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Multimorbidity patterns and the relation to self-rated health among older Japanese people: a nationwide cross-sectional study

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ABSTRACT

Objectives: Classifying individuals into multimorbidity patterns can be useful to identify the target population with poorer clinical outcomes. Self-rated health (SRH) is one of the core outcomes in multimorbidity patients. Although studies have reported that multimorbidity is associated with poor SRH, whether certain patterns have stronger associations remains unknown. Therefore, this study aimed to identify the prevalence and patterns of multimorbidity and investigate the association between multimorbidity patterns and SRH in an older Japanese population.

Design: Cross-sectional study

Setting: Data were obtained from the 2013 Comprehensive Survey of Living Conditions, a nationally representative survey of the general Japanese population.

Participants: This study examined 23,730 participants aged ≥65 years who were not hospitalised or institutionalised.

Primary outcome measure: Poor SRH was defined as choosing 'not very good' or 'bad' from five options: 'excellent', 'fairly good', 'average', 'not very good', and 'bad'.

Results: The prevalence of multimorbidity was 19.5% in participants aged ≥20 years and 40.9% in those aged ≥65 years. The prevalence of poor SRH was 23.8% among older participants. Three multimorbidity patterns were identified by exploratory factor analysis: i) degenerative/mental health, ii) malignant/digestive/urologic/haematologic, and iii)

cardiovascular/metabolic. Multivariable modified Poisson regression analysis revealed that high malignant/digestive/urologic/haematologic, degenerative/mental health, and cardiovascular/metabolic pattern scores, corresponding to the number of affected body systems in each pattern, were significantly associated with poor SRH [adjusted risk ratio (aRR) = 1.68, 95% confidence interval (CI): 1.60-1.76, aRR = 1.63, 95% CI: 1.58-1.69; and aRR = 1.31, 95% CI: 1.26-1.36, respectively]. When including the Kessler 6 score, a screening scale for depression, as a covariate in the analysis, the association between each multimorbidity pattern score and poor SRH decreased.

Conclusions: Malignant/digestive/urologic/haematologic and degenerative/mental health patterns may be associated with a high risk for poor SRH. Further research should focus on interventions to improve SRH in multimorbidity patients.

Strengths and limitations of this study

- This study reports the prevalence and patterns of multimorbidity, which is important in an ageing society, based on nationally representative data randomly selected from the general population in Japan.
- This is the first report to investigate associations between certain multimorbidity patterns and SRH.
- Health care professionals can recognise multimorbidity patients at high risk for poor

SRH and consider possible interventions.

- Because of the study's cross-sectional design, it was impossible to determine whether there was a causal relationship between multimorbidity patterns and poor SRH.
- Because chronic diseases were examined using self-report questionnaires, the prevalence of chronic diseases might be underestimated or conditions might be misclassified.

INTRODUCTION

Multimorbidity is defined as the co-occurrence of two or more chronic conditions within a person and is common in older people, requiring individualised management. In Europe, North America, and Australia, the prevalence of multimorbidity was reported as approximately 10-50% in individuals aged 20-65 years and 70-80% in those aged ≥65 years.[1] A study from Japan showed similar results, with a prevalence of multimorbidity of 29.9% for those aged ≥18 years and 62.8% for those aged ≥65 years.[2] However, the prevalence of multimorbidity varies widely from a few percent to 80% among older people in China[3] and is approximately 20% among adults in South Korea.[4] Multimorbidity is associated with several health care outcomes, including mortality, hospitalisation, functional limitations, and health care utilisation and costs.[5] Furthermore, the management of multimorbidity is difficult because applying a combination of individual clinical practice guidelines for each disease to

multimorbidity patients may increase the treatment burden and negatively affect the patients.[6] Multimorbidity is highly complex and heterogeneous, with various disease combinations, and the guidelines for multimorbidity recommend individualised management.[7]

Multimorbidity patterns and their association with health care outcomes have been the focus of much attention. A systematic review of 51 studies showed that mental health and cardiometabolic patterns were the two most replicable multimorbidity patterns based on specific combinations of conditions.[8] In a study of 3,256 Japanese general people, five multimorbidity patterns were identified: cardiovascular/renal/metabolic, neuro/psychiatric, skeletal/articular/digestive, respiratory/dermal, and malignant/digestive/urologic.[2] Furthermore, previous studies have reported associations between certain multimorbidity patterns and clinical outcomes, such as mortality,[9] functional ability,[10] and reduced health-related quality of life.[11] In caring for patients with multimorbidity, classifying individuals into multimorbidity patterns can be useful in identifying the target population with poorer clinical outcomes.

Self-rated health (SRH), the subjective perception of an individual's overall health, is a simple and powerful predictor of outcomes, such as mortality[12] and health care expenditure.[13] SRH is also one of the core outcomes in patients with multimorbidity.[14] Although several studies have shown that multimorbidity is associated with poor SRH,[15,[16]

it is unknown whether certain multimorbidity patterns are associated with poor SRH.

Therefore, the present study aimed i) to identify the prevalence of multimorbidity and multimorbidity patterns and ii) to investigate the association between multimorbidity patterns and poor SRH in the older population in Japan using large nationwide data from the 2013 Comprehensive Survey of Living Conditions (CSLC). We focused on the older population in this study because stratifying multimorbidity patterns by age group is recommended to better understand the evolution of multimorbidity over a lifespan.[8]

METHODS

Design, setting, and participants

In this nationwide cross-sectional study, we used data from the CSLC conducted by the Ministry of Health, Labour, and Welfare (MHLW) of the Japanese government in June 2013.[17] The CSLC is a nationwide repeated cross-sectional survey of households and household members. In 2013, the CSLC covered all households and household members in 5,530 districts stratified and randomly selected from the census tracts. Trained investigators visited households to distribute and collect self-administered questionnaires. The survey items included household questionnaire that inquiring about sex, age, educational level, and work status as well as health questionnaire that inquiring about health conditions, difficulties in daily life, and the status of medical check-ups. The MHLW provided anonymised data from the

CSLC for 97,345 individuals in 2013.

For investigating the prevalence of multimorbidity, we excluded individuals who were aged <20 years or had missing age data and those who were hospitalised, institutionalised, or had missing residence data at the time of the survey because they were not included for the questions on health conditions. In the analysis of multimorbidity patterns, we excluded those aged <65 years because we wanted to investigate multimorbidity patterns in older people. Finally, we excluded individuals with missing SRH data from the analysis of the association between multimorbidity patterns and poor SRH.

Measures

Chronic health conditions

In the CSLC survey, participants chose from 42 options about health conditions for which they were attending medical institutions. The options included diabetes mellitus, obesity, dyslipidaemia, thyroid diseases, depression and other mental disorders, dementia, Parkinson's disease, other nervous system diseases, eye diseases, ear diseases, hypertension, stroke, angina pectoris or myocardial infarction, other circulatory system diseases, acute nasopharyngitis, allergic rhinitis, chronic obstructive pulmonary disease, asthma, other respiratory system diseases, stomach and duodenal diseases, liver and gallbladder diseases, other digestive system diseases, dental diseases, atopic dermatitis, other skin diseases, gout, rheumatoid arthritis,

arthropathy, stiff neck, back pain, osteoporosis, kidney diseases, benign prostatic hyperplasia, perimenopausal or postmenopausal disorders, fracture, injury or burn other than fracture, anaemia and other blood diseases, malignancies, pregnancy or puerperium, infertility, others, and unknown. We used 34 conditions after excluding eight conditions: acute nasopharyngitis, dental diseases, fracture, injury or burn other than fracture, pregnancy or puerperium, infertility, others, and unknown, as they were not considered chronic conditions. For individuals aged ≥65 years, 33 chronic conditions were included because none of the participants reported perimenopausal or postmenopausal disorders. To investigate multimorbidity patterns, 33 chronic diseases were grouped into 13 body system-dependent clusters based on International Classification of Diseases (ICD)-10 chapters: malignancies, haematologic diseases (anaemia and other blood diseases), endocrine and metabolic diseases (diabetes mellitus, obesity, dyslipidaemia, and thyroid diseases), mental disorders (depression and other mental disorders), nervous system diseases (dementia, Parkinson's disease, and other nervous system diseases), eye diseases, ear diseases, circulatory system diseases (hypertension, stroke, angina pectoris or myocardial infarction, and other circulatory system diseases), respiratory system diseases (allergic rhinitis, chronic obstructive pulmonary disease, asthma, and other respiratory system diseases), digestive system diseases (stomach and duodenal diseases, liver and gallbladder diseases, and other digestive system diseases), skin diseases (atopic dermatitis and other skin diseases), musculoskeletal system diseases (gout, rheumatoid arthritis, arthropathy, stiff neck,

back pain, and osteoporosis), and urinary system diseases (kidney diseases and benign prostatic hyperplasia). The reason for this grouping was that it was difficult to treat 'other' diseases, such as other neurological diseases, when analysing multimorbidity patterns. Assessment of multimorbidity by grouping conditions based on body systems, such as complex multimorbidity that can identify patients needing complex healthcare interventions rather than conventional multimorbidity, could be useful.[18] In addition, since the multimorbidity patterns in the previous studies were mostly classified by organ systems,[2, 8, 19] we thought that grouping by organ system in advance would not have a significant effect on the pattern composition.

We defined multimorbidity as the coexistence of ≥2 chronic health conditions out of 34 conditions and complex multimorbidity as the presence of ≥3 affected body systems out of 13 systems based on the ICD-10 chapters within one person.

Self-rated health

Data on SRH were obtained through the question 'What is your present general health status?' Participants chose from five options: 'excellent', 'fairly good', 'average', 'not very good', and 'bad'. Those who chose 'excellent', 'fairly good', or 'average' were regarded as being in a 'fine SRH' condition, whereas those who chose 'not very good' or 'bad' were regarded as being in a 'poor SRH' condition. The distribution of responses to the five scale

items differs depending on the country owing to cultural differences. When dividing the five scale items into two values, it is common in Europe and the United States to classify the middle 'average' or 'good' as 'poor SRH',[20] whereas in Japan and Korea, it is common to classify 'average' or 'good' as 'fine SRH'.[21, 22]

Covariates

Previous studies have reported that older age, female sex, and lower educational levels are associated with poor SRH.[23] An incremental association between depressive symptoms and multimorbidity with SRH has also been reported.[20, 24] Therefore, we used age, sex, educational level, and Kessler 6 (K6) score[25, 26] as covariates. Data on age were provided in five-year categories. Data on educational level were divided into three categories: less than high school, high school, and more than high school. The Japanese version of the K6 scale of psychological distress is a validated screening scale for depression and anxiety that consists of six questions answered on a scale of 0-4, with a total score of 0-24.[27] We classified the scores into three categories: 0-4 (normal), 5-12 (psychological distress), and 13-24 (severe mental illness).[28]

Statistical analysis

We applied a two-step procedure to determine the extent to which multimorbidity

patterns are associated with poor SRH.

Identification of multimorbidity patterns: Multimorbidity patterns were determined using exploratory factor analysis based on polychoric correlations. We used 13 body system-dependent clusters grouped into 33 chronic health conditions, which were coded as dichotomous variables. We applied the maximum likelihood method and promax rotation. The number of factors was determined based on a parallel analysis. A factor loading greater than 0.30 is considered meaningful and was used as the criterion for item selection. In addition, multimorbidity patterns were also determined based on clinical plausibility, as assessed by two primary care physicians (YH and TA).

Associations between multimorbidity patterns and poor SRH: For each participant, a multimorbidity pattern score was calculated for each identified pattern. These scores correspond to the number of affected body system-dependent clusters in each pattern.[11] Modified Poisson regression analyses (i.e. Poisson regression with robust error variance)[29] were conducted to investigate the association between each multimorbidity pattern score and poor SRH. The following possible confounding variables were included as covariates in the analyses: age, sex, educational level, and K6 score. Each multimorbidity pattern score was individually included in the model to avoid multicollinearity. We also analysed the association between a simple count of affected body systems, regardless of multimorbidity pattern, and poor SRH. Missing values for covariates were analysed as missing categories. As a sensitivity

analysis, we also performed modified Poisson regression analyses after handling missing data with multiple imputations using a fully conditional specification. We created and analysed 100 multiple-imputed datasets.

All P-values were two-tailed, and statistical significance was set at $P < 0.05$. We used IBM SPSS Statistics 28.0 (IBM Japan, Tokyo, Japan) and R 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) for the analysis.

Ethics

Ethical approval was not required for this study because it involved a secondary analysis of the national surveillance data that did not contain any personally identifiable information. According to Article 36 of Japan's Statistics Act, anonymised data from the CSLC can be used for scientific research after approval by the MHLW of Japan.

Patient and public involvement

No patients or public were involved.

RESULTS

Figure shows a flowchart of the participants. The descriptive statistics of multimorbidity included 77,120 participants, factor analysis to identify multimorbidity patterns

included 23,730 participants, and analyses to investigate the association between multimorbidity patterns and poor SRH included 23,340 participants.

The prevalence of multimorbidity was 20% in participants aged ≥20 years, 41% in those aged ≥65 years, and 48% in those aged ≥75 years. The prevalence of complex multimorbidity was 6.5% in participants aged ≥20 years, 16% in those aged ≥65 years, and 20% in those aged ≥75 years.

We conducted a parallel analysis to examine the maximum number of factors for exploratory factor analysis to identify multimorbidity patterns and a seven-factor solution was suggested. After factor analyses using two- to seven-factor solutions, a four-factor solution was adopted because the multimorbidity pattern was the most clinically plausible and consistent with previous reports. Table 1 shows the factor loadings for the four-factor solution following an exploratory factor analysis in older participants who were not hospitalised or institutionalised in care facilities (N = 23,730).

Table 1. Factor loadings for the four-factor solution following an exploratory factor analysis in older participants (N = 23,730)

Chronic conditions (ICD-10 chapter no.)	No. of affected participants (%)	Factor 1	Factor 2	Factor 3	Factor 4
Malignancies (2)	364 (1.5)	-0.15	**0.66**	-0.04	-0.15
Haematologic diseases (3)	260 (1.1)	0.00	**0.41**	0.11	0.13
Endocrine and metabolic diseases (4)	5,062 (21.3)	0.19	-0.05	-0.02	**0.31**
Mental disorders (5)	329 (1.4)	**0.37**	-0.05	0.16	-0.14
Nervous system diseases (6)	880 (3.7)	-0.03	0.01	**0.99**	0.13
Eye diseases (7)	3,474 (14.6)	**0.56**	-0.02	-0.08	0.16

Ear diseases (8)	608 (2.6)	**0.69**	-0.07	-0.01	-0.06
Circulatory system diseases (9)	9,213 (38.8)	-0.11	-0.07	0.06	**0.71**
Respiratory system diseases (10)	1,421 (6.0)	0.27	0.20	0.00	0.00
Digestive system diseases (11)	1,866 (7.9)	0.17	**0.46**	-0.07	-0.13
Skin diseases (12)	705 (3.0)	0.17	0.24	0.02	0.08
Musculoskeletal system diseases (13)	4,959 (20.9)	**0.36**	0.02	-0.06	0.15
Urinary system diseases (14)	1,437 (6.1)	-0.06	**0.42**	0.04	0.16

ICD, International Statistical Classification of Diseases and Related Health Problems

Maximum likelihood method and promax rotation are applied.

Loadings are bolded if they exceed 0.30.

Three multimorbidity patterns were identified and labelled as follows: i) degenerative/mental health (Factor 1), ii) malignant/digestive/urologic/haematologic (Factor 2), and iii) cardiovascular/metabolic pattern (Factor 4). Factor 3 included only nervous system diseases, which was not considered a multimorbidity pattern. The respiratory system and skin diseases were not classified into any factor. Two primary care clinicians (YH and TA) agreed that the three multimorbidity patterns were clinically plausible.

Table 2 presents the characteristics of older participants with SRH data who were not hospitalised or institutionalised in care facilities (N = 23,340). Poor SRH was found in 5,554 participants (23.8%).

Table 2. Characteristics of older participants with SRH data who were not hospitalised or institutionalised

Characteristic	**All participants (N = 23,340)**	**Fine SRH (N = 17,786)**	**Poor SRH (N = 5,554)**
Age (years)			
65-69	6,818	5,704 (83.6)	1,114 (16.4)
70-74	6,029	4,816 (79.9)	1,213 (20.1)

75-79	4,910	3,625 (73.8)	1,285 (26.2)
80-84	3,149	2,111 (67.0)	1,038 (33.0)
85-89	1,686	1,056 (62.6)	630 (37.4)
≥90	748	474 (63.4)	274 (36.6)
Sex			
Male	10,266	7,956 (77.5)	2,310 (22.5)
Female	13,074	9,830 (75.2)	3,244 (24.8)
Educational level			
Less than high school	7,660	5,544 (72.4)	2,116 (27.6)
High school	8,810	6,841 (77.7)	1,969 (22.3)
More than high school	3,460	2,777 (80.3)	683 (19.7)
Data missing	3,410	2,624 (77.0)	786 (23.0)
K6 score			
0-4 (normal)	15,721	13,425 (85.4)	2,296 (14.6)
5-12 (psychological distress)	4,830	2,848 (59.0)	1,982 (41.0)
13-24 (severe mental illness)	696	171 (24.6)	525 (75.4)
Data missing	2,093	1,342 (64.1)	751 (35.9)
No. of morbidities			
0	7,308	6,546 (89.6)	762 (10.4)
1	6,458	5,145 (79.7)	1,313 (20.3)
2	4,648	3,383 (72.8)	1,265 (27.2)
3	2,560	1,585 (61.9)	975 (38.1)
4	1,245	700 (56.2)	545 (43.8)
≥5	1,121	427 (38.1)	694 (61.9)
Multimorbidity*			
Yes	9,574	6,095 (63.7)	3,479 (36.3)
No	13,766	11,691 (84.9)	2,075 (15.1)
Complex multimorbidity†			
Yes	3,637	1,933 (53.1)	1,704 (46.9)
No	19,703	15,853 (80.5)	3,850 (19.5)

Data were presented as the number (percentage) of participants.

SRH, self-rated health; K6, Kessler 6

*Multimorbidity was defined as the coexistence of ≥2 chronic health conditions.

†Complex multimorbidity was defined as the presence of ≥3 affected body systems.

The association between multimorbidity pattern scores and poor SRH adjusted for age,

sex, and educational level as covariates is summarised in Table 3 and that adjusted for age, sex, educational level, and K6 is shown in Table 4. Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern (e.g. the malignant/digestive/urologic/haematologic pattern score for a person with malignancy and anaemia was two). In the model with age, sex, and educational level as covariates, high malignant/digestive/urologic/haematologic, degenerative/mental health, and cardiovascular/metabolic pattern scores were significantly associated with poor SRH (adjusted risk ratio [aRR] = 1.68, 95% confidence interval [CI]: 1.60-1.76, aRR = 1.63, 95% CI: 1.58-1.69, and aRR = 1.31, 95% CI: 1.26-1.36, respectively) (Table 3). In the model with age, sex, educational level, and K6 as covariates, high malignant/digestive/urologic/haematologic, degenerative/mental health, and cardiovascular/metabolic pattern scores were significantly associated with poor SRH (aRR = 1.47, 95% CI: 1.40-1.54, aRR = 1.44, 95% CI: 1.39-1.49, and aRR = 1.24, 95% CI: 1.19-1.28, respectively) (Table 4). The association between multimorbidity pattern scores and poor SRH was reduced when K6 was added to the model as a covariate, particularly for the malignant/digestive/urologic/haematologic and degenerative/mental health patterns. Although the simple count of affected body systems, regardless of multimorbidity pattern, was also significantly associated with poor SRH when adjusted for age, sex, and educational level with and without K6 as covariates (aRR = 1.35, 95% CI: 1.34-1.37 and aRR = 1.27, 95% CI: 1.25-1.29, respectively), the association was

smaller than the malignant/digestive/urologic/haematologic and degenerative/mental health pattern scores and equivalent to cardiovascular/metabolic pattern scores.

Table 3. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses without K6.

	Malignant/digestive/urologic /haematologic pattern		Degenerative /mental health pattern*		Cardiovascular/metabolic pattern	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.68 (1.60-1.76)	<0.001	1.63 (1.58-1.69)	<0.001	1.31 (1.26-1.36)	<0.001
Age (years)						
65-69	ref		ref		ref	
70-74	1.19 (1.10-1.30)	<0.001	1.14 (1.06-1.24)	<0.001	1.22 (1.13-1.33)	<0.001
75-79	1.52 (1.40-1.65)	<0.001	1.38 (1.28-1.50)	0.001	1.58 (1.46-1.72)	<0.001
80-84	1.87 (1.72-2.04)	<0.001	1.69 (1.55-1.85)	<0.001	1.99 (1.82-2.17)	<0.001
85-89	2.11 (1.91-2.34)	<0.001	1.92 (1.74-2.12)	<0.001	2.24 (2.03-2.48)	<0.001
≥90	2.06 (1.80-2.36)	<0.001	1.94 (1.70-2.23)	<0.001	2.19 (1.92-2.51)	<0.001
Female sex	1.14 (1.08-1.21)	<0.001	0.97 (0.92-1.03)	0.34	1.03 (0.98-1.09)	0.27
Educational level						
Less than high school	ref		ref		ref	
High school	0.91 (0.85-0.97)	0.003	0.91 (0.86-0.97)	0.005	0.91 (0.86-0.97)	0.004
More than high school	0.83 (0.76-0.91)	<0.001	0.84 (0.77-0.92)	<0.001	0.83 (0.76-0.91)	<0.001
Data missing	0.92 (0.84-1.00)	0.038	0.93 (0.86-1.02)	0.13	0.93 (0.86-1.01)	0.091

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, and educational level.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern. Each pattern score was individually included in the model, adjusted for age, sex, and educational level.

Table 4. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses with K6.

	Malignant/digestive/urologic /haematologic pattern		Degenerative /mental health pattern*		Cardiovascular/metabolic pattern	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.47 (1.40-1.54)	<0.001	1.44 (1.39-1.49)	<0.001	1.24 (1.19-1.28)	<0.001
Age (years)						
65-69	ref		ref		ref	
70-74	1.15 (1.06-1.25)	<0.001	1.12 (1.03-1.22)	0.007	1.15 (1.06-1.25)	<0.001
75-79	1.41 (1.30-1.53)	<0.001	1.32 (1.22-1.44)	<0.001	1.43 (1.31-1.55)	<0.001
80-84	1.64 (1.50-1.79)	<0.001	1.55 (1.42-1.69)	<0.001	1.68 (1.54-1.83)	<0.001
85-89	1.78 (1.61-1.96)	<0.001	1.70 (1.54-1.88)	<0.001	1.82 (1.64-2.01)	<0.001
≥90	1.67 (1.46-1.92)	<0.001	1.65 (1.45-1.90)	<0.001	1.71 (1.50-1.96)	<0.001
Female sex	1.05 (0.99-1.11)	0.10	0.93 (0.88-0.98)	0.006	0.97 (0.92-1.03)	0.29
Educational level						
Less than high school	ref		ref		ref	
High school	0.95 (0.89-1.01)	0.081	0.95 (0.89-1.01)	0.089	0.95 (0.89-1.02)	0.14
More than high school	0.90 (0.82-0.98)	0.020	0.92 (0.84-1.00)	0.054	0.91 (0.84-1.00)	0.051
Data missing	0.88 (0.80-0.95)	0.002	0.89 (0.82-0.97)	0.007	0.89 (0.82-0.97)	0.006
K6 score						
0-4 (normal)	ref		ref		ref	
5-12 (psychological distress)	2.66 (2.51-2.83)	<0.001	2.51 (2.36-2.67)	<0.001	2.74 (2.57-2.91)	<0.001
13-24 (severe mental illness)	4.31 (3.91-4.75)	<0.001	3.94 (3.57-4.34)	<0.001	4.60 (4.18-5.07)	<0.001
Data missing	2.35 (2.16-2.56)	<0.001	2.25 (2.07-2.45)	<0.001	2.39 (2.20-2.60)	<0.001

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, educational level, and K6.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern. Each pattern score was individually included in the model, adjusted for age, sex, educational level, and K6 score.

For sensitivity analyses, we performed modified Poisson regression analyses after handling missing data with multiple imputations (Supplemental Tables 1 and 2). The proportion of missing values was 14.6% for educational level and 9.0% for K6. In total, 4,806

of the 23,340 records (20.6%) were incomplete. The association of each multimorbidity pattern score and covariate with poor SRH did not differ considerably between the analyses using multiple imputations and the analyses on the subset of complete cases.

DISCUSSION

In the present study of nationally representative data from 77,120 participants in Japan who were not hospitalised or institutionalised, we found a prevalence of multimorbidity. Analysis using data from 23,730 older participants aged ≥65 years revealed three multimorbidity patterns: i) degenerative/mental health, ii) malignant/digestive/urologic/haematologic, and iii) cardiovascular/metabolic. To the best of our knowledge, this is the first study to investigate the association between certain multimorbidity patterns and SRH. We found a positive association between each multimorbidity pattern score and poor SRH. This association was stringer for degenerative/mental health and malignant/digestive/urologic/haematologic patterns than for cardiovascular/metabolic patterns. Health care professionals can use the results to recognise multimorbidity in patients at high risk for poor SRH and consider possible interventions.

Although the prevalence of multimorbidity in the present study was relatively lower than that reported in previous studies from Europe, North America, Australia, and Japan,[1, 2] it would considerably reflect the prevalence in the free-living general population in Japan. The

prevalence of multimorbidity could have been lower in our study because the survey excluded hospitalised or institutionalised people who were expected to have more chronic conditions. The results reflect the state of the community residents who visit medical institutions and are subject to health care policies. In addition, differences in the method of ascertainment of chronic conditions could contribute to differences in the prevalence. Various methods have been used in previous studies, including self-reporting, administrative health records, and clinical assessments.[1] Moreover, within self-reports, questions about chronic conditions varied among surveys. Although the participants in this study were asked about the health conditions for which they were attending medical institutions at the time of the survey, participants in another study were asked about chronic conditions that had been reported by healthcare professionals.[2] As this study did not cover inactive conditions that were not being attended to in medical institutions at the time, it could reflect only the conditions that were currently burdening participants.

Because the multimorbidity patterns in this study were plausible based on previous reports and clinical perspectives, they can be widely generalised to older people in developed countries. Mental health pattern and cardiometabolic pattern were reported as the two most replicable multimorbidity patterns in a systematic review in 2019,[8] whereas another systematic review in Asia reported the following five patterns: cardiovascular/metabolic, mental health, degenerative, pulmonary, and cancer.[19] The systematic review in Asia

contained one study from Japan that reported five patterns: cardiovascular/renal/metabolic, neuropsychiatric, skeletal/articular/digestive, respiratory/dermal, and malignant/digestive/urologic.[2] We found that the cardiovascular/metabolic pattern was consistent with that reported in previous studies. The degenerative/mental health pattern in this study was close to the falls/fractures/vision disorders/cognitive impairment and falls/vision impairment/cognitive impairment/urinary incontinence/hearing impairment reported in the systematic review in 2019, and mental patterns and degenerative patterns in the systematic review in Asia. As a mechanism for the construction of this pattern, we speculate that communication disability, social isolation, functional disability, limited mobility, and poorly treated pain due to vision and hearing impairment[30] or musculoskeletal diseases led to mental disorders such as depression. The malignant/digestive/urologic/haematologic pattern in this study was similar to the pattern reported in the previous study in Japan. As a mechanism for the construction of this pattern, we speculate that digestive and urologic organs are relatively frequent as sites of primary lesions in cancer survivors.[31] Furthermore, anaemia is one of the common complications of malignancy and its treatment and can also be associated with chronic kidney disease or bleeding from gastrointestinal diseases. The multimorbidity patterns revealed by the data limited to the older population in this study may differ from those reported in previous studies involving younger generations. We believe it is valuable to report multimorbidity patterns in the older in Japan, where the population is ageing ahead of the rest

of the world.

The association between multimorbidity pattern scores and poor SRH was greater for malignant/digestive/urologic/haematologic and degenerative/mental health patterns than for cardiovascular/metabolic patterns. The strong association between malignant/digestive/urologic/haematologic patterns and poor SRH in the present study is consistent with the findings of a previous study that reported poorer SRH in older cancer survivors than in people without cancer.[32] Symptoms of digestive or urological conditions can affect eating and elimination, which may exacerbate SRH. The strong association between degenerative/mental health patterns and poor SRH in this study is consistent with the findings of previous studies. Rheumatic and musculoskeletal diseases have been reported to have the strongest association with poor SRH among the chronic conditions.[33] SRH in older people with multimorbidity is exacerbated by vision impairment, hearing impairment, depression, and anxiety.[34] Mental disorders and/or musculoskeletal diseases have been reported as combinations of chronic conditions associated with poor SRH.[35] Communication disability, social isolation, functional disability, limited mobility, and poorly treated pain due to vision and hearing impairment or musculoskeletal diseases can worsen SRH. In contrast, the association between cardiovascular/metabolic patterns and poor SRH was weaker than that between other patterns and poor SRH. We suspect that this is because stable conditions of cardiovascular/metabolic diseases, such as diabetes or ischaemic heart disease, may not have

severe symptoms and may not affect daily life significantly. However, one previous study reported that cardiometabolic diseases contribute the most to the worsening of SRH in the general population aged 30-79 years in China.[36] Differences in participants' ages across studies may affect multimorbidity patterns and the association between these patterns and SRH.

The K6, a screening scale for depression and anxiety, partially mediated the association between multimorbidity pattern scores and poor SRH. Comparing the models of multivariate regression analysis that included K6 as a covariate and those that did not include it as a covariate revealed that the association between multimorbidity pattern scores and poor SRH was weaker in the model that included K6 for all three patterns. We speculate that the growing patient burden due to the increasing number of chronic conditions may have partially caused mood disorders, resulting in the worsening of SRH.

The results of this study will help clinicians recognise patients with multimorbidity patterns, which are highly associated with poor SRH, and consider possible interventions. Because the multimorbidity pattern score we used was simple and easy to apply in clinical practice, clinicians could calculate the score for each patient and assess the risk of poor SRH. Given that a previous study reported that the association between multimorbidity and poor SRH could be reduced by increasing physical activity,[37] clinicians may improve SRH by prescribing exercise to patients with multimorbidity at risk for poor SRH. Further research is warranted to confirm whether such interventions can improve SRH in patients with

multimorbidity.

Our study has several limitations. First, because of the cross-sectional design, it was impossible to determine whether there was a causal relationship between multimorbidity patterns and SRH. Additional research using a longitudinal design is needed to confirm the association between multimorbidity patterns and SRH. Second, because chronic diseases were measured using self-report questionnaires, it is possible that the prevalence of chronic diseases was underestimated or that the conditions were misclassified. However, previous studies have demonstrated that assessment of morbidity using self-reported data can predict clinical outcomes, including SRH, compared with measures based on administrative data.[38] Finally, it is unclear whether the results of this study can be applied to older adults who require hospitalisation or institutionalisation, such as those with severe chronic diseases or functional decline, because the survey did not include such patients.

CONCLUSIONS

We found differences in the association between multimorbidity patterns and poor SRH. Malignant/digestive/urologic/haematologic and degenerative/mental health patterns may be associated with a high risk for poor SRH. Further research should focus on interventions to improve SRH in patients with multimorbidity.

Statements

Author contributions: All authors (YH, MN, TA, and TO) contributed to the conception or design of the study, reviewed and edited the manuscript, contributed to the interpretation of the data and the analyses, performed critical review of the manuscript, and gave the final approval of the manuscript before submission. YH performed the statistical analyses and drafted the manuscript. MN, TA, and TO supervised the work.

Competing interest: TA received a grant from Pfizer Health Research Foundation, Japan for another research project related to multimorbidity (Grant No. 21-E-01).

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Data availability: These data were derived from the CSLC in June 2013, which was conducted by the MHLW of Japan. You can use the anonymous data if you apply for and receive permission from the ministry. [https://www.mhlw.go.jp/toukei/itaku/tokumei.html]

Participant consent: Not applicable.

Ethical approval: Ethical approval was not required for this study because it involved a secondary analysis of the national surveillance data that did not contain any personally identifiable information. According to Article 36 of Japan's Statistics Act, anonymised data from the CSLC can be used for scientific research after approval by the MHLW of Japan.

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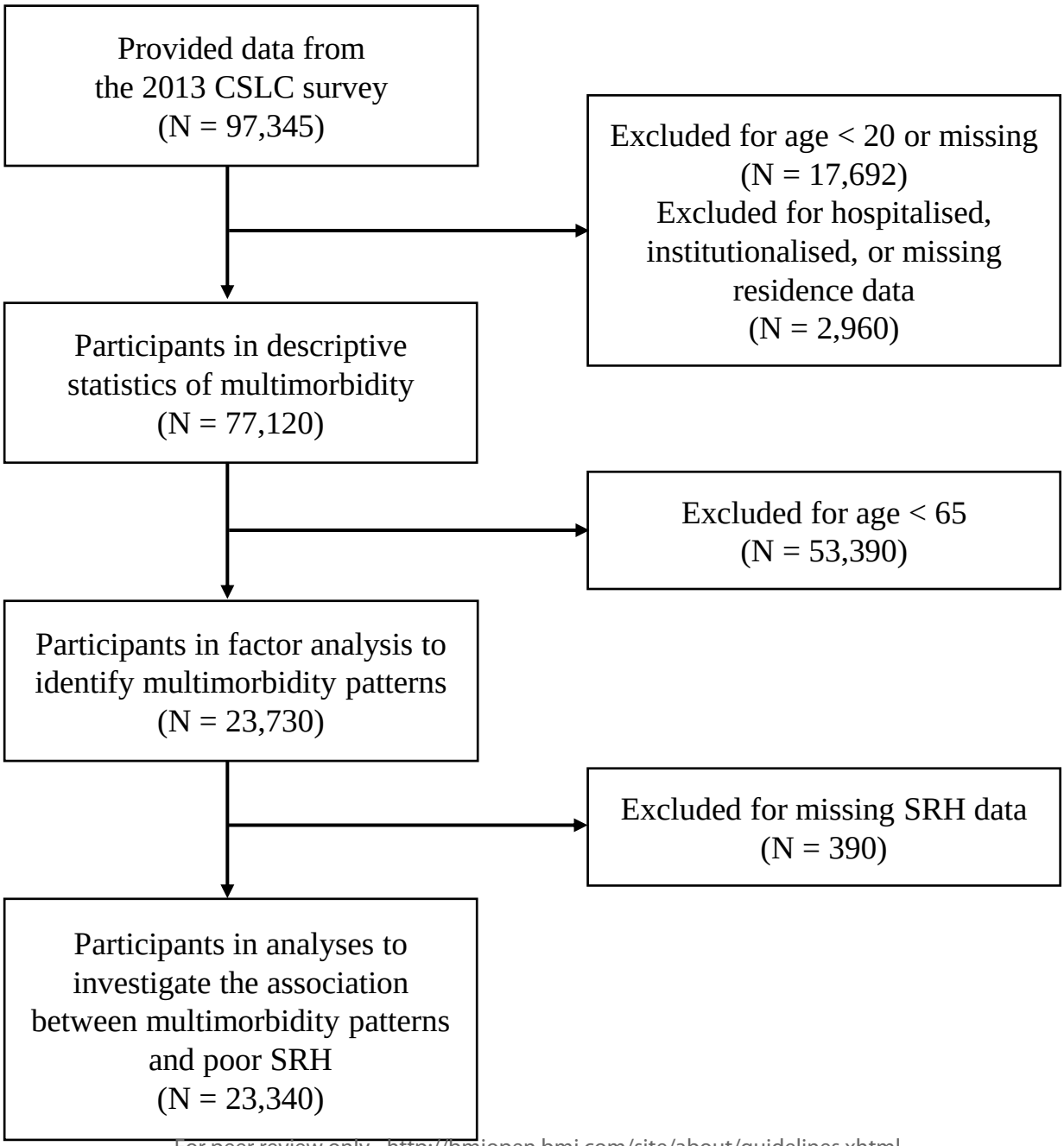
doi:10.1370/afm.1364

Figure legend

Figure. Participant flow chart

CSLC, the Comprehensive Survey of Living Conditions; SRH, self-rated health


Provided data from the 2013 CSLC survey (N = 97,345)
Excluded for age < 20 or missing (N = 17,692)
Excluded for hospitalised, institutionalised, or missing residence data (N = 2,960)
Participants in descriptive statistics of multimorbidity (N = 77,120)
Excluded for age < 65 (N = 53,390)
Participants in factor analysis to identify multimorbidity patterns (N = 23,730)
Excluded for missing SRH data (N = 390)
Participants in analyses to investigate the association between multimorbidity patterns and poor SRH (N = 23,340)

Supplemental Table 1. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses without K6.

	Malignant/digestive/urologic/haematologic pattern				Degenerative/mental health pattern*				Cardiovascular/metabolic pattern			
	Complete case analysis (N = 19,930)		Multiple imputation (N = 23,340)		Complete case analysis (N = 19,930)		Multiple imputation (N = 23,340)		Complete case analysis (N = 19,930)		Multiple imputation (N = 23,340)	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.68 (1.62-1.75)	<0.001	1.69 (1.63-1.75)	<0.001	1.65 (1.60-1.69)	<0.001	1.65 (1.61-1.69)	<0.001	1.30 (1.25-1.34)	<0.001	1.29 (1.26-1.34)	<0.001
Age (years)												
65-69	ref		ref		ref		ref		ref		ref	
70-74	1.18 (1.09-1.28)	<0.001	1.19 (1.10-1.28)	<0.001	1.14 (1.06-1.24)	0.001	1.15 (1.07-1.23)	<0.001	1.19 (1.10-1.29)	<0.001	1.19 (1.11-1.28)	<0.001
75-79	1.53 (1.41-1.65)	<0.001	1.49 (1.39-1.60)	<0.001	1.41 (1.30-1.52)	<0.001	1.38 (1.29-1.49)	<0.001	1.55 (1.43-1.67)	<0.001	1.51 (1.41-1.63)	<0.001
80-84	1.83 (1.69-1.98)	<0.001	1.82 (1.69-1.96)	<0.001	1.69 (1.56-1.83)	<0.001	1.69 (1.57-1.82)	<0.001	1.98 (1.75-2.06)	<0.001	1.89 (1.75-2.04)	<0.001
85-89	2.05 (1.87-2.24)	<0.001	2.06 (1.90-2.24)	<0.001	1.90 (1.74-2.08)	<0.001	1.92 (1.77-2.09)	<0.001	2.23 (1.95-2.33)	<0.001	2.13 (1.96-2.32)	<0.001
≥90	2.08 (1.85-2.33)	<0.001	2.00 (1.79-2.24)	<0.001	2.01 (1.79-2.26)	<0.001	1.95 (1.74-2.17)	<0.001	2.26 (1.92-2.42)	<0.001	2.08 (1.87-2.33)	<0.001
Female sex	1.13 (1.08-1.19)	<0.001	1.13 (1.08-1.19)	<0.001	0.96 (0.92-1.01)	0.15	0.96 (0.92-1.01)	0.12	1.03 (0.98-1.09)	0.21	1.03 (0.98-1.08)	0.21
Educational level												
Less than high school	ref		ref		ref		ref		ref		ref	
High school	0.91 (0.86-0.96)	<0.001	0.91 (0.86-0.96)	<0.001	0.91 (0.87-0.96)	<0.001	0.91 (0.87-0.96)	<0.001	0.91 (0.87-0.96)	<0.001	0.91 (0.87-0.96)	<0.001
More than high school	0.83 (0.77-0.89)	<0.001	0.83 (0.77-0.90)	<0.001	0.85 (0.78-0.91)	<0.001	0.85 (0.79-0.92)	<0.001	0.84 (0.78-0.91)	<0.001	0.85 (0.79-0.92)	<0.001

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, and educational level.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern.

Each pattern score was individually included in the model, adjusted for age, sex, and educational level.

Supplemental Table 2. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses with K6.

	Malignant/digestive/urologic/haematologic pattern				Degenerative/mental health pattern*				Cardiovascular/metabolic pattern			
	Complete case analysis (N = 18,534)		Multiple imputation (N = 23,340)		Complete case analysis (N = 18,534)		Multiple imputation (N = 23,340)		Complete case analysis (N = 18,534)		Multiple imputation (N = 23,340)	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.49 (1.44-1.56)	<0.001	1.49 (1.44-1.54)	<0.001	1.47 (1.43-1.51)	<0.001	1.46 (1.42-1.50)	<0.001	1.24 (1.20-1.29)	<0.001	1.24 (1.20-1.28)	<0.001
Age (years)												
65-69	ref		ref		ref		ref		ref		ref	
70-74	1.15 (1.06-1.25)	<0.001	1.17 (1.09-1.25)	<0.001	1.12 (1.04-1.21)	0.005	1.14 (1.06-1.22)	<0.001	1.16 (1.07-1.25)	<0.001	1.17 (1.09-1.25)	<0.001
75-79	1.51 (1.40-1.63)	<0.001	1.46 (1.37-1.57)	<0.001	1.41 (1.31-1.53)	<0.001	1.38 (1.29-1.48)	<0.001	1.52 (1.40-1.64)	<0.001	1.48 (1.38-1.58)	<0.001
80-84	1.75 (1.61-1.90)	<0.001	1.71 (1.59-1.84)	<0.001	1.64 (1.51-1.78)	<0.001	1.61 (1.50-1.73)	<0.001	1.78 (1.64-1.93)	<0.001	1.74 (1.63-1.87)	<0.001
85-89	1.86 (1.69-2.04)	<0.001	1.85 (1.71-2.01)	<0.001	1.76 (1.61-1.93)	<0.001	1.77 (1.63-1.92)	<0.001	1.89 (1.73-2.07)	<0.001	1.89 (1.74-2.05)	<0.001
≥90	1.82 (1.62-2.05)	<0.001	1.73 (1.56-1.92)	<0.001	1.81 (1.61-2.04)	<0.001	1.72 (1.54-1.91)	<0.001	1.86 (1.66-2.10)	<0.001	1.76 (1.59-1.96)	<0.001
Female sex	1.06 (1.01-1.12)	0.031	1.05 (1.00-1.10)	0.039	0.93 (0.88-0.98)	0.005	0.92 (0.88-0.97)	<0.001	0.98 (0.93-1.03)	0.45	0.97 (0.93-1.02)	0.25
Educational level												
Less than high school	ref		ref		ref		ref		ref		ref	
High school	0.93 (0.88-0.98)	0.009	0.94 (0.89-0.98)	0.009	0.93 (0.88-0.99)	0.012	0.94 (0.89-0.99)	0.011	0.95 (0.89-0.99)	0.018	0.94 (0.90-0.99)	0.023
More than high school	0.89 (0.83-0.97)	0.004	0.89 (0.83-0.96)	0.002	0.91 (0.84-0.98)	0.016	0.91 (0.85-0.98)	0.009	0.92 (0.84-0.98)	0.014	0.91 (0.85-0.98)	0.012
K6 score												
0-4 (normal)	ref		ref		ref		ref		ref		ref	
5-12 (psychological distress)	2.57 (2.44-2.71)	<0.001	2.61 (2.48-2.74)	<0.001	2.47 (2.34-2.61)	<0.001	2.50 (2.38-2.63)	<0.001	2.64 (2.50-2.78)	<0.001	2.66 (2.53-2.79)	<0.001
13-24 (severe mental illness)	4.31 (4.04-4.60)	<0.001	4.29 (4.05-4.55)	<0.001	3.98 (3.71-4.26)	<0.001	3.97 (3.72-4.23)	<0.001	4.57 (4.29-4.86)	<0.001	4.56 (4.31-4.83)	<0.001

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, educational level, and K6.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern.

Each pattern score was individually included in the model, adjusted for age, sex, educational level, and K6 score.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-10
Bias	9	Describe any efforts to address potential sources of bias	7-12
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-12
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	11-12
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	11-12
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12-13 and Figure
		(b) Give reasons for non-participation at each stage	12-13
		(c) Consider use of a flow diagram	Figure
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14 and Table 2
		(b) Indicate number of participants with missing data for each variable of interest	Table 2
Outcome data	15*	Report numbers of outcome events or summary measures	14 and Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15-17 and Tables 3 and 4
		(*b*) Report category boundaries when continuous variables were categorized	Table 4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	18-19 and Supplemental Tables 1 and 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	23-24
Generalisability	21	Discuss the generalisability (external validity) of the study results	19-21
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Multimorbidity patterns and the relation to self-rated health among older Japanese people: a nationwide cross-sectional study

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ABSTRACT

Objectives: Classifying individuals into multimorbidity patterns can be useful to identify the target population with poorer clinical outcomes. Self-rated health (SRH) is one of the core outcomes in multimorbidity patients. Although studies have reported that multimorbidity is associated with poor SRH, whether certain patterns have stronger associations remains unknown. Therefore, this study aimed to identify the prevalence and patterns of multimorbidity and investigate the association between multimorbidity patterns and SRH in an older Japanese population.

Design: Cross-sectional study

Setting: Data were obtained from the 2013 Comprehensive Survey of Living Conditions, a nationally representative survey of the general Japanese population.

Participants: This study mainly examined 23,730 participants aged ≥65 years who were not hospitalised or institutionalised.

Primary outcome measure: Poor SRH was defined as choosing 'not very good' or 'bad' from five options: 'excellent', 'fairly good', 'average', 'not very good', and 'bad'.

Results: The prevalence of multimorbidity was 40.9% and that of poor SRH was 23.8%. Three multimorbidity patterns were identified by exploratory factor analysis: i) degenerative/mental health, ii) malignant/digestive/urologic/haematologic, and iii) cardiovascular/metabolic. Multivariable modified Poisson regression analysis revealed that high

malignant/digestive/urologic/haematologic, degenerative/mental health, and cardiovascular/metabolic pattern scores, corresponding to the number of affected body systems in each pattern, were significantly associated with poor SRH [adjusted risk ratio (aRR) = 1.68, 95% confidence interval (CI): 1.60-1.76, aRR = 1.63, 95% CI: 1.58-1.69; and aRR = 1.31, 95% CI: 1.26-1.36, respectively]. When including the Kessler 6 score, a screening scale for psychological distress, in the analysis, the association between each multimorbidity pattern score and poor SRH decreased.

Conclusions: Malignant/digestive/urologic/haematologic and degenerative/mental health patterns may be associated with a high risk for poor SRH. Further research should focus on interventions to improve SRH in multimorbidity patients.

Strengths and limitations of this study

- Randomly selected nationally representative data from the general population in Japan were used to determine the prevalence and patterns of multimorbidity in older people.
- The modified Poisson regression model allowed for an appropriate estimate of the risk ratio of poor SRH to multimorbidity patterns because the incidence of the outcome was common.
- The multimorbidity pattern score, which is the sum of affected conditions in each pattern, was easy to calculate to assess each patient's condition in the clinical practice

setting.

- The cross-sectional design of the study limited the causality between multimorbidity patterns and poor SRH.
- Self-reporting of affected conditions could cause underestimation or misclassification, but the influence would not differ between participants with and without poor SRH.

INTRODUCTION

Multimorbidity is defined as the co-occurrence of two or more chronic conditions within a person and is common in older people, requiring individualised management. In Europe, North America, and Australia, the prevalence of multimorbidity was reported as approximately 10-50% in individuals aged 20-65 years and 70-80% in those aged ≥65 years.[1] A study from Japan showed similar results, with a prevalence of multimorbidity of 29.9% for those aged ≥18 years and 62.8% for those aged ≥65 years.[2] However, the prevalence of multimorbidity varies widely from a few percent to 80% among older people in China[3] and is approximately 20% among adults in South Korea.[4] Multimorbidity is associated with several health care outcomes, including mortality, hospitalisation, functional limitations, and health care utilisation and costs.[5] Furthermore, the management of multimorbidity is difficult because applying a combination of individual clinical practice guidelines for each disease to multimorbidity patients may increase the treatment burden and negatively affect the

patients.[6] Multimorbidity is highly complex and heterogeneous, with various disease combinations, and the guidelines for multimorbidity recommend individualised management.[7]

Multimorbidity patterns and their association with health care outcomes have been the focus of much attention. A systematic review of 51 studies showed that mental health and cardiometabolic patterns were the two most replicable multimorbidity patterns based on specific combinations of conditions.[8] In a study of 3,256 Japanese general people, five multimorbidity patterns were identified: cardiovascular/renal/metabolic, neuro/psychiatric, skeletal/articular/digestive, respiratory/dermal, and malignant/digestive/urologic.[2] Furthermore, previous studies have reported associations between certain multimorbidity patterns and clinical outcomes, such as mortality,[9] functional ability,[10] and reduced health-related quality of life.[11] In caring for patients with multimorbidity, classifying individuals into multimorbidity patterns can be useful in identifying the target population with poorer clinical outcomes.

Self-rated health (SRH), the subjective perception of an individual's overall health, is a simple and powerful predictor of outcomes, such as mortality[12] and health care expenditure.[13] SRH is also one of the core outcomes in patients with multimorbidity.[14] Although several studies have shown that multimorbidity is associated with poor SRH,[15,16] it is unknown whether certain multimorbidity patterns are associated with poor SRH.

Therefore, the present study aimed i) to identify the prevalence of multimorbidity and multimorbidity patterns and ii) to investigate the association between multimorbidity patterns and poor SRH in the older population in Japan using large nationwide data from the 2013 Comprehensive Survey of Living Conditions (CSLC). We focused on the older population in this study because stratifying multimorbidity patterns by age group is recommended to better understand the evolution of multimorbidity over a lifespan.[8]

METHODS

Design, setting, and participants

In this nationwide cross-sectional study, we used data from the CSLC conducted by the Ministry of Health, Labour, and Welfare (MHLW) of the Japanese government in June 2013.[17] The CSLC is a nationwide repeated cross-sectional survey of households and household members. In 2013, the CSLC covered all households and household members in 5,530 districts stratified and randomly selected from the census tracts. Trained investigators visited households to distribute and collect self-administered questionnaires. The survey items included a household-related questionnaire that inquired about sex, age, educational level, and work status and a health-related questionnaire that inquired about health conditions, difficulties in daily life, and status of medical check-ups. The MHLW provided anonymised data from the CSLC for 97,345 individuals in 2013.

For investigating the prevalence of multimorbidity, we excluded individuals who were aged <20 years or had missing age data and those who were hospitalised, institutionalised, or had missing residence data at the time of the survey because they were not included for the questions on health conditions. In the analysis of multimorbidity patterns, we excluded those aged <65 years because we wanted to investigate multimorbidity patterns in older people. Finally, we excluded individuals with missing SRH data from the analysis of the association between multimorbidity patterns and poor SRH.

Measures

Chronic health conditions

In the CSLC survey, participants chose from 42 options about health conditions for which they were attending medical institutions. The options included diabetes mellitus, obesity, dyslipidaemia, thyroid diseases, depression and other mental disorders, dementia, Parkinson's disease, other nervous system diseases, eye diseases, ear diseases, hypertension, stroke, angina pectoris or myocardial infarction, other circulatory system diseases, acute nasopharyngitis, allergic rhinitis, chronic obstructive pulmonary disease, asthma, other respiratory system diseases, stomach and duodenal diseases, liver and gallbladder diseases, other digestive system diseases, dental diseases, atopic dermatitis, other skin diseases, gout, rheumatoid arthritis, arthropathy, stiff neck, back pain, osteoporosis, kidney diseases, benign prostatic hyperplasia,

perimenopausal or postmenopausal disorders, fracture, injury or burn other than fracture, anaemia and other blood diseases, malignancies, pregnancy or puerperium, infertility, others, and unknown. We included 35 conditions after excluding the following seven conditions. Acute nasopharyngitis, fracture, injury or burn other than fracture, pregnancy or puerperium, others, and unknown were excluded because they were acute conditions or conditions whose acute or chronic state was difficult to determine. Although there are some previous studies on multimorbidity treated dental diseases as one of the chronic conditions,[18,19] most studies did not contain dental diseases in the list of chronic conditions.[1,8,20] Therefore, we excluded dental diseases. For individuals aged ≥65 years, 33 chronic conditions were included because none of the participants reported perimenopausal or postmenopausal disorders and infertility. To investigate multimorbidity patterns, 33 chronic diseases were grouped into 13 body system-dependent clusters based on the International Classification of Diseases (ICD)-10 chapters (Table 1). The reason for this grouping was that treatment of 'other' diseases, such as other neurological diseases, was difficult when analysing multimorbidity patterns. Assessment of multimorbidity by grouping conditions based on body systems, such as complex multimorbidity that can identify patients needing complex healthcare interventions rather than conventional multimorbidity, could be useful.[21] Moreover, since the multimorbidity patterns in the previous studies were mostly classified by organ systems,[2,8,19] we thought that grouping by organ system in advance would not have a significant effect on the pattern

composition.

Table 1. Grouping and prevalence of chronic conditions in older participants (N = 23,730)

13 body system-dependent clusters (ICD-10 chapter no.)	**33 chronic conditions included in the analyses**	**No. of affected participants (%)**
Malignancies (2)	Malignancies	364 (1.5)
Haematologic diseases (3)	Anaemia and other blood diseases	260 (1.1)
Endocrine and metabolic diseases (4)	Diabetes mellitus	2,578 (10.9)
	Obesity	256 (1.1)
	Dyslipidaemia	2,456 (10.3)
	Thyroid diseases	454 (1.9)
Mental disorders (5)	Depression and other mental disorders	329 (1.4)
Nervous system diseases (6)	Dementia	489 (2.1)
	Parkinson's disease	137 (0.6)
	Other nervous system diseases	296 (1.2)
Eye diseases (7)	Eye diseases	3,474 (14.6)
Ear diseases (8)	Ear diseases	608 (2.6)
Circulatory system diseases (9)	Hypertension	7,353 (31.0)
	Stroke	854 (3.6)
	Angina pectoris or myocardial infarction	1,359 (5.7)
	Other circulatory system diseases	1,085 (4.6)
Respiratory system diseases (10)	Allergic rhinitis	557 (2.3)
	Chronic obstructive pulmonary disease	90 (0.4)
	Asthma	419 (1.8)
	Other respiratory system diseases	467 (2.0)
Digestive system diseases (11)	Stomach and duodenal diseases	907 (3.8)
	Liver and gallbladder diseases	525 (2.2)
	Other digestive system diseases	553 (2.3)
Skin diseases (12)	Atopic dermatitis	98 (0.4)
	Other skin diseases	614 (2.6)
Musculoskeletal system diseases (13)	Gout	375 (1.6)
	Rheumatoid arthritis	374 (1.6)
	Arthropathy	1,382 (5.8)
	Stiff neck	1,344 (5.7)
	Back pain	2,921 (12.3)
	Osteoporosis	1,304 (5.5)

Urinary system diseases (14)	Kidney diseases	534 (2.3)
	Benign prostatic hyperplasia	949 (4.0)

ICD, International Statistical Classification of Diseases and Related Health Problems

We defined multimorbidity as the coexistence of ≥2 chronic health conditions out of 35 conditions and complex multimorbidity as the presence of ≥3 affected body systems out of 13 systems based on the ICD-10 chapters within one person.

Self-rated health

Data on SRH were obtained through the question 'What is your present general health status?' Participants chose from five options: 'excellent', 'fairly good', 'average', 'not very good', and 'bad'. Those who chose 'excellent', 'fairly good', or 'average' were regarded as being in a 'fine SRH' condition, whereas those who chose 'not very good' or 'bad' were regarded as being in a 'poor SRH' condition. The distribution of responses to the five scale items differs depending on the country owing to cultural differences. When dividing the five scale items into two values, it is common in Europe and the United States to classify the middle 'average' or 'good' as 'poor SRH',[22] whereas in Japan and Korea, it is common to classify 'average' or 'good' as 'fine SRH'.[23,24]

Covariates

Previous studies have reported that older age, female sex, and lower educational levels

are associated with multimorbidity and poor SRH;[24–26] therefore, we used age, sex, and educational level as covariates. Data on age were provided in 5-year categories. Data regarding educational level were divided into three categories: less than high school, high school, and more than high school.

The risk of psychological distress is reportedly higher in people with multimorbidity,[27] and psychological distress is an independent predictor of change in SRH;[28] therefore, we hypothesised that psychological distress serves as a mediator between multimorbidity and SRH and evaluated the impact of psychological distress on the relationship between multimorbidity and SRH using the Kessler 6 (K6) score, a screening scale for psychological distress.[29,30] The Japanese version of the K6 scale is a validated scale that comprises six questions answered on a scale of 0-4, with a total score of 0-24.[31] We classified the scores into three categories: 0-4 (normal), 5-12 (psychological distress), and 13-24 (severe mental illness).[32]

Statistical analysis

We applied a two-step procedure to determine the extent to which multimorbidity patterns are associated with poor SRH.

Identification of multimorbidity patterns (exploratory factor analysis)

Multimorbidity patterns were determined using exploratory factor analysis based on polychoric correlations. We used 13 body system-dependent clusters grouped into 33 chronic health conditions, which were coded as dichotomous variables. We applied the maximum likelihood method and promax rotation. The number of factors was determined based on a parallel analysis. A factor loading greater than 0.30 is considered meaningful and was used as the criterion for item selection. Moreover, multimorbidity patterns were also determined based on clinical plausibility, as assessed by two primary care physicians (YH and TA).

Investigation of the associations between multimorbidity patterns and poor SRH (multivariable modified Poisson regression analyses)

For each participant, a multimorbidity pattern score was calculated for each identified pattern. These scores correspond to the number of affected body system-dependent clusters in each pattern.[11] Modified Poisson regression analyses (i.e. Poisson regression with robust error variance)[33] were conducted to investigate the association between each multimorbidity pattern score and poor SRH. We estimated the risk ratio directly using modified Poisson regression because the odds ratio derived from the logistic regression can no longer approximate the risk ratio due to the high prevalence of >10% of poor SRH.[34] The possible confounding variables—age, sex, and educational level—were included as covariates in the analyses. Each multimorbidity pattern score was individually included in the model to avoid

multicollinearity. To evaluate the impact of the K6 score as a mediator on the relationship between multimorbidity and SRH, we compared the results of two multivariable models with and without the K6 score. We analysed the association between a simple count of affected body systems, regardless of multimorbidity pattern, and poor SRH. Missing values for covariates were analysed as missing categories. As sensitivity analyses, we performed modified Poisson regression analyses with complete cases and after handling missing data with multiple imputations using a fully conditional specification. We created and analysed 100 multiple-imputed datasets. Because unmeasured confounding factors, such as income,[24–26] could be present, we calculated the E-value, which estimates how strong unmeasured confounders would need to be to overturn the association between each multimorbidity pattern score and poor SRH.[35,36]

All P-values were two-tailed, and statistical significance was set at $P < 0.05$. We used IBM SPSS Statistics 28.0 (IBM Japan, Tokyo, Japan) and R 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria) for the analysis.

Ethics

Ethical approval was not required for this study because it involved a secondary analysis of the national surveillance data that did not contain any personally identifiable

information. According to Article 36 of Japan's Statistics Act, anonymised data from the CSLC can be used for scientific research after approval by the MHLW of Japan.

Patient and public involvement

No patients or public were involved.

RESULTS

Supplemental Figure 1 shows a flowchart of the participants. The descriptive statistics of multimorbidity included 77,120 participants, factor analysis to identify multimorbidity patterns included 23,730 participants, and analyses to investigate the association between multimorbidity patterns and poor SRH included 23,340 participants.

The prevalence of multimorbidity was 20% in participants aged ≥20 years, 41% in those aged ≥65 years, and 48% in those aged ≥75 years. The prevalence of complex multimorbidity was 6.5% in participants aged ≥20 years, 16% in those aged ≥65 years, and 20% in those aged ≥75 years.

Table 1 shows the grouping and prevalence of chronic conditions in older participants. We conducted a parallel analysis to examine the maximum number of factors for exploratory factor analysis to identify multimorbidity patterns and a seven-factor solution was suggested. After factor analyses using two- to seven-factor solutions, a four-factor solution was adopted

because the multimorbidity pattern was the most clinically plausible and consistent with previous reports. Table 2 shows the factor loadings for the four-factor solution following an exploratory factor analysis in older participants who were not hospitalised or institutionalised in care facilities (N = 23,730).

Table 2. Factor loadings for the four-factor solution following an exploratory factor analysis in older participants (N = 23,730)

Chronic conditions (ICD-10 chapter no.)	No. of affected participants (%)	Factor 1	Factor 2	Factor 3	Factor 4
Malignancies (2)	364 (1.5)	-0.15	**0.66**	-0.04	-0.15
Haematologic diseases (3)	260 (1.1)	0.00	**0.41**	0.11	0.13
Endocrine and metabolic diseases (4)	5,062 (21.3)	0.19	-0.05	-0.02	**0.31**
Mental disorders (5)	329 (1.4)	**0.37**	-0.05	0.16	-0.14
Nervous system diseases (6)	880 (3.7)	-0.03	0.01	**0.99**	0.13
Eye diseases (7)	3,474 (14.6)	**0.56**	-0.02	-0.08	0.16
Ear diseases (8)	608 (2.6)	**0.69**	-0.07	-0.01	-0.06
Circulatory system diseases (9)	9,213 (38.8)	-0.11	-0.07	0.06	**0.71**
Respiratory system diseases (10)	1,421 (6.0)	0.27	0.20	0.00	0.00
Digestive system diseases (11)	1,866 (7.9)	0.17	**0.46**	-0.07	-0.13
Skin diseases (12)	705 (3.0)	0.17	0.24	0.02	0.08
Musculoskeletal system diseases (13)	4,959 (20.9)	**0.36**	0.02	-0.06	0.15
Urinary system diseases (14)	1,437 (6.1)	-0.06	**0.42**	0.04	0.16

ICD, International Statistical Classification of Diseases and Related Health Problems

Maximum likelihood method and promax rotation are applied.

Loadings are bolded if they exceed 0.30.

Three multimorbidity patterns were identified and labelled as follows: i) degenerative/mental health (Factor 1), ii) malignant/digestive/urologic/haematologic (Factor 2), and iii) cardiovascular/metabolic pattern (Factor 4). Factor 3 included only nervous system

diseases. There were very few participants with nervous system multimorbidity: only 37 participants (0.16% of the total older participants) had two or more nervous system diseases. Therefore, we have not considered this factor as a multimorbidity pattern. The respiratory system and skin diseases were not classified into any factor. Two primary care clinicians (YH and TA) agreed that the three multimorbidity patterns were clinically plausible.

Table 3 presents the characteristics of older participants with SRH data who were not hospitalised or institutionalised in care facilities (N = 23,340). Poor SRH was found in 5,554 participants (23.8%).

Table 3. Characteristics of older participants with SRH data who were not hospitalised or institutionalised

Characteristic	All participants (N = 23,340)	Fine SRH (N = 17,786)	Poor SRH (N = 5,554)
Age (years)			
65-69	6,818	5,704 (83.6)	1,114 (16.4)
70-74	6,029	4,816 (79.9)	1,213 (20.1)
75-79	4,910	3,625 (73.8)	1,285 (26.2)
80-84	3,149	2,111 (67.0)	1,038 (33.0)
85-89	1,686	1,056 (62.6)	630 (37.4)
≥90	748	474 (63.4)	274 (36.6)
Sex			
Male	10,266	7,956 (77.5)	2,310 (22.5)
Female	13,074	9,830 (75.2)	3,244 (24.8)
Educational level			
Less than high school	7,660	5,544 (72.4)	2,116 (27.6)
High school	8,810	6,841 (77.7)	1,969 (22.3)
More than high school	3,460	2,777 (80.3)	683 (19.7)
Data missing	3,410	2,624 (77.0)	786 (23.0)
K6 score			
0-4 (normal)	15,721	13,425 (85.4)	2,296 (14.6)

5-12 (psychological distress)	4,830	2,848 (59.0)	1,982 (41.0)
13-24 (severe mental illness)	696	171 (24.6)	525 (75.4)
Data missing	2,093	1,342 (64.1)	751 (35.9)
No. of morbidities			
0	7,308	6,546 (89.6)	762 (10.4)
1	6,458	5,145 (79.7)	1,313 (20.3)
2	4,648	3,383 (72.8)	1,265 (27.2)
3	2,560	1,585 (61.9)	975 (38.1)
4	1,245	700 (56.2)	545 (43.8)
≥5	1,121	427 (38.1)	694 (61.9)
Multimorbidity*			
Yes	9,574	6,095 (63.7)	3,479 (36.3)
No	13,766	11,691 (84.9)	2,075 (15.1)
Complex multimorbidity†			
Yes	3,637	1,933 (53.1)	1,704 (46.9)
No	19,703	15,853 (80.5)	3,850 (19.5)

Data were presented as the number (percentage) of participants.

SRH, self-rated health; K6, Kessler 6

*Multimorbidity was defined as the coexistence of ≥2 chronic health conditions.

†Complex multimorbidity was defined as the presence of ≥3 affected body systems.

The association between multimorbidity pattern scores and poor SRH adjusted for age, sex, and educational level as covariates is summarised in Table 4 and that adjusted for age, sex, educational level, and K6 is shown in Table 5. Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern (e.g. the malignant/digestive/urologic/haematologic pattern score for a person with malignancy and anaemia was two). In the model with age, sex, and educational level as covariates, high malignant/digestive/urologic/haematologic, degenerative/mental health, and cardiovascular/metabolic pattern scores were significantly associated with poor SRH (adjusted

risk ratio [aRR] = 1.68, 95% confidence interval [CI]: 1.60-1.76, aRR = 1.63, 95% CI: 1.58-1.69, and aRR = 1.31, 95% CI: 1.26-1.36, respectively) (Table 4). The E-value for the association between each multimorbidity pattern score and poor SRH was 2.75 (lower limit of 95% CI: 2.58) for malignant/digestive/urologic/haematologic pattern, 2.64 (lower limit of 95% CI: 2.54) for degenerative/mental health pattern, and 1.95 (lower limit of 95% CI: 1.83) for cardiovascular/metabolic pattern. In the model with age, sex, educational level, and K6 as covariates, high malignant/digestive/urologic/haematologic, degenerative/mental health, and cardiovascular/metabolic pattern scores were significantly associated with poor SRH (aRR = 1.47, 95% CI: 1.40-1.54, aRR = 1.44, 95% CI: 1.39-1.49, and aRR = 1.24, 95% CI: 1.19-1.28, respectively) (Table 5). The E-value for the association between each multimorbidity pattern score and poor SRH was 2.30 (lower limit of 95% CI: 2.15) for malignant/digestive/urologic/haematologic pattern, 2.24 (lower limit of 95% CI: 2.13) for degenerative/mental health pattern, and 1.79 (lower limit of 95% CI: 1.67) for cardiovascular/metabolic pattern. The association between multimorbidity pattern scores and poor SRH was reduced when K6 was added to the model as a covariate, particularly for the malignant/digestive/urologic/haematologic and degenerative/mental health patterns. Although the simple count of affected body systems, regardless of multimorbidity pattern, was also significantly associated with poor SRH when adjusted for age, sex, and educational level with and without K6 as covariates (aRR = 1.35, 95% CI: 1.34-1.37 and aRR = 1.27, 95% CI: 1.25-

295 1.29, respectively), the association was smaller than the
296 malignant/digestive/urologic/haematologic and degenerative/mental health pattern scores and
297 equivalent to cardiovascular/metabolic pattern scores.
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Table 4. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses without K6.

	Malignant/digestive/urologic /haematologic pattern		Degenerative /mental health pattern*		Cardiovascular/metabolic pattern	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.68 (1.60-1.76)	<0.001	1.63 (1.58-1.69)	<0.001	1.31 (1.26-1.36)	<0.001
Age (years)						
65-69	ref		ref		ref	
70-74	1.19 (1.10-1.30)	<0.001	1.14 (1.06-1.24)	<0.001	1.22 (1.13-1.33)	<0.001
75-79	1.52 (1.40-1.65)	<0.001	1.38 (1.28-1.50)	0.001	1.58 (1.46-1.72)	<0.001
80-84	1.87 (1.72-2.04)	<0.001	1.69 (1.55-1.85)	<0.001	1.99 (1.82-2.17)	<0.001
85-89	2.11 (1.91-2.34)	<0.001	1.92 (1.74-2.12)	<0.001	2.24 (2.03-2.48)	<0.001
≥90	2.06 (1.80-2.36)	<0.001	1.94 (1.70-2.23)	<0.001	2.19 (1.92-2.51)	<0.001
Female sex	1.14 (1.08-1.21)	<0.001	0.97 (0.92-1.03)	0.34	1.03 (0.98-1.09)	0.27
Educational level						
Less than high school	ref		ref		ref	
High school	0.91 (0.85-0.97)	0.003	0.91 (0.86-0.97)	0.005	0.91 (0.86-0.97)	0.004
More than high school	0.83 (0.76-0.91)	<0.001	0.84 (0.77-0.92)	<0.001	0.83 (0.76-0.91)	<0.001
Data missing	0.92 (0.84-1.00)	0.038	0.93 (0.86-1.02)	0.13	0.93 (0.86-1.01)	0.091

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, and educational level.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern. Each pattern score was individually included in the model, adjusted for age, sex, and educational level.

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Table 5. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses with K6.

	Malignant/digestive/urologic /haematologic pattern		Degenerative /mental health pattern*		Cardiovascular/metabolic pattern	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.47 (1.40-1.54)	<0.001	1.44 (1.39-1.49)	<0.001	1.24 (1.19-1.28)	<0.001
Age (years)						
65-69	ref		ref		ref	
70-74	1.15 (1.06-1.25)	<0.001	1.12 (1.03-1.22)	0.007	1.15 (1.06-1.25)	<0.001
75-79	1.41 (1.30-1.53)	<0.001	1.32 (1.22-1.44)	<0.001	1.43 (1.31-1.55)	<0.001
80-84	1.64 (1.50-1.79)	<0.001	1.55 (1.42-1.69)	<0.001	1.68 (1.54-1.83)	<0.001
85-89	1.78 (1.61-1.96)	<0.001	1.70 (1.54-1.88)	<0.001	1.82 (1.64-2.01)	<0.001
≥90	1.67 (1.46-1.92)	<0.001	1.65 (1.45-1.90)	<0.001	1.71 (1.50-1.96)	<0.001
Female sex	1.05 (0.99-1.11)	0.10	0.93 (0.88-0.98)	0.006	0.97 (0.92-1.03)	0.29
Educational level						
Less than high school	ref		ref		ref	
High school	0.95 (0.89-1.01)	0.081	0.95 (0.89-1.01)	0.089	0.95 (0.89-1.02)	0.14
More than high school	0.90 (0.82-0.98)	0.020	0.92 (0.84-1.00)	0.054	0.91 (0.84-1.00)	0.051
Data missing	0.88 (0.80-0.95)	0.002	0.89 (0.82-0.97)	0.007	0.89 (0.82-0.97)	0.006
K6 score						
0-4 (normal)	ref		ref		ref	
5-12 (psychological distress)	2.66 (2.51-2.83)	<0.001	2.51 (2.36-2.67)	<0.001	2.74 (2.57-2.91)	<0.001
13-24 (severe mental illness)	4.31 (3.91-4.75)	<0.001	3.94 (3.57-4.34)	<0.001	4.60 (4.18-5.07)	<0.001
Data missing	2.35 (2.16-2.56)	<0.001	2.25 (2.07-2.45)	<0.001	2.39 (2.20-2.60)	<0.001

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, educational level, and K6.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern.

Each pattern score was individually included in the model, adjusted for age, sex, educational level, and K6 score.

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For sensitivity analyses, we performed modified Poisson regression analyses with complete cases and after handling missing data with multiple imputations (Supplemental Tables 1 and 2). The proportion of missing values was 14.6% for educational level and 9.0% for K6. In total, 4,806 of the 23,340 records (20.6%) were incomplete. The association of each multimorbidity pattern score and covariate with poor SRH did not differ considerably between the analyses using multiple imputations and the analyses on the subset of complete cases.

DISCUSSION

In the present study of nationally representative data from 77,120 participants in Japan who were not hospitalised or institutionalised, we found a prevalence of multimorbidity. Analysis using data from 23,730 older participants aged ≥65 years revealed three multimorbidity patterns: i) degenerative/mental health, ii) malignant/digestive/urologic/haematologic, and iii) cardiovascular/metabolic. To the best of our knowledge, this is the first study to investigate the association between certain multimorbidity patterns and SRH. We found a positive association between each multimorbidity pattern score and poor SRH. This association was stronger for degenerative/mental health and malignant/digestive/urologic/haematologic patterns than for cardiovascular/metabolic patterns. Health care professionals can use the results to recognise multimorbidity in patients at high risk for poor SRH and consider possible interventions.

Although the prevalence of multimorbidity in the present study was relatively lower than that reported in previous studies from Europe, North America, Australia, and Japan,[1,2] it would considerably reflect the prevalence in the free-living general population in Japan. The prevalence of multimorbidity could have been lower in our study because the survey excluded hospitalised or institutionalised people who were expected to have more chronic conditions. The results reflect the state of the community residents who visit medical institutions and are subject to health care policies. In addition, differences in the method of ascertainment of chronic conditions could contribute to differences in the prevalence. Various methods have been used in previous studies, including self-reporting, administrative health records, and clinical assessments.[1] Moreover, within self-reports, questions about chronic conditions varied among surveys. Although the participants in this study were asked about the health conditions for which they were attending medical institutions at the time of the survey, participants in another study were asked about chronic conditions that had been reported by healthcare professionals.[2] As this study did not cover inactive conditions that were not being attended to in medical institutions at the time, it could reflect only the conditions that were currently burdening participants.

Because the multimorbidity patterns in this study were plausible based on previous reports and clinical perspectives, they can be widely generalised to older people in developed countries. Mental health pattern and cardiometabolic pattern were reported as the two most

replicable multimorbidity patterns in a systematic review in 2019,[8] whereas another systematic review in Asia reported the following five patterns: cardiovascular/metabolic, mental health, degenerative, pulmonary, and cancer.[20] The systematic review in Asia contained one study from Japan that reported five patterns: cardiovascular/renal/metabolic, neuropsychiatric, skeletal/articular/digestive, respiratory/dermal, and malignant/digestive/urologic.[2] We found that the cardiovascular/metabolic pattern was consistent with that reported in previous studies. The degenerative/mental health pattern in this study was close to the falls/fractures/vision disorders/cognitive impairment and falls/vision impairment/cognitive impairment/urinary incontinence/hearing impairment reported in the systematic review in 2019, and mental patterns and degenerative patterns in the systematic review in Asia. As a mechanism for the construction of this pattern, we speculate that communication disability, social isolation, functional disability, limited mobility, and poorly treated pain due to vision and hearing impairment[37] or musculoskeletal diseases led to mental disorders such as depression. Moreover, patients with musculoskeletal diseases have a high risk of depression and anxiety, and those with both musculoskeletal diseases and anxiety or depression show increased pain,[38] explaining the interrelationship between musculoskeletal diseases and mental health disorders in degenerative/mental health patterns. The malignant/digestive/urologic/haematologic pattern in this study was similar to the pattern reported in the previous study in Japan. As a mechanism for the construction of this pattern,

we speculate that digestive and urologic organs are relatively frequent as sites of primary lesions in cancer survivors.[39] Furthermore, anaemia is a common complication of malignancy and its treatment[40,41] and can also be associated with chronic kidney disease[42] or bleeding due to gastrointestinal diseases. The multimorbidity patterns revealed by the data limited to the older population in this study may differ from those reported in previous studies involving younger generations. We believe it is valuable to report multimorbidity patterns in the older in Japan, where the population is ageing ahead of the rest of the world.

The association between multimorbidity pattern scores and poor SRH was greater for malignant/digestive/urologic/haematologic and degenerative/mental health patterns than for cardiovascular/metabolic patterns. The strong association between malignant/digestive/urologic/haematologic patterns and poor SRH in the present study is consistent with the findings of a previous study that reported poorer SRH in older cancer survivors than in people without cancer.[43] Symptoms of digestive or urological conditions can affect eating and elimination, which may exacerbate SRH. The strong association between degenerative/mental health patterns and poor SRH in this study is consistent with the findings of previous studies. Rheumatic and musculoskeletal diseases have been reported to have the strongest association with poor SRH among the chronic conditions.[44] SRH in older people with multimorbidity is exacerbated by vision impairment, hearing impairment, depression, and anxiety.[45] Mental disorders and/or musculoskeletal diseases have been reported as

combinations of chronic conditions associated with poor SRH.[46] Communication disability, social isolation, functional disability, limited mobility, and poorly treated pain due to vision and hearing impairment or musculoskeletal diseases can worsen SRH. Reportedly, multimorbidity, depressive symptoms, and disability synergistically exacerbate SRH.[47] The combined involvement of these factors in degenerative/mental health patterns could explain the strong association with poor SRH. In contrast, the association between cardiovascular/metabolic patterns and poor SRH was weaker than that between other patterns and poor SRH. We suspect that this is because stable conditions of cardiovascular/metabolic diseases, such as diabetes or ischaemic heart disease, may not have severe symptoms and may not affect daily life significantly. However, one previous study reported that cardiometabolic diseases contribute the most to the worsening of SRH in the general population aged 30-79 years in China.[48] Differences in participants' ages across studies may affect multimorbidity patterns and the association between these patterns and SRH.

The K6, a screening scale for psychological distress, partially mediated the association between multimorbidity pattern scores and poor SRH. Comparing the models of multivariable regression analysis that included K6 and those that did not include it revealed that the association between multimorbidity pattern scores and poor SRH was weaker in the model that included K6 for all three patterns. We speculate that the growing patient burden due to the increasing number of chronic conditions may have partially caused psychological distress,

resulting in the worsening of SRH.[27,28] There might be a correlation between the degenerative/mental health pattern score and K6 conceptually. However, because the Pearson correlation coefficient between the degenerative/mental health pattern score and K6 was 0.053 and the variance inflation factor of the degenerative/mental health pattern score and K6 was 1.025 and 1.035 in the multivariable model, respectively, no significant multicollinearity was noted of concern in statistical analysis.

The results of this study will help clinicians recognise patients with multimorbidity patterns, which are highly associated with poor SRH, and consider possible interventions. Because the multimorbidity pattern score we used was simple and easy to apply in clinical practice, clinicians could calculate the score for each patient and assess the risk of poor SRH. Given that a previous study reported that the association between multimorbidity and poor SRH could be reduced by increasing physical activity,[49] clinicians may improve SRH by prescribing exercise to patients with multimorbidity at risk for poor SRH. Further research is warranted to confirm whether such interventions can improve SRH in patients with multimorbidity.

Our study has several limitations. First, because of the cross-sectional design, it was impossible to determine whether there was a causal relationship between multimorbidity patterns and SRH. Additional research using a longitudinal design is needed to confirm the association between multimorbidity patterns and SRH. Second, because chronic diseases were

measured using self-report questionnaires, it is possible that the prevalence of chronic diseases was underestimated or that the conditions were misclassified. However, previous studies have demonstrated that assessment of morbidity using self-reported data can predict clinical outcomes, including SRH, compared with measures based on administrative data.[50] Third, there might be unmeasured confounding factors, such as income.[24–26] However, the E-values for the association between each multimorbidity pattern score and poor SRH were reasonably high, making it unlikely that unmeasured confounders would overturn the observed association between each multimorbidity pattern score and poor SRH. Fourth, we could not show the magnitude of mediation by the psychological distress of the relationship between multimorbidity and SRH, as it is beyond the study scope. This should be examined in future studies using causal mediation analysis. Finally, it is unclear whether the results of this study can be applied to older adults who require hospitalisation or institutionalisation, such as those with severe chronic diseases or functional decline, because the survey did not include such patients.

CONCLUSIONS

We found differences in the association between multimorbidity patterns and poor SRH. Malignant/digestive/urologic/haematologic and degenerative/mental health patterns may be associated with a high risk for poor SRH. Further research should focus on interventions to

improve SRH in patients with multimorbidity.

Statements

Author contributions: All authors (YH, MN, TA, and TO) contributed to the conception or design of the study, reviewed and edited the manuscript, contributed to the interpretation of the data and the analyses, performed critical review of the manuscript, and gave the final approval of the manuscript before submission. YH performed the statistical analyses and drafted the manuscript. MN, TA, and TO supervised the work.

Competing interest: TA received a grant from Pfizer Health Research Foundation, Japan for another research project related to multimorbidity (Grant No. 21-E-01).

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Data availability: These data were derived from the CSLC in June 2013, which was conducted by the MHLW of Japan. You can use the anonymous data if you apply for and receive permission from the ministry. [https://www.mhlw.go.jp/toukei/itaku/tokumei.html]

Participant consent: Not applicable.

Ethical approval: Ethical approval was not required for this study because it involved a secondary analysis of the national surveillance data that did not contain any personally identifiable information. According to Article 36 of Japan's Statistics Act, anonymised data

from the CSLC can be used for scientific research after approval by the MHLW of Japan.

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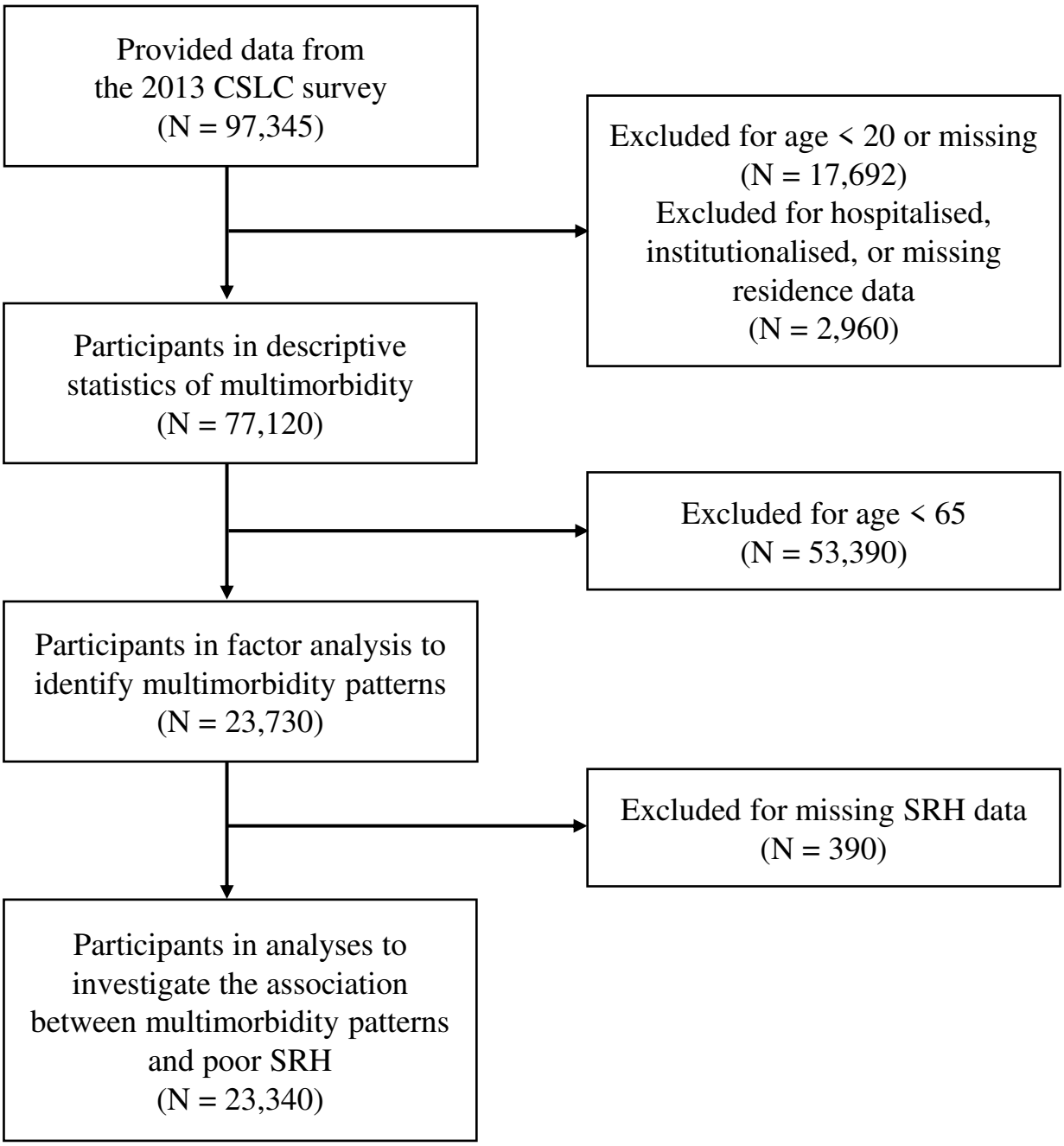
Supplemental Figure 1. Participant flow chart.



CSLC, the Comprehensive Survey of Living Conditions; SRH, self-rated health

Supplemental Table 1. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses without K6.

	Malignant/digestive/urologic/haematologic pattern				Degenerative/mental health pattern*				Cardiovascular/metabolic pattern			
	Complete case analysis (N = 19,930)		Multiple imputation (N = 23,340)		Complete case analysis (N = 19,930)		Multiple imputation (N = 23,340)		Complete case analysis (N = 19,930)		Multiple imputation (N = 23,340)	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.68 (1.62-1.75)	<0.001	1.69 (1.63-1.75)	<0.001	1.65 (1.60-1.69)	<0.001	1.65 (1.61-1.69)	<0.001	1.30 (1.25-1.34)	<0.001	1.29 (1.26-1.34)	<0.001
Age (years)												
65-69	ref		ref		ref		ref		ref		ref	
70-74	1.18 (1.09-1.28)	<0.001	1.19 (1.10-1.28)	<0.001	1.14 (1.06-1.24)	0.001	1.15 (1.07-1.23)	<0.001	1.19 (1.10-1.29)	<0.001	1.19 (1.11-1.28)	<0.001
75-79	1.53 (1.41-1.65)	<0.001	1.49 (1.39-1.60)	<0.001	1.41 (1.30-1.52)	<0.001	1.38 (1.29-1.49)	<0.001	1.55 (1.43-1.67)	<0.001	1.51 (1.41-1.63)	<0.001
80-84	1.83 (1.69-1.98)	<0.001	1.82 (1.69-1.96)	<0.001	1.69 (1.56-1.83)	<0.001	1.69 (1.57-1.82)	<0.001	1.90 (1.75-2.06)	<0.001	1.89 (1.75-2.04)	<0.001
85-89	2.05 (1.87-2.24)	<0.001	2.06 (1.90-2.24)	<0.001	1.90 (1.74-2.08)	<0.001	1.92 (1.77-2.09)	<0.001	2.13 (1.95-2.33)	<0.001	2.13 (1.96-2.32)	<0.001
≥90	2.08 (1.85-2.33)	<0.001	2.00 (1.79-2.24)	<0.001	2.01 (1.79-2.26)	<0.001	1.95 (1.74-2.17)	<0.001	2.16 (1.92-2.42)	<0.001	2.08 (1.87-2.33)	<0.001
Female sex	1.13 (1.08-1.19)	<0.001	1.13 (1.08-1.19)	<0.001	0.96 (0.92-1.01)	0.15	0.96 (0.92-1.01)	0.12	1.03 (0.98-1.09)	0.21	1.03 (0.98-1.08)	0.21
Educational level												
Less than high school	ref		ref		ref		ref		ref		ref	
High school	0.91 (0.86-0.96)	<0.001	0.91 (0.86-0.96)	<0.001	0.91 (0.87-0.96)	<0.001	0.91 (0.87-0.96)	<0.001	0.91 (0.87-0.96)	<0.001	0.91 (0.87-0.96)	<0.001
More than high school	0.83 (0.77-0.89)	<0.001	0.83 (0.77-0.90)	<0.001	0.85 (0.78-0.91)	<0.001	0.85 (0.79-0.92)	<0.001	0.84 (0.78-0.91)	<0.001	0.85 (0.79-0.92)	<0.001

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, and educational level.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern.

Each pattern score was individually included in the model, adjusted for age, sex, and educational level.

Supplemental Table 2. Associations between multimorbidity pattern scores and poor SRH. Modified Poisson regression analyses with K6.

	Malignant/digestive/urologic/haematologic pattern				Degenerative/mental health pattern*				Cardiovascular/metabolic pattern			
	Complete case analysis (N = 18,534)		Multiple imputation (N = 23,340)		Complete case analysis (N = 18,534)		Multiple imputation (N = 23,340)		Complete case analysis (N = 18,534)		Multiple imputation (N = 23,340)	
	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value	Poor SRH (aRR (95% CI))	P value
Multimorbidity pattern score†	1.49 (1.44-1.56)	<0.001	1.49 (1.44-1.54)	<0.001	1.47 (1.43-1.51)	<0.001	1.46 (1.42-1.50)	<0.001	1.24 (1.20-1.29)	<0.001	1.24 (1.20-1.28)	<0.001
Age (years)												
65-69	ref		ref		ref		ref		ref		ref	
70-74	1.15 (1.06-1.25)	<0.001	1.17 (1.09-1.25)	<0.001	1.12 (1.04-1.21)	0.005	1.14 (1.06-1.22)	<0.001	1.16 (1.07-1.25)	<0.001	1.17 (1.09-1.25)	<0.001
75-79	1.51 (1.40-1.63)	<0.001	1.46 (1.37-1.57)	<0.001	1.41 (1.31-1.53)	<0.001	1.38 (1.29-1.48)	<0.001	1.52 (1.40-1.64)	<0.001	1.48 (1.38-1.58)	<0.001
80-84	1.75 (1.61-1.90)	<0.001	1.71 (1.59-1.84)	<0.001	1.64 (1.51-1.78)	<0.001	1.61 (1.50-1.73)	<0.001	1.78 (1.64-1.93)	<0.001	1.74 (1.63-1.87)	<0.001
85-89	1.86 (1.69-2.04)	<0.001	1.85 (1.71-2.01)	<0.001	1.76 (1.61-1.93)	<0.001	1.77 (1.63-1.92)	<0.001	1.89 (1.73-2.07)	<0.001	1.89 (1.74-2.05)	<0.001
≥90	1.82 (1.62-2.05)	<0.001	1.73 (1.56-1.92)	<0.001	1.81 (1.61-2.04)	<0.001	1.72 (1.54-1.91)	<0.001	1.87 (1.66-2.10)	<0.001	1.76 (1.59-1.96)	<0.001
Female sex	1.06 (1.01-1.12)	0.031	1.05 (1.00-1.10)	0.039	0.93 (0.88-0.98)	0.005	0.92 (0.88-0.97)	<0.001	0.98 (0.93-1.03)	0.45	0.97 (0.93-1.02)	0.25
Educational level												
Less than high school	ref		ref		ref		ref		ref		ref	
High school	0.93 (0.88-0.98)	0.009	0.94 (0.89-0.98)	0.009	0.93 (0.88-0.99)	0.012	0.94 (0.89-0.99)	0.011	0.94 (0.89-0.99)	0.018	0.94 (0.90-0.99)	0.023
More than high school	0.89 (0.83-0.97)	0.004	0.89 (0.83-0.96)	0.002	0.91 (0.84-0.98)	0.016	0.91 (0.85-0.98)	0.009	0.91 (0.84-0.98)	0.014	0.91 (0.85-0.98)	0.012
K6 score												
0-4 (normal)	ref		ref		ref		ref		ref		ref	
5-12 (psychological distress)	2.57 (2.44-2.71)	<0.001	2.61 (2.48-2.74)	<0.001	2.47 (2.34-2.61)	<0.001	2.50 (2.38-2.63)	<0.001	2.64 (2.50-2.78)	<0.001	2.66 (2.53-2.79)	<0.001
13-24 (severe mental illness)	4.31 (4.04-4.60)	<0.001	4.29 (4.05-4.55)	<0.001	3.98 (3.71-4.26)	<0.001	3.97 (3.72-4.23)	<0.001	4.57 (4.29-4.86)	<0.001	4.56 (4.31-4.83)	<0.001

SRH, self-rated health; K6, Kessler 6; aRR, adjusted risk ratio; CI, confidence interval

Adjusted for age, sex, educational level, and K6.

*Degenerative/mental health pattern consisted of ear, eye, and musculoskeletal system diseases and mental disorders.

†Multimorbidity pattern scores corresponded to the number of affected body system-dependent clusters in each pattern.

Each pattern score was individually included in the model, adjusted for age, sex, educational level, and K6 score.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-11
Bias	9	Describe any efforts to address potential sources of bias	7-13
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11-13
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	13
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6
		(*e*) Describe any sensitivity analyses	13
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14 and Supplemental Figure 1
		(b) Give reasons for non-participation at each stage	Supplemental Figure 1
		(c) Consider use of a flow diagram	Supplemental Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	16 and Table 3
		(b) Indicate number of participants with missing data for each variable of interest	Table 3
Outcome data	15*	Report numbers of outcome events or summary measures	16 and Table 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	17-19 and Tables 4 and 5
		(*b*) Report category boundaries when continuous variables were categorized	Table 5
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	21 and Supplemental Tables 1 and 2
Discussion			
Key results	18	Summarise key results with reference to study objectives	21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	26-27
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	26
Generalisability	21	Discuss the generalisability (external validity) of the study results	22, 24, and 27
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	28

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.