


# BMJ Open Association between multimorbidity, self-rated health and life satisfaction among independent, community-dwelling very old persons in Japan: longitudinal cohort analysis from the Kawasaki Ageing and Well-being Project

Takayuki Ando,<sup>1</sup> Yoshinori Nishimoto,<sup>2</sup> Takumi Hirata,<sup>3</sup> Yukiko Abe,<sup>4</sup> Midori Takayama,<sup>5</sup> Takashi Maeno,<sup>6</sup> Seitaro Fujishima,<sup>1</sup> Toru Takebayashi,<sup>7</sup> Yasumichi Arai <sup>4</sup>

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For numbered affiliations see end of article.

## Correspondence to

Professor Yasumichi Arai;  
[yasumich@keio.jp](mailto:yasumich@keio.jp)

## ABSTRACT

**Objective** This study aimed to identify associations between multimorbidity and subjective health outcomes among the very old persons, after adjusting for coexisting conditions such as frailty and depression.

**Study setting and participants** This was an observational cross-sectional study involving 1012 independent, community-dwelling very old persons (507 men, 505 women; aged 85–89 years) in Kawasaki city, Japan.

**Outcome measures** The primary outcome was the cross-sectional associations between multimorbidity and poor self-rated health (SRH) and life satisfaction using binary logistic regression. The secondary outcome was the association of subjective health with each chronic condition.

**Results** The prevalence of multimorbidity ( $\geq 2$  conditions) was 94.7%, and the average number of chronic conditions was  $4.47 \pm 1.9$ . Multimorbidity was significantly associated with poor SRH in the adjusted model only when six or more chronic conditions were present (OR 4.80; 95% CI 1.34 to 17.11;  $p=0.016$ ). Cerebrovascular disease, heart disease, respiratory disease, connective tissue disease and arthritis showed significant associations with poor SRH after multivariate adjustment. Sex-specific analysis replicated associations between multimorbidity with six or more conditions and SRH in both men and women, while the diseases with the greatest impact on SRH differed between men and women. Most conditions were not associated with low satisfaction with life scale, with the exception of arthritis (OR 1.92, 95% CI 1.32 to 2.78,  $p=0.001$ ).

**Conclusions** Multimorbidity is prevalent in the independent, community-dwelling very old persons and is associated with poor SRH when six or more conditions are present; conditions causing mobility limitations, such as cerebrovascular disease, connective tissue disease and arthritis, have a negative impact on SRH.

## Strengths and limitations of this study

- The data for this study were obtained from a relatively large sample of approximately 1000 independent, community-dwelling, very old persons aged 85 years and older.
- The number of chronic diseases among the subjects was measured not only by self-report, but also by medical interviews to ensure the accuracy of the data.
- The analysis was conducted using a multivariate model that adjusted for factors that influence the health of the old, such as frailty, depression and instrumental activities of daily living.
- A stratified analysis is performed for male and female subjects to examine the effects of sex differences.
- Our inclusion criteria of only those who are independent in daily living limits the validation of the association between dementia and self-rated health.

**Trial registration number** UMIN000026053.

## INTRODUCTION

Multimorbidity, defined as the presence of two or more chronic conditions, has become increasingly common among older adults.<sup>1</sup> With the rapidly ageing global population, multimorbidity is becoming a public health priority, as it is associated with an increased risk of functional decline,<sup>2</sup> greater healthcare burden<sup>3</sup> and increased mortality.<sup>4</sup> The outcome measures in multimorbidity research include not only objective outcomes such as mortality and disability, but also subjective health outcomes such as quality

of life, well-being and self-rated health (SRH).<sup>5</sup> SRH is an important measure of a person's physical and psychological state, which can be surveyed with a simple question, 'How is your health now?' SRH has been reported to be associated with physical functioning, well-being and mortality in various countries and ages.<sup>6–10</sup> A cohort study of postmidlife populations indicated that multimorbidity is associated with a decline in subjective health.<sup>11</sup> Multimorbidity is recognised as a public health burden in Japan's rapidly ageing society, in which life expectancy is over 80 years. The prevalence of multimorbidity is reported to increase with age, reaching 65% at 65 years and nearly 100% at 85 years.<sup>12–14</sup> The prevalence of frailty also increases with age, and the effects of the two conditions on physical and mental health overlap. It has been reported that poor SRH and grip strength are associated with multimorbidity in the older Japanese population, suggesting that multimorbidity is linked to frailty and affects subjective health.<sup>15</sup> However, little is known about the extent to which multimorbidity independently affects health and well-being in the very old persons. This study aimed to clarify the impact of multimorbidity on subjective health outcomes in very old persons aged >85 years, adjusting for frailty, depression and other potential confounders. In order to clarify the impact of each chronic condition on SRH and life satisfaction within the context of multimorbidity, a condition-specific analysis was also conducted.

## METHODS

### Study design and data source

The Kawasaki Ageing and Well-being Project (KAWP) is an ongoing longitudinal cohort study aiming to observe a decline of independence in very old persons who are physically independent at baseline. The inclusion criteria for the KAWP are as follows: (1) be a resident of Kawasaki city, a city with a population of 1.5 million, located in the Greater Tokyo Area and aged 85–89 years, (2) have no limitations related to basic activities of daily living (ADLs) and (3) able to visit the study site and the Kawasaki Municipal Hospitals independently.<sup>16</sup> Between March 2017 and December 2018, we identified 9978 eligible individuals from the residential registry and long-term care insurance in collaboration with the Kawasaki Municipality. We sent an invitation letter to all of these individuals, and 1464 responded expressing their willingness to participate in the KAWP survey. Among the positive responders, 438 (16; not meeting inclusion criteria, 83; unable to telephone contact, 99; acute illness, 139; declined after telephone instruction, 68; unable to consent, 21; family circumstances, 12; unknown) were excluded, thus a total of 1026 individuals (513 men and 513 women) were examined at one of three Kawasaki Municipal Hospitals (Kawasaki, Ida or Tama) and enrolled in the KAWP. In the current study, we excluded 14 participants with missing values in the past and present medical history, and 1012 were included in the final analysis. Written informed

consent to participate in the KAWP was obtained from all participants.

### Assessment

The assessment questionnaires of the KAWP were designed to harmonise with the Tokyo Oldest Old Survey on Total Health<sup>17</sup> and Japan Semi-supercentenarian Study,<sup>18</sup> both of which are managed by the Center for Supercentenarian Medical Research, Keio University School of Medicine. The questionnaire included socio-economic status; previous medical histories and present medical conditions; current medication use; and various lifestyle factors including smoking, alcohol consumption, and physical and cognitive function. For the assessment, all the participants were interviewed and examined directly by experienced physicians. The past and present medical diagnoses included 18 categories: cerebrovascular disease, cardiac disease, hypertension, diabetes, dyslipidaemia, respiratory disease, gastrointestinal disease, renal disease, prostate disease, thyroid disease, Parkinson's disease, connective tissue disease, eye disease, osteoporosis, arthritis, hyperuricaemia, malignancy and dementia (online supplemental table 1). Instrumental ADL (IADLs) were assessed using the Lawton scale (0–5 points),<sup>19</sup> cognitive function was evaluated using the Mini-Mental State Examination (MMSE; 0–30 points),<sup>20</sup> and depression was assessed using the Geriatric Depression Scale (GDS-15).<sup>21</sup> Independent IADL was defined as a score of 5 points on the Lawton Scale. Frailty was evaluated using the Japanese version of the Cardiovascular Health Study (J-CHS) criteria. (0: robust, 1–2: prefrail, and 3–5: frail). Results of the GDS-15 were classified into three categories: 0–4, 5–9, and 10–15 indicated normal, mild depression, depression, respectively.<sup>22 23</sup>

### Outcome

Both SRH and life satisfaction were selected as the main outcomes. SRH was evaluated by asking, 'How is your health in general?'. The response option was a five-point Likert scale, with 1 denoting very healthy and 5 denoting very unhealthy. The main outcome was poor SRH, which was defined as poor (a score of 4) or very poor (a score of 5). We used the Satisfaction with Life Scale (SWLS) as a measure of life satisfaction, which consists of five questions with seven possible rating options. The scores ranged from 5 to 35, with high scores reflecting high satisfaction.<sup>24</sup> An SWLS score <20 indicated poor life satisfaction.<sup>25</sup>

### Statistical analysis

Baseline characteristics were expressed as means±SD or medians and IQRs; categorical variables were shown as numbers and proportions. Age, sex, current drinking history, current smoking history, body mass index, IADL, education (high school graduation or higher), frailty (J-CHS criteria),<sup>26</sup> depression (GDS-15), and number of chronic conditions were considered independent variables. IADL, frailty and GDS were analysed as categorical

variables. We conducted univariate and multivariate logistic regression analyses to examine the association between multimorbidity and subjective health outcomes. We also performed a multivariable logistic regression analysis to examine the independent association between subjective health outcomes and each chronic condition with *p* values of <0.10 in the univariate analysis. We reported unadjusted and adjusted ORs and 95% CIs for poor SRH and poor life satisfaction. Supplementary analyses by stratification by sex were also performed to examine the interaction effect of sex and multimorbidity. All analyses were conducted using SPSS V.27 software (SPSS), and the results were considered statistically significant at a two-sided *p*<0.05.

### Patient and public involvement

Participants (healthy older adults) and/or the public were not involved in the design, or conduct, or reporting of this study. To disseminate the results of this research,

Kawasaki City and Keio University have been holding an annual public lecture since 2017, to which the participants are invited.

## RESULTS

The characteristics of the participants are displayed in [table 1](#). Most participants (86.5%) were independent of IADLs, and 13.2% met the J-CHS criteria of frailty. Further, 85.4% rated their health as moderate to very good. The mean MMSE score was 26.04, and 16.4% of the participants had an MMSE score of ≤23. The mean SWLS score was 24.95, and 70.2% scored ≥20 points. In addition, 26.9% of the participants had a GDS score of ≥5, which suggests the presence of depressive mood or depression.

A histogram of chronic conditions is shown in [figure 1](#). The prevalence of multimorbidity (two or more conditions) was 94.7%, and the average number of chronic conditions was 4.47±1.94. [Figure 2](#) indicates the prevalence of each condition. Eye disease (75.5%), hypertension (64.1%) and gastrointestinal disease (60.0%) were the most prevalent conditions, while Parkinson's disease (0.3%), dementia (2.5%) and connective tissue disease (3.2%) were rare in our very old cohort. The sex-specific prevalence of chronic conditions is shown in online supplemental figure 1. The prevalence of hypertension and gastrointestinal diseases did not show much difference between the sexes. Dyslipidaemia, osteoporosis, thyroid disease, arthritis and eye disease were prevalent in female participants, while hyperuricaemia, cerebrovascular disease, cardiovascular disease, respiratory disease and malignancy were prevalent in male participants.

### Factors associated with SRH and life satisfaction

[Table 2](#) presents the results of the univariate and multivariate logistic regression analyses. IADL, frailty, depression and multimorbidity were associated with poor SRH in both the unadjusted and adjusted models. As the

**Table 1** Characteristics of study participants and mean number of chronic conditions

	Total (n=1012)	No of chronic conditions, mean (SD)
Age, mean(SD)	86.57 (1.37)	
Sex, n(%)		
male	507 (50.1)	4.55 (2.01)
female	505 (49.9)	4.39 (1.87)
BMI, n(%)		
<18.5	62 (6.1)	3.98(1.79)
18.5–24.689	681 (67.3)	4.43 (1.92)
≥25.0	269 (26.6)	4.71 (2.02)
Smoking, n(%)		
Current	41 (4.1)	3.98 (1.92)
Past	382 (37.7)	4.73 (1.91)
Never	587 (58.0)	4.35 (1.95)
Drinking, n(%)		
Current	404 (39.9)	4.38 (1.91)
Past	159 (15.7)	4.76 (2.17)
Never	448 (44.3)	4.46 (1.89)
IADL independent, n(%)		
independent	875 (86.5)	4.64 (1.83)
dependent	136 (13.4)	4.45 (1.96)
Education, n(%)		
≥12 years	460 (45.5)	4.46 (1.83)
<12 years	552 (54.5)	4.49 (2.07)
Frailty, n(%)		
Robust	162 (16.0)	4.65 (1.82)
Prefrail	698 (69.0)	4.41 (1.95)
Frail	134 (13.2)	4.58 (1.95)
MMSE, n(%)		
≥24	842 (83.2)	4.51 (1.94)
0–23	166 (16.4)	4.28 (1.98)
Self-rated health, n(%)		
Very good	73 (7.2)	3.38 (1.69)
Good	336 (33.2)	4.43 (1.76)
Moderate	455 (45.0)	4.27 (1.90)
Poor	134 (13.2)	5.68 (1.96)
Very poor	9 (0.9)	7.11 (2.57)
SWLS, n(%)		
30–35	188 (18.6)	4.06 (2.0)
25–29	262 (25.9)	4.54 (1.8)
20–24	260 (25.7)	5.52 (2.0)
15–19	92 (9.1)	4.67 (2.1)
10–14	15 (1.5)	5.13 (1.9)
5–9	9 (0.9)	5.11 (1.8)

Continued

**Table 1** Continued

	Total (n=1012)	No of chronic conditions, mean (SD)
GDS, n(%)		
0–4	736(72.7)	4.37 (1.9)
5–9	234 (23.1)	4.75 (1.8)
10–15	38 (3.8)	4.68 (2.4)

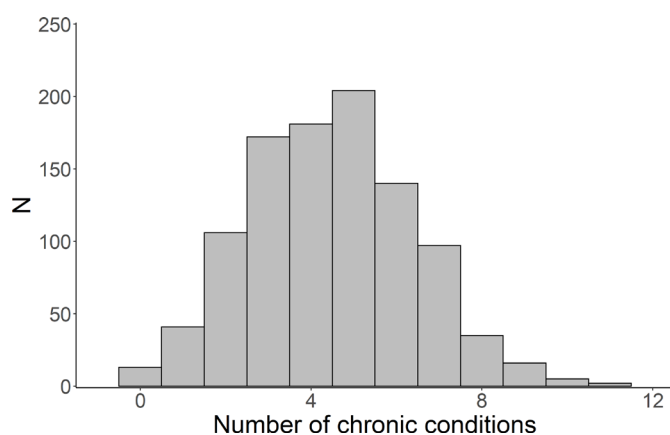
BMI, body mass index; GDS, Geriatric Depression Scale; IADL, Instrumental activities of daily living; MMSE, Mini-Mental State Examination; SWLS, Satisfaction with Life Scale.

number of co-occurring chronic conditions increased, subjective health tended to be impaired and having six or more conditions was statistically significantly associated with poor SRH even after adjustment for other variables including depression. When the number of co-occurring conditions was six, compared with zero or one, the OR for impaired SRH was 4.80 (95% CI 1.34 to 17.11,  $p=0.016$ ) in the adjusted model.

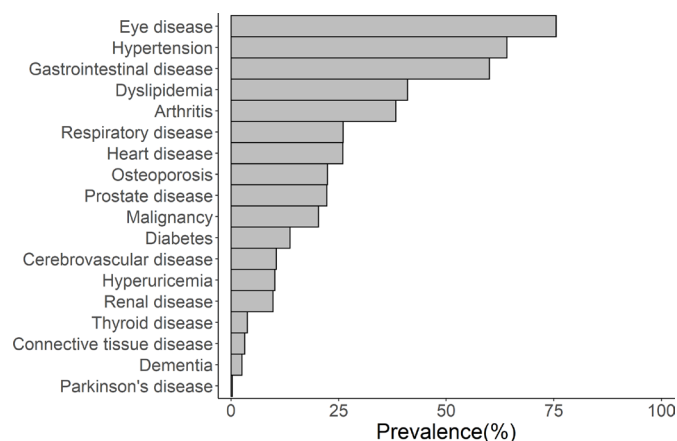
High BMI, smoking and frailty were associated with low SWLS in the unadjusted model, but the association disappeared in the adjusted model. No association was observed between multimorbidity and low SWLS, even in the presence of nine or more conditions. Only depression was associated with low SWLS in the adjusted model.

### Type of conditions and subjective health outcomes

Table 3 shows the association of each condition with subjective health outcomes. Cerebrovascular disease, heart disease, respiratory disease, connective tissue disease and arthritis showed significant associations with poor SRH after adjustment. Connective tissue disease had the highest OR (OR 3.21; 95% CI 1.19 to 8.66,  $p=0.021$ ), followed by cerebrovascular disease (OR 2.68; 95% CI 1.51 to 4.78,  $p<0.001$ ). Most of the conditions were not associated with low SWLS, but arthritis exhibited a statistically significant association (OR 1.92; 95% CI 1.32 to 2.78;  $p<0.001$  in the adjusted model).



**Figure 1** Histogram of the number of comorbid chronic conditions. N, number of participants.



**Figure 2** Prevalence of each chronic condition among study population.

The sex-specific analyses showed a similar trend of impaired SRH as the number of chronic conditions increased, although the confidence intervals were wider due to the limited sample size (online supplemental table 2). There was no association between the number of chronic conditions and life satisfaction in the separate analyses for male and female participants. In the disease-specific analyses, the diseases with the greatest impact on SRH differed between men and women. In men, cerebrovascular disease, gastrointestinal disease, respiratory disease, and arthritis had a significant association. In females, hyperuricaemia, cerebrovascular disease, arthritis and malignancy were associated with poor SRH. Meanwhile, few conditions were associated with low life satisfaction in both sexes. In the multivariable-adjusted model, gastrointestinal diseases in men and arthritis in women were associated with low life satisfaction (online supplemental table 3).

### DISCUSSION

With the ageing global population, the prevalence of multimorbidity has increased in various countries.<sup>13 27</sup> Although the prevalence varies by definition of multimorbidity, previous studies have demonstrated that the prevalence of multimorbidity increases with age and is reported to be nearly 100% among patients aged  $\geq 85$  years.<sup>13 14 28</sup> This study revealed that multimorbidity is very common even in a population of physically independent very old community-dwelling persons. The presence of six or more conditions was associated with poor SRH in this population, and the odds increased with the number of conditions. Multimorbidity has been defined by WHO as the presence of two or more chronic health conditions.<sup>29</sup> Since multimorbidity is the norm among the very old persons, our results suggest that those who have six or more chronic conditions need to be monitored closely in clinical settings, particularly with regard to poor subjective health.

Our findings are consistent with those of past studies reporting that depression impairs subjective health.<sup>30–32</sup>



**Table 2** OR of baseline characteristics on poor self-rated health and low life satisfaction

	Poor Self-rated health				Low life satisfaction			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	0.93 (0.81 to 1.06)	0.255	0.88 (0.76 to 1.03)	0.118	0.95 (0.84 to 1.08)	0.446	0.95 (0.83 to 1.09)	0.456
Sex	0.73 (0.51 to 1.04)	0.085	0.73 (0.47 to 1.13)	0.155	0.89 (0.64 to 1.24)	0.494	0.90 (0.60 to 1.33)	0.588
<b>BMI</b>								
<18.5	0.98 (0.47 to 2.06)	0.964	1.28 (0.53 to 3.08)	0.582	0.77 (0.36 to 1.64)	0.498	0.78 (0.34 to 1.77)	0.548
18–25	Reference		Reference		Reference		Reference	
25≤	0.85 (0.56 to 1.29)	0.441	0.73 (0.45 to 1.18)	0.198	0.60 (0.39 to 0.91)	0.016	0.64 (0.41 to 1.00)	0.050
Current drinking	0.88 (0.61 to 1.27)	0.489	1.05 (0.68 to 1.64)	0.811	0.95 (0.67 to 1.34)	0.774	1.04 (0.70 to 1.55)	0.847
Current smoking	1.25 (0.54 to 2.88)	0.595	0.88 (0.33 to 2.39)	0.808	2.98 (1.49 to 5.94)	0.002	1.83 (0.83 to 4.03)	0.136
Education (<12 years)	1.18 (0.82 to 1.68)	0.375	1.29 (0.84 to 1.98)	0.243	1.14 (0.82 to 1.59)	0.440	1.17 (0.80 to 1.72)	0.417
IADL (dependent)	2.13 (1.36 to 3.32)	0.001	1.83 (1.09 to 3.08)	0.023	0.72 (0.42 to 1.25)	0.244	0.62 (0.34 to 1.13)	0.117
<b>Frailty</b>								
Robust	Reference		Reference		Reference		Reference	
Prefrail	1.07 (0.63 to 1.82)	0.799	1.05 (0.60 to 1.87)	0.856	1.26 (0.77 to 2.06)	0.363	1.19 (0.71 to 2.01)	0.506
Frail	2.16 (1.15 to 4.04)	0.016	1.57 (0.77 to 3.19)	0.215	1.99 (1.08 to 3.69)	0.027	1.33 (0.68 to 2.61)	0.405
<b>GDS</b>								
0–4	Reference		Reference		Reference		Reference	
5–9	2.66 (1.80 to 3.93)	<0.001	2.41 (1.55 to 3.75)	<0.001	3.12 (2.12 to 4.57)	<0.001	2.90 (1.92 to 4.40)	<0.001
10–15	6.57 (3.30 to 13.06)	<0.001	6.90 (2.97 to 16.04)	<0.001	11.22 (4.90 to 25.72)	<0.001	13.93 (5.48 to 35.42)	<0.001
<b>No of chronic conditions</b>								
0–1	Reference		Reference		Reference		Reference	
2	0.36 (0.08 to 1.69)	0.197	0.53 (0.10 to 2.85)	0.463	0.69 (0.28 to 1.69)	0.416	0.80 (0.30 to 2.13)	0.657
3	0.94 (0.29 to 3.06)	0.923	1.53 (0.40 to 5.80)	0.534	0.72 (0.32 to 1.65)	0.437	0.77 (0.32 to 1.88)	0.566
4	1.23 (0.39 to 3.84)	0.725	1.49 (0.40 to 5.59)	0.551	0.90 (0.40 to 2.03)	0.805	0.89 (0.37 to 2.16)	0.795
5	1.91 (0.64 to 5.71)	0.248	2.45 (0.69 to 8.73)	0.166	1.06 (0.48 to 2.34)	0.877	0.94 (0.40 to 2.22)	0.884
6	3.30 (1.10 to 9.88)	0.033	4.80 (1.34 to 17.11)	0.016	0.88 (0.38 to 2.04)	0.763	0.95 (0.38 to 2.38)	0.921
7	4.82 (1.59 to 14.64)	0.006	6.42 (1.76 to 23.33)	0.005	0.91 (0.37 to 2.22)	0.830	0.77 (0.29 to 2.07)	0.604
8	6.82 (1.98 to 23.51)	0.002	10.68 (2.58 to 44.26)	0.001	1.53 (0.53 to 4.40)	0.430	1.70 (0.54 to 5.37)	0.362

Continued

**Table 2** Continued

	Poor Self-rated health				Low life satisfaction			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
9 or more	16.25 (4.38 to 60.24)	<0.001	37.75 (8.29 to 171.92)	<0.001	1.70 (0.51 to 5.69)	0.389	2.21 (0.58 to 8.45)	0.247

BMI, body mass index; GDS, Geriatric Depression Scale; IADL, instrumental activities of daily living.

It has been reported that depressive symptoms are associated with an increase in the number of comorbidities.<sup>33</sup> Depression is also known to increase non-suicidal mortality in the old population,<sup>34</sup> so it is important to evaluate the presence of depression when treating patients with multimorbidity. In our study, multimorbidity was associated with poor SRH, independent of depression, frailty and IADL. This suggests that multimorbidity affects subjective health not only via depression or physical disability but via its own pathogenesis. In the patient-centred clinical method model, patient perception of a health issue is described

as ‘illness’, and perception of ‘health’ is described as the patients’ ability to realise aspirations and purpose in their lives.<sup>35</sup> It is not clear whether each condition causes symptoms or disability and impairs health. The combination of multiple chronic conditions affects patients’ health in a complicated manner by affecting patients’ perception of chronic condition complex and their life purpose. To understand this complexity, social and spiritual aspects need to be considered in multimorbidity research.

This study did not show an association between multimorbidity and life satisfaction. There are several

**Table 3** Effect of each chronic condition on poor self-rated health and low life satisfaction

	Poor self-rated health				Low life satisfaction			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Hypertension	1.47 (0.99 to 2.16)	0.053	1.41 (0.86 to 2.31)	0.178	0.94 (0.67 to 1.33)	0.721	–	–
Diabetes	1.39 (0.86 to 2.25)	0.181	–	–	1.18 (0.73 to 1.90)	0.493	–	–
Dyslipidaemia	1.63 (1.15 to 2.33)	0.007	1.28 (0.82 to 2.02)	0.281	0.96 (0.69 to 1.36)	0.836	–	–
Hyperuricaemia	2.07 (1.25 to 3.43)	0.005	1.88 (0.99 to 3.60)	0.056	1.15 (0.68 to 1.96)	0.601	–	–
Cerebrovascular disease	3.42 (2.17 to 5.39)	<0.001	2.68 (1.51 to 4.78)	<0.001	1.22 (0.72 to 2.08)	0.463	–	–
Parkinson's disease	3.03 (0.27 to 33.65)	0.366	–	–	1.86 (0.17 to 20.66)	0.613	–	–
Dementia	0.58 (0.13 to 2.49)	0.461	–	–	0.45 (0.10 to 2.00)	0.296	–	–
Heart disease	2.00 (1.38 to 2.90)	<0.001	1.69 (1.05 to 2.72)	0.030	0.86 (0.58 to 1.27)	0.439	–	–
Respiratory disease	2.35 (1.63 to 3.39)	<0.001	2.04 (1.29 to 3.24)	0.002	1.09 (0.75 to 1.59)	0.662	–	–
Gastrointestinal disease	1.72 (1.17 to 2.53)	0.006	1.62 (1.00 to 2.64)	0.051	1.24 (0.88 to 1.76)	0.216	–	–
Renal disease	1.96 (1.17 to 3.27)	0.010	1.52 (0.79 to 2.91)	0.208	1.17 (0.67 to 2.05)	0.573	–	–
Thyroid disease	1.94 (0.90 to 4.20)	0.091	2.16 (0.85 to 5.48)	0.105	1.76 (0.84 to 3.66)	0.132	–	–
Connective tissue disease	2.88 (1.33 to 6.21)	0.007	3.21 (1.19 to 8.66)	0.021	2.76 (1.20 to 6.32)	0.017	2.11 (0.82 to 5.43)	0.121
Osteoporosis	1.53 (1.02 to 2.28)	0.040	1.65 (0.93 to 2.91)	0.087	1.01 (0.67 to 1.52)	0.969	–	–
Arthritis	2.41 (1.68 to 3.46)	<0.001	2.41 (1.55 to 3.76)	<0.001	1.75 (1.25 to 2.46)	0.001	1.92 (1.32 to 2.78)	<0.001
Eye disease	1.35 (0.87 to 2.10)	0.183	–	–	0.76 (0.52 to 1.10)	0.143	–	–
Prostate disease	1.43 (0.96 to 2.14)	0.078	0.86 (0.48 to 1.56)	0.623	1.10 (0.76 to 1.65)	0.567	–	–
Malignancy	1.48 (0.98 to 2.23)	0.064	1.47 (0.90 to 2.40)	0.125	1.35 (0.91 to 2.02)	0.140	–	–

The adjusted models include age, sex, current drinking, current smoking, BMI, IADL, education (high school graduation or higher), frailty and depression.

BMI, body mass index; IADL, instrumental activities of daily living.

explanations for this. For example, one of the items in the SWLS involves an implicit reference to the past, meaning it might be a long-term psychometric data. Older people who were satisfied with their lives when they were young may score high on the SWLS even if they were not satisfied with their current state with multimorbidity. The SWLS has been validated in many countries, but some components of the SWLS vary across countries.<sup>36</sup> For instance, Asian people tend to value social connections rather than individual achievement.<sup>37</sup> In this study, social connection or social participation was not considered, which might have masked the impact of multimorbidity on life satisfaction. Furthermore, the impact of multimorbidity on life satisfaction is reported to be small in older adults with independent ADLs.<sup>38</sup> Longitudinal follow-up surveys of this cohort are needed to address the potential effects of disability on life satisfaction, as our participants become older and frail.

In the condition-specific analysis, we found a correlation with poor SRH in conditions that are likely to cause symptoms and functional limitations in daily life. Cerebrovascular disease, heart disease and arthritis are associated with mobility limitation and are subsequently linked to long-term care dependency. Respiratory diseases such as chronic obstructive pulmonary disease are typical chronic symptomatic conditions in the very old persons. Dementia tended to be associated with poor SRH, but the correlation was not statistically significant. This could result from the small number of participants with dementia in our cohort, but previous studies in patients with dementia have also shown an inconsistent association between SRH and mortality.<sup>39 40</sup> Studies investigating the structure of SRH in the very old persons have shown that the influence of disease on SRH differs with the existence of dementia.<sup>41</sup> Because patients with dementia may have a different awareness of their condition, the impact of multimorbidity on subjective health and well-being could be different. Future studies with people with various degree of dementia and cognitive impairment are warranted to examine the actual association between multimorbidity and SRH.

### Study limitations

Due to the nature of the cross-sectional study, inferences could not be determined on the causality of the relationship. Although we obtained medical history via physician-led interviews, the accuracy might have been limited because this strategy depends on the participant's memory. The accuracy could be improved with the use of information regarding the number of conditions by referring to medical records and medical claim data. The prevalence of dementia and disability was relatively low in this study because we enrolled community-dwelling and physically independent people. Thus, the generalisability of our findings is limited. The strength of this study is that we included a relatively large sample size of very old persons aged  $\geq 85$  years. Our comprehensive assessment allowed us to examine the associations

between multimorbidity and subjective health adjusted for a spectrum of coexisting conditions from frailty and physical function to depression. Future studies involving follow-up of this cohort will allow a comparison of the predictive power of multimorbidity, frailty and depression for predicting incident disability and mortality.

Several studies have reported different effects of subjective health perception and mortality in males and females.<sup>42 43</sup> It has been reported that females tend to estimate their own health lower than males, and males tend to place more emphasis on physical functioning.<sup>44 45</sup> In our study, there was no difference in subjective health perceptions between the sexes, but some conditions may influence subjective health perceptions differently in males and females. Further research is needed to reveal the process by which each condition affects subjective health perception and mortality in males and females.

In conclusion, our results demonstrate that multimorbidity, defined as having two or more chronic conditions, is prevalent (94.7%) in the independent, very old community-dwelling persons. Multimorbidity was associated with poor SRH when six or more conditions were present, and stroke and arthritis may have strong impacts. Our study contributes to the current knowledge of the psychometric impact of multimorbidity in the very old persons, whose primary care physicians are expected to play an increasingly important role in the maintenance of health and well-being.

### Author affiliations

<sup>1</sup>Center for General Medicine Education, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan

<sup>2</sup>Department of Neurology, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan

<sup>3</sup>Department of Public Health, Hokkaido University Graduate School of Medicine, Sapporo, Hokkaido, Japan

<sup>4</sup>Center for Supercentenarian Medical Research, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan

<sup>5</sup>Faculty of Science and Technology, Keio University, Yokohama, Kanagawa, Japan

<sup>6</sup>Graduate School of System Design and Management, Keio University, Yokohama, Kanagawa, Japan

<sup>7</sup>Department of Preventive Medicine and Public Health, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan

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## ORCID iD

Yasumichi Arai <http://orcid.org/0000-0003-1746-965X>

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## Supplementary Material

Supplementary Figure1:

Sex difference in prevalence of each chronic condition.

Supplementary Table 1:

Classification of 18 conditions and the corresponding ICD-10 codes.

Supplementary Table 2a:

Odds ratio of baseline characteristics on poor self-rated health in female and male participants.

Supplementary Table 2b:

Odds ratio of baseline characteristics on low life satisfaction in female and male participants.

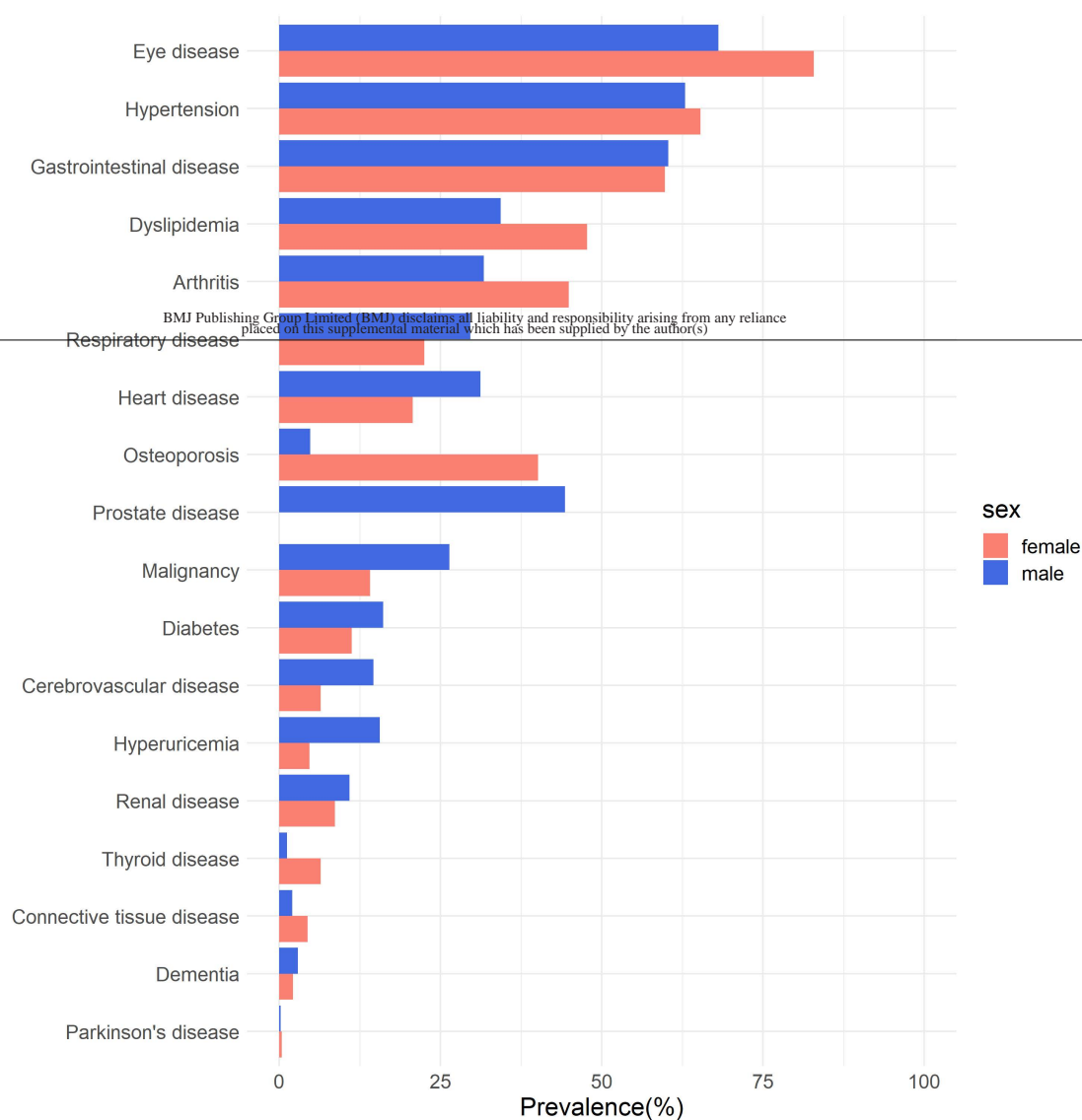
Supplementary Table 3a:

Condition specific effect on poor self-rated health in female and male participants.

Supplementary Table 3b:

Condition specific effect on low life satisfaction in female and male participants.

Supplementary Figure 1. Sex difference in prevalence of each chronic condition.



Following conditions showed statistically significant differences between the sexes in the chi-square test: diabetes, dyslipidemia, hyperuricemia, cerebrovascular disease, heart disease, respiratory disease, thyroid disease, connective tissue disease, osteoporosis, arthritis, eye disease and malignancy.

Supplementary Table 1. Classification of 18 conditions and the corresponding ICD-10 codes.

Classification	Example	ICD-10 codes
Cerebrovascular disease	Ischemic stroke, intracranial bleeding, transient ischemic attack, subdural hematoma	I60-I69
Cardiac disease	Heart failure, angina, myocardial infarction, atrial fibrillation, valvular disease	I20-I25
Hypertension	Essential hypertension	I10-I15
Diabetes	Type2 diabetes mellitus,	E10-14
Dyslipidemia	Hyperlipidemia, hypertriglycemia	E78
Respiratory disease	Asthma, COPD, Tuberculosis	A15-16, J40-47, J60-7, J80-84,
Gastrointestinal disease	Gastroesophageal reflux disease, gastritis, peptic ulcer disease, hepatitis,	K20-K31, K35-K38, K40-K46, K50-K52, K55-K64, K70-K77, K80-K87, K90-K93,
Renal disease	Chronic kidney disease, End stage renal disease, Nephritis	N00-N08, N10-N16, N17-N19, N25-N29
Prostate disease	Benign prostate hyperplasia	N40-N51
Thyroid disease	Hyperthyroidism(Grave's disease), Hypothyroidism(Hashimoto's disease)	E00-E07
Parkinson's disease		G20-G22
Connective tissue disease	Rheumatoid arthritis, Systemic Lupus Erythematosus,	M05-M14, M30-M36,
Eye disease	Glaucoma, Cataract, Dry eye	H10-H13, H15-H22, H25-H28, H30-H36, H40-H59
Osteoporosis	Postmenopausal osteoporosis	M80-M82
Arthritis	Osteoarthritis	M15-M19
Hyperuricemia	Asymptomatic hyperuricemia, Gout	E79, M10
Malignancy	Any kinds of malignancy	C00-C97
Dementia	Alzheimer's disease, Dementia with Lewy Bodies	F00-F03



Supplementary Table 2a. Odds ratio of baseline characteristics on poor self-rated health in female and male participants.

	Poor Self-rated health							
	female				male			
	unadjusted		adjusted		unadjusted		adjusted	
	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value
Age	0.85(0.69-1.04)	0.115	0.81(0.64-1.04)	0.096	1.00(0.84-1.19)	0.966	0.96(0.78-1.18)	0.714
BMI								
<18.5	1.05(0.42-2.63)	0.913	0.98(0.32-3.03)	0.971	0.98(0.28-3.47)	0.973	1.45(0.35-6.03)	0.610
18-25	Reference		Reference		Reference		Reference	
25≤	0.63(0.32-1.26)	0.195	0.67(0.30-1.49)	0.328	1.01(0.59-1.72)	0.975	0.77(0.41-1.44)	0.413
Current Drinking	0.94(0.50-1.77)	0.838	1.24(0.60-2.55)	0.559	0.69(0.43-1.12)	0.135	0.95(0.54-1.67)	0.853
Current Smoking	3.63(0.65-20.26)	0.141	1.10(0.10-12.77)	0.938	0.86(0.32-2.29)	0.762	0.77(0.25-2.37)	0.646
Education (<12 years)	1.05(0.60-1.85)	0.853	1.43(0.71-2.87)	0.318	1.45(0.90-2.33)	0.128	1.45(0.82-2.55)	0.203
IADL( Dependent)	1.75(0.90-3.43)	0.101	1.52(0.66-3.50)	0.320	2.57(1.41-4.68)	0.002	2.36(1.18-4.75)	0.016
Frailty								
Robust	Reference		Reference		Reference		Reference	
Prefrail	2.64(0.92-7.58)	0.072	3.37(1.06-10.72)	0.040	0.64(0.34-1.22)	0.180	0.51(0.25-1.05)	0.066
Frail	5.13(1.59-16.63)	0.006	5.70(1.52-21.37)	0.010	1.32(0.60-2.90)	0.485	0.70(0.27-1.79)	0.453
GDS								
0-4	Reference		Reference		Reference		Reference	
5-9	3.72(2.10-6.62)	<0.001	3.36(1.71-6.63)	<0.001	1.98(1.16-3.39)	0.013	2.01(1.08-3.75)	0.028
10-15	5.93(1.90-18.52)	0.002	4.20(0.97-18.12)	0.055	6.56(2.73-15.77)	<0.001	9.32(3.02-28.76)	<0.001
Number of chronic conditions								
0-1	Reference		Reference		Reference		Reference	
2	0.18(0.02-2.07)	0.168	0.36(0.03-4.42)	0.425	0.66(0.09-4.94)	0.685	0.71(0.05-9.14)	0.792
3	1.02(0.20-5.19)	0.977	1.64(0.30-9.01)	0.567	0.75(0.13-4.34)	0.751	1.46(0.15-14.03)	0.742
4	1.02(0.20-5.19)	0.977	1.06(0.19-6.04)	0.950	1.43(0.29-7.14)	0.661	2.37(0.27-20.49)	0.433
5	0.87(0.17-4.37)	0.862	1.15(0.20-6.50)	0.872	3.44(0.75-15.71)	0.110	5.27(0.65-42.45)	0.118
6	1.78(0.36-8.80)	0.480	2.69(0.50-14.61)	0.252	5.40(1.17-24.86)	0.030	9.13(1.12-74.41)	0.039
7	4.34(0.88-21.49)	0.072	7.43(1.35-40.93)	0.021	5.30(1.13-25.00)	0.035	7.51(0.90-62.67)	0.062
8	8.17(1.41-47.22)	0.019	12.32(1.90-79.71)	0.008	5.58(0.95-32.59)	0.056	7.72(0.75-79.93)	0.087
9 or more	15.75(2.30-107.93)	0.005	27.86(3.54-218.99)	0.002	16.92(2.79-102.40)	0.002	59.41(5.41-652.67)	0.001

Abbreviations: OR, Odds ratio; CI, Confidence interval; IADL, Instrumental activities of daily living; GDS, Geriatric Depression Scale

Supplementary Table 2b. Odds ratio of baseline characteristics on low life satisfaction in female and male participants.

	Low life satisfaction							
	female				male			
	unadjusted		adjusted		unadjusted		adjusted	
	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value
Age	0.83(0.69-0.99)	0.042	0.82(0.66-1.02)	0.071	1.08(0.92-1.28)	0.344	1.06(0.87-1.27)	0.576
BMI								
<18.5	0.24(0.05-1.01)	0.052	0.10(0.01-0.86)	0.036	2.25(0.83-6.15)	0.112	2.56(0.86-7.64)	0.091
18-25	Reference		Reference		Reference		Reference	
25≤	0.60(0.33-1.12)	0.107	0.70(0.36-1.38)	0.304	0.59(0.33-1.05)	0.072	0.64(0.34-1.21)	0.169
Current Drinking	0.72(0.39-1.33)	0.292	0.77(0.39-1.51)	0.447	1.04(0.65-1.65)	0.882	1.20(0.71-2.04)	0.501
Current Smoking	2.71(0.45-16.49)	0.279	0.25(0.01-6.73)	0.409	2.96(1.38-6.35)	0.005	1.96(0.83-4.63)	0.124
Education (<12 years)	1.03(0.63-1.70)	0.897	1.17(0.64-2.14)	0.602	1.31(0.82-2.08)	0.253	1.12(0.66-1.91)	0.664
IADL( Dependent)	0.76(0.35-1.62)	0.469	1.68(0.71-3.99)	0.240	0.70(0.31-1.54)	0.372	1.66(0.68-4.03)	0.265
Frailty								
Robust	Reference		Reference		Reference		Reference	
Prefrail	1.10(0.55-2.20)	0.779	0.99(0.47-2.09)	0.986	1.42(0.70-2.87)	0.331	1.13(0.52-2.43)	0.764
Frail	1.96(0.81-4.72)	0.135	1.53(0.57-4.12)	0.401	2.04(0.86-4.81)	0.105	1.18(0.44-3.15)	0.737
GDS								
0-4	Reference		Reference		Reference		Reference	
5-9	2.67(1.52-4.67)	0.001	2.45(1.28-4.66)	0.007	3.58(2.11-6.08)	<0.001	3.32(1.86-5.93)	<0.001
10-15	15.04(3.85-58.74)	<0.001	15.48(3.58-66.90)	<0.001	9.31(3.23-26.80)	<0.001	13.27(3.79-46.47)	<0.001
Number of chronic conditions								
0-1	Reference		Reference		Reference		Reference	
2	0.39(0.12-1.30)	0.126	0.46(0.13-1.72)	0.251	1.06(0.26-4.44)	0.931	0.94(0.20-4.45)	0.935
3	0.33(0.10-1.06)	0.063	0.40(0.11-1.42)	0.155	1.44(0.43-4.83)	0.557	1.34(0.36-4.98)	0.659
4	0.48(0.15-1.54)	0.219	0.43(0.12-1.56)	0.202	1.53(0.46-5.07)	0.484	1.46(0.40-5.35)	0.570
5	0.39(0.12-1.21)	0.103	0.34(0.10-1.18)	0.088	2.49(0.78-7.93)	0.122	1.90(0.54-6.64)	0.315
6	0.43(0.13-1.43)	0.167	0.41(0.11-1.55)	0.191	1.62(0.48-5.54)	0.438	1.62(0.43-6.13)	0.475
7	0.51(0.14-1.88)	0.315	0.38(0.09-1.59)	0.184	1.48(0.41-5.37)	0.552	1.28(0.31-5.28)	0.731
8	1.37(0.32-5.88)	0.667	1.62(0.35-7.63)	0.539	1.44(0.28-7.50)	0.667	1.46(0.21-9.99)	0.701
9 or more	1.37(0.23-8.30)	0.728	1.85(0.25-13.83)	0.550	2.16(0.39-11.80)	0.376	3.14(0.45-21.75)	0.246

Abbreviations: OR, Odds ratio; CI, Confidence interval; IADL, Instrumental activities of daily living; GDS, Geriatric Depression Scale

Supplementary Table 3a. Condition specific effect on poor self-rated health in female and male participants.

	Poor Self-rated health							
	Female				Male			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value
Hypertension	1.48(0.82-2.67)	0.195	-	-	1.48(0.88-2.48)	0.136	-	-
Diabetes	1.25(0.56-2.79)	0.586	-	-	1.41(0.77-2.60)	0.267	-	-
Dyslipidemia	1.74(1.02-3.00)	0.044	1.55(0.75-3.19)	0.233	1.73(1.06-2.80)	0.027	1.34(0.73-2.44)	0.342
Hyperuricemia	5.51(2.27-13.39)	<0.001	4.55(1.32-15.74)	0.017	1.25(0.66-2.37)	0.490	-	-
Cerebrovascular disease	2.57(1.10-6.00)	0.029	3.05(1.05-8.85)	0.040	3.68(2.11-6.42)	<0.001	2.90(1.48-5.68)	0.002
Parkinson's disease	NA	NA	-	-	NA	NA	-	-
Dementia	NA	NA	-	-	0.91(0.20-4.15)	0.903	-	-
Heart disease	2.02(1.13-3.62)	0.018	1.91(0.86-4.23)	0.110	1.89(1.16-3.07)	0.011	1.56(0.84-2.90)	0.157
Respiratory disease	1.78(1.00-3.17)	0.052	1.11(0.48-2.56)	0.813	2.77(1.70-4.50)	<0.001	2.73(1.51-4.96)	0.001
Gastrointestinal disease	1.37(0.78-2.39)	0.273	-	-	2.09(1.23-3.57)	0.007	2.00(1.05-3.80)	0.034
Renal disease	2.42(1.13-5.20)	0.024	1.70(0.62-4.67)	0.300	1.62(0.81-3.24)	0.172	-	-
Thyroid disease	2.62(1.12-6.13)	0.026	2.01(0.64-6.28)	0.232	1.04(0.12-9.02)	0.972	-	-
Connective tissue disease	3.62(1.42-9.28)	0.007	2.91(0.73-11.58)	0.129	2.28(0.58-9.01)	0.240	-	-
Osteoporosis	2.16(1.25-3.74)	0.006	1.64(0.82-3.29)	0.165	1.87(0.72-4.87)	0.201	-	-
Arthritis	2.25(1.29-3.90)	0.004	2.14(1.02-4.49)	0.043	2.88(1.77-4.69)	<0.001	2.64(1.50-4.65)	0.001
Eye disease	1.06(0.51-2.18)	0.876	-	-	1.72(0.98-3.02)	0.059	1.66(0.85-3.27)	0.139
Prostate disease	NA	NA	-	-	1.26(0.78-2.02)	0.347	-	-
Malignancy	3.06(1.64-5.69)	<0.001	3.43(1.53-7.68)	0.003	0.84(0.48-1.46)	0.529	-	-

The adjusted models include age, current drinking, current smoking, BMI, IADL, education (high school graduation or higher), frailty and depression. Abbreviations: BMI, body mass index; IADL, Instrumental activities of daily living

Supplementary Table 3b. Condition specific effect on low life satisfaction in female and male participants.

	Low life satisfaction							
	Female				Male			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value	OR(95%CI)	P value
Hypertension	1.20(0.72-2.02)	0.488	-		0.77(0.48-1.23)	0.269	-	-
Diabetes	1.02(0.47-2.22)	0.957	-		1.27(0.69-2.34)	0.438	-	-
Dyslipidemia	1.04(0.64-1.70)	0.861	-		0.92(0.56-1.51)	0.747	-	-
Hyperuricemia	2.02(0.73-5.56)	0.173	-		0.91(0.48-1.74)	0.784	-	-
Cerebrovascular disease	1.19(0.46-3.07)	0.716	-		1.20(0.63-2.31)	0.581	-	-
Parkinson's disease	NA	NA	-		NA	NA	-	-
Dementia	0.49(0.06-3.97)	0.503	-		0.42(0.05-3.44)	0.422	-	-
Heart disease	0.87(0.47-1.62)	0.665	-		0.82(0.49-1.36)	0.446	-	-
Respiratory disease	1.20(0.67-2.14)	0.544	-		0.99(0.60-1.64)	0.975	-	-
Gastrointestinal disease	0.78(0.48-1.26)	0.308	-		1.99(1.19-3.30)	0.008	2.01(1.13-3.56)	0.017
Renal disease	1.36(0.59-3.15)	0.472	-		1.03(0.49-2.18)	0.929	-	-
Thyroid disease	2.10(0.94-4.67)	0.070	1.49(0.57-3.92)	0.417	0.89(0.10-8.04)	0.915	-	-
Connective tissue disease	2.76(0.95-8.00)	0.061	2.88(0.62-13.41)	0.177	2.89(0.76-11.00)	0.119	-	-
Osteoporosis	0.94(0.57-1.54)	0.796	-		1.53(0.57-4.06)	0.397	-	-
Arthritis	1.85(1.13-3.03)	0.014	2.04(1.14-3.66)	0.016	1.76(1.09-2.82)	0.020	1.67(0.98-2.82)	0.058
Eye disease	0.54(0.31-0.97)	0.040	0.37(0.19-0.73)	0.004	0.97(0.59-1.59)	0.898	-	-
Prostate disease	NA	NA			1.05(0.66-1.67)	0.825	-	-
Malignancy	1.79(0.94-3.40)	0.074	1.73(0.83-3.58)	0.144	1.10(0.65-1.86)	0.713	-	-

The adjusted models include age, current drinking, current smoking, BMI, IADL, education (high school graduation or higher), frailty and depression.  
Abbreviations: BMI, body mass index; IADL, Instrumental activities of daily living