobDFLE <sup>a</sup>	mobDLE <sup>b</sup>	TLE <sup>c</sup>
None	3.1 (2.0-4.1)	4.0 (3.2-4.7)	7.1 (5.5-8.2)	2.6 (1.8-3.5)	6.1 (5.3-7.0)	8.7 (7.6-9.8)
1	2.4 (1.6-3.1)	3.9 (3.3-4.5)	6.3 (5.4-7.2)	2.0 (1.5-2.5)	5.9 (5.3-6.6)	7.9 (7.2-8.7)
2	1.9 (1.4-2.4)	3.7 (3.2-4.2)	5.6 (4.9-6.3)	1.5 (1.3-1.8)	5.6 (5.2-6.1)	7.1 (6.7-7.7)
3	1.5 (1.2-1.8)	3.5 (3.1-4.0)	5.0 (4.4-5.6)	1.1 (1.0-1.3)	5.3 (4.9-5.6)	6.4 (6.0-6.8)
4	1.2 (1.0-1.4)	3.2 (2.9-3.7)	4.4 (4.0-5.0)	0.9 (0.8-1.1)	4.9 (4.6-5.3)	5.8 (5.5-6.2)
5	1.0 (0.8-1.1)	3.0 (2.7-3.4)	4.0 (3.6-4.5)	0.7 (0.5-0.9)	4.6 (4.0-5)	5.2 (5.0-5.7)
6	0.8 (0.6-1.0)	2.8 (2.4-3.2)	3.6 (3.2-4.1)	0.5 (0.4-0.7)	4.2 (3.8-4.8)	4.8 (4.4-5.3)
7	0.7 (0.4-0.9)	2.5 (2.2-2.9)	3.2 (2.8-3.7)	0.4 (0.3-0.6)	3.9 (3.4-4.5)	4.3 (3.9-5.0)
8	0.6 (0.3-0.8)	2.3 (2.0-2.8)	2.9 (2.4-3.4)	0.4 (0.2-0.5)	3.6 (3.0-4.3)	3.9 (3.4-4.7)
9	0.5 (0.3-0.7)	2.1 (1.8-2.6)	2.6 (2.1-3.1)	0.3 (0.2-0.5)	3.3 (2.6-4.1)	3.5 (3.0-4.4)

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<sup>a</sup> mobDFLE = mobility disability-free life expectancy; <sup>b</sup> mobDLE = mobility disability life expectancy, <sup>c</sup> TLE = Total life expectancy

301 The inverse association between increasing numbers of diseases and the decrease in the proportion of  
302 remaining time spent mobility disability-free can be seen in Figure 4: males without disease spend the greatest  
303 proportion of time mobility disability-free (44%), and as the number of diseases increase this reduces, to 18%  
304 in males with nine diseases.

305 For adjacent diseases, the relationship between the number of diseases and mobDFLE was not statistically  
306 significant. However, males with 3 diseases had a statistically significantly shorter ( $p<0.05$ ) mobDFLE than  
307 males without disease (1.5 years [95% CI: 1.2-1.8] compared to 3.1 years [95% CI: 2.0-4.1]); males with 5  
308 diseases had a statistically significantly shorter ( $p<0.05$ ) mobDFLE than males with 3 diseases (1.0 years  
309 [95% CI: 0.8-1.1] compared to 1.5 years [95% CI: 1.2-1.8]), and males with 9 diseases had a statistically  
310 significantly shorter ( $p<0.05$ ) mobDFLE than males with 5 diseases (0.5 years [95% CI: 0.3-0.7] compared to  
311 1.0 years [95% CI: 0.8-1.1]) (Table 3, Figure 5).

312 A similar pattern prevailed for the female participants with one key difference: multimorbidity was associated  
313 with mobility disability to a greater extent in females than males, yet females lived longer. At age 85, females  
314 without disease have a remaining life expectancy of 8.7 years: 6.1 years of which are spent with mobility  
315 disability and 2.6 without mobility disability. Females with 1 diagnosed disease can expect to live 0.8 years  
316 less than females without disease (with their 7.9 years of remaining life comprising 5.9 years with and 2.0  
317 years without mobility disability). Further increases in multiple long-term conditions followed a similar  
318 pattern, with fewer years of remaining life spent mobility disability-free as the number of diseases increased.  
319 85-year-old females with nine diagnosed diseases can, for example, expect to live 5.1 years less than females  
320 without disease (spending 3.3 of their remaining 3.6 years with mobility disability, and only 0.3 years without  
321 mobility disability, on average) (Figure 3).

322 Females without any diseases therefore spent 30% of their remaining life mobility disability-free, and as the  
323 number of diseases increased this proportion reduced, to 8% in females with nine diseases (Figure 4).

324 Females with 2 diseases had a statistically significantly shorter ( $p<0.05$ ) mobDFLE than females without  
325 disease (1.5 years [95% CI: 1.3-1.8] compared to 2.6 years [95% CI: 1.8-3.5]); females with 4 diseases had a  
326 statistically significantly shorter ( $p<0.05$ ) mobDFLE than females with 2 diseases (0.9 years [95% CI: 0.8-1.1]  
327 compared to 1.5 years [95% CI: 1.3-3.8]), and females with 6 diseases had a statistically significantly shorter  
328 ( $p<0.05$ ) mobDFLE than females with 4 diseases (0.5 years [95% CI: 0.4-0.7] compared to 0.9 years [95% CI:  
329 0.8-1.1]) (Table 3, Figure 5).

330 **Figure 3: Remaining life-expectancy (in years) spent with and without mobility disability for each**  
331 **disease group count, in male and female participants at age 85**

332 **Figure 4: Remaining life-expectancy (as a proportion) spent with and without mobility disability for**  
333 **each disease group count, in male and female participants at age 85**

334

335 **Figure 5: Graphical representation of point estimates with 95% confidence intervals for mobility**  
336 **disability-free life-expectancy (in years) at each disease group count, in male and female participants at**  
337 **age 85**

## 338 **Discussion**

339 To the best of our knowledge, our paper is the first to explore the association between multimorbidity and  
340 transitions in mobility disability in those aged  $\geq 85$ , and to present estimates of mobDFLE at age 85 in the  
341 presence of multimorbidity. For every additional disease, the risk of incident mobility disability was  
342 increased, and the chance of recovery reduced. Female participants had a higher risk of incident mobility  
343 disability than the male participants, and a lower risk of death with mobility disability. Reductions in  
344 mobDFLE were observed with increasing numbers of multiple long-term conditions, and this association was  
345 more pronounced in the female participants.

### 346 **Comparison with existing literature**

347 Multimorbidity is the norm in those aged  $\geq 85$  [24] and is projected to increase [25]. Conceptual models of the  
348 disablement process place disease or active pathology at the start [26], and previous studies have shown that  
349 each additional chronic condition increases the risk of mobility disability [7,27]. Consistent with this, our  
350 analysis accounting for body mass index and age suggests that the increasing prevalence of mild disability  
351 amongst older people is not just a consequence of population ageing and significant reversible factors  
352 contributing to multimorbidity such as obesity, as measured by BMI [28].

353 Previous studies have shown that continued reductions in mortality at older ages will result in more years with  
354 disability [29]. Attention is now focussing more on the quality of those extra years (healthy versus unhealthy  
355 life expectancy) [29]. To date few studies have examined the effect of multimorbidity on life expectancy with  
356 and without disability [30,31], and none have examined its influence on mobDFLE in those aged  $\geq 85$ . The  
357 reductions in mobDFLE that we observed with increasing numbers of multiple long-term conditions is  
358 therefore an interesting finding of our study. What is also apparent from previous research is the profound  
359 impact of mobility disability: it increases the risk of mortality, morbidity and hospital admission; self-care  
360 disability, social isolation and depression, a poorer quality of life and loss of independence [7,32,33]. It is  
361 also a risk-factor for long-term care admission [7,32] yet most people would prefer to remain in their own  
362 homes as they age [34].

363 Regarding sex differences, females are known to live longer than males but with more disability [18]. This  
364 disability-survival paradox is still evident in people aged 85 years and over probably due to sex differences in  
365 the type and disabling impacts of diseases [18]; compared to males aged  $\geq 85$ , females this age have a higher  
366 prevalence of long-term disabling conditions, such as arthritis, and a higher risk of incident disability from  
367 certain fatal conditions, like cerebrovascular disease [18]. Our observation that multimorbidity is disabling  
368 females more than males therefore extends previous research. Females aged  $\geq 85$  are also more likely to live  
369 alone through widowhood (Table 1), and therefore potentially manage mobility disability alone and have



370 unmet needs in this regard [35], especially as informal care networks (e.g. children) are becoming more fragile  
371 for reasons including extended working life, greater female labour market participation and more  
372 geographically disparate families [36].

### 373 **Strengths and limitations**

374 The strengths of our work include the long-term follow-up of a large sample of 85-year-olds, inclusive of  
375 those living in care homes, using an established measure of mobility disability [5,17]. Multiple long-term  
376 conditions were obtained from general practice medical records, as opposed to the less reliable method of self-  
377 report [13], and we accounted for pertinent confounding factors (for example body mass index) [37]. Multi-  
378 state models also account for interval censored data, i.e., we know that transitions between mobility disability  
379 states took place between the study waves, based on multidimensional health assessment data, though not  
380 necessarily when. However, our work has limitations. It was beyond the scope of this work to examine the  
381 synergistic effects of specific combinations of diseases on mobility disability, but the literature highlights  
382 important disease pairs (such as arthritis and high blood pressure [38,39]). Furthermore, certain diseases may  
383 have had a stronger association with mobility disability than others. We might have missed episodes of  
384 intermittent disability and recovery of independence as mobility disability is a highly dynamic process in older  
385 people [40]. The possibility of residual and unmeasured confounding influencing our estimates also cannot be  
386 excluded. For example, the number of covariates that we could introduce was limited by the number of  
387 transitions; comparisons with available health assessment data show that rates of undiagnosed hypertension  
388 and ischaemic heart disease in the baseline sample were high [13], and we restricted multimorbidity to nine  
389 disease groups though the number of conditions included in studies of multimorbidity does vary widely [41].  
390 Diseases were also grouped by body systems to increase power, and as has been the case elsewhere we did not  
391 have information on disease severity [42]. In addition, we adjusted for education level instead of area-level  
392 deprivation [20], but the latter is the more complex measure. Loss to follow-up was primarily related to  
393 mortality [15] which we accounted for in our multi-state model, but we were unable to account for other  
394 losses to follow-up that were assumed to be random. Finally, in terms of generalisability, there is little ethnic  
395 diversity in the Newcastle 85+ Study [13] so our results may not apply to non-white populations. In addition,  
396 future populations who go on to reach 85-years-of age will have different diseases to those in our analytic  
397 sample (a 1912 birth cohort), as their earlier life-experiences (and subsequent health trajectories) will be  
398 different: non-exposure to the First World War aftermath, for example. Other factors such as rising levels of  
399 multimorbidity [25] will also change the makeup of subsequent inception cohorts of 85-year-olds.

### 400 **Implications and future research**

401 Our results suggest that there is no threshold beyond which multimorbidity becomes disabling in those aged  
402  $\geq 85$ , rather each additional disease group is associated with a 16% increased risk of incident mobility  
403 disability. This translates to statistically significant reductions in mobDFLE at age 85, at several disease  
404 group cut-points. Thus, multimorbidity (diagnoses in  $\geq 2$  disease groups for females and  $\geq 3$  for males)  
405 significantly shortens mobDFLE, and complex multimorbidity (diagnoses in  $\geq 4$  disease groups for females

406 and  $\geq 5$  for males) reduces this even further. In terms of implications for practice, this reinforces calls for a  
407 greater focus on the prevention of multimorbidity [43] and further accrual of disease [25] as populations age.  
408 Approaches might include a primary care system that focuses on a multi, rather than single, disease paradigm,  
409 that promotes continuity of care [44], and reducing risk factor exposure (via smoking cessation, weight and  
410 blood pressure reduction, for example) from earlier in the life course [43].

411 More time spent with mobility disability could potentially lead to greater care needs and solutions for this will  
412 be required on several levels. Firstly, maintaining independence with increasing age should be a key focus for  
413 health/social care and reablement services [45]. Secondly, our results question-whether an assessment of  
414 functional ability for older people with multimorbidity should become part of usual primary care practice,  
415 where the majority of multimorbidity management occurs, in order to proactively intervene in a timelier  
416 manner to maintain both health and independence [46,47]. Thirdly, the assessment and maintenance of  
417 physical function requires an integrated health care and social care approach [47].

418 The numbers of people aged  $\geq 85$  living with multimorbidity ( $\geq 2$  conditions) and complex multimorbidity ( $\geq 4$   
419 conditions) in particular are also projected to increase [25]. Therefore, without interventions, we can infer that  
420 there will be more people aged 85 and over living with mobility disability in the coming years, so there is a  
421 need to consider the implications of this for future health and social service provision.

422 In terms of future research, we need to better understand the most common disease clusters, how can we stop  
423 diseases A, B and C from accruing, and potentially require the integration of single-condition clinical  
424 guidelines to help prevent conditions that a patient may not yet have but is at risk of developing in the future  
425 [48]. Targeting ageing hallmarks might be another way to prevent multimorbidity, and clinical trials are  
426 underway [49]. We also need a consensus definition of multimorbidity [41] in order to synthesise evidence  
427 about a) the effects of different interventions for prevention and b) predictive factors; this will help in the  
428 development of healthcare policy around the provision of preventative services [48]. Future research could  
429 also investigate whether (and at what age) multimorbidity becomes disabling in younger populations,  
430 including those of lower socioeconomic status, given the wide health inequalities that exist between rich and  
431 poor and the well documented social patterning of multimorbidity, being more common and developing some  
432 10-15 years earlier in deprived areas compared to affluent areas [50]. Finally, studies could examine the  
433 association between individual diseases and mobility disability, adjusting for residual disease count.

#### 434 **Conclusion**

435 In summary, our findings based on an observational cohort study suggest that, in those aged  $\geq 85$ ,  
436 multimorbidity is an important determinant of mobility disability, and the number of years spent living with it.  
437 The prevention, or postponement, of multimorbidity from earlier in the life-course will thus have significant  
438 benefit to both the health and independence of people as they age, in addition to profound effects on their  
439 health and social care needs.

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446 their families and carers.

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## 592 **Supporting information files**

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- 594 • S1 Appendix: STROBE Statement—Checklist of items that should be included in reports of cohort  
595 studies
- 596 • S2 Appendix: Recruitment and retention in the Newcastle 85+ Study
- 597 • S3 Appendix: Disease group construction
- 598 • S4 Appendix: Baseline sociodemographic and health characteristics of the Newcastle 85+ participants  
599 according to the number of disease groups

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