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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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4 **Multimorbidity patterns and the relation to self-rated health among older Japanese**
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7 **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)

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4 cardiovascular/metabolic. Multivariable modified Poisson regression analysis revealed that
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7 high malignant/digestive/urologic/haematologic, degenerative/mental health, and
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10 cardiovascular/metabolic pattern scores, corresponding to the number of affected body systems
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13 in each pattern, were significantly associated with poor SRH [adjusted risk ratio (aRR) = 1.68,
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16 95% confidence interval (CI): 1.60-1.76, aRR = 1.63, 95% CI: 1.58-1.69; and aRR = 1.31, 95%
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19 CI: 1.26-1.36, respectively]. When including the Kessler 6 score, a screening scale for
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22 depression, as a covariate in the analysis, the association between each multimorbidity pattern
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25 score and poor SRH decreased.
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28 **Conclusions:** Malignant/digestive/urologic/haematologic and degenerative/mental health
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31 patterns may be associated with a high risk for poor SRH. Further research should focus on
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34 interventions to improve SRH in multimorbidity patients.
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41 **Strengths and limitations of this study**

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43 • This study reports the prevalence and patterns of multimorbidity, which is important in
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46 an ageing society, based on nationally representative data randomly selected from the
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49 general population in Japan.
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52 • This is the first report to investigate associations between certain multimorbidity
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55 patterns and SRH.
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58 • Health care professionals can recognise multimorbidity patients at high risk for poor
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4 SRH and consider possible interventions.
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- 8 • Because of the study's cross-sectional design, it was impossible to determine whether
9
10 there was a causal relationship between multimorbidity patterns and poor SRH.
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 - 13 • Because chronic diseases were examined using self-report questionnaires, the
14
15 prevalence of chronic diseases might be underestimated or conditions might be
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17 misclassified.
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25 INTRODUCTION

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28 Multimorbidity is defined as the co-occurrence of two or more chronic conditions
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30 within a person and is common in older people, requiring individualised management. In
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32 Europe, North America, and Australia, the prevalence of multimorbidity was reported as
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34 approximately 10-50% in individuals aged 20-65 years and 70-80% in those aged ≥ 65 years.[1]
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37 A study from Japan showed similar results, with a prevalence of multimorbidity of 29.9% for
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39 those aged ≥ 18 years and 62.8% for those aged ≥ 65 years.[2] However, the prevalence of
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41 multimorbidity varies widely from a few percent to 80% among older people in China[3] and
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43 is approximately 20% among adults in South Korea.[4] Multimorbidity is associated with
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45 several health care outcomes, including mortality, hospitalisation, functional limitations, and
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47 health care utilisation and costs.[5] Furthermore, the management of multimorbidity is difficult
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49 because applying a combination of individual clinical practice guidelines for each disease to
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4 multimorbidity patients may increase the treatment burden and negatively affect the
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7 patients.[6] Multimorbidity is highly complex and heterogeneous, with various disease
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10 combinations, and the guidelines for multimorbidity recommend individualised
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13 management.[7]
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16 Multimorbidity patterns and their association with health care outcomes have been the
17
18 focus of much attention. A systematic review of 51 studies showed that mental health and
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20 cardiometabolic patterns were the two most replicable multimorbidity patterns based on
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22 specific combinations of conditions.[8] In a study of 3,256 Japanese general people, five
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24 multimorbidity patterns were identified: cardiovascular/renal/metabolic, neuro/psychiatric,
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26 skeletal/articular/digestive, respiratory/dermal, and malignant/digestive/urologic.[2]
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29 Furthermore, previous studies have reported associations between certain multimorbidity
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31 patterns and clinical outcomes, such as mortality,[9] functional ability,[10] and reduced health-
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33 related quality of life.[11] In caring for patients with multimorbidity, classifying individuals
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35 into multimorbidity patterns can be useful in identifying the target population with poorer
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37 clinical outcomes.
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49 Self-rated health (SRH), the subjective perception of an individual's overall health, is
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51 a simple and powerful predictor of outcomes, such as mortality[12] and health care
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53 expenditure.[13] SRH is also one of the core outcomes in patients with multimorbidity.[14]
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56 Although several studies have shown that multimorbidity is associated with poor SRH,[15],[16]
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4 it is unknown whether certain multimorbidity patterns are associated with poor SRH.
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7 Therefore, the present study aimed i) to identify the prevalence of multimorbidity and
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10 multimorbidity patterns and ii) to investigate the association between multimorbidity patterns
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13 and poor SRH in the older population in Japan using large nationwide data from the 2013
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16 Comprehensive Survey of Living Conditions (CSLC). We focused on the older population in
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19 this study because stratifying multimorbidity patterns by age group is recommended to better
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22 understand the evolution of multimorbidity over a lifespan.[8]
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28 **METHODS**

29 **Design, setting, and participants**

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32 In this nationwide cross-sectional study, we used data from the CSLC conducted by
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35 the Ministry of Health, Labour, and Welfare (MHLW) of the Japanese government in June
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38 2013.[17] The CSLC is a nationwide repeated cross-sectional survey of households and
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41 household members. In 2013, the CSLC covered all households and household members in
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43
44 5,530 districts stratified and randomly selected from the census tracts. Trained investigators
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47 visited households to distribute and collect self-administered questionnaires. The survey items
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50 included household questionnaire that inquiring about sex, age, educational level, and work
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53 status as well as health questionnaire that inquiring about health conditions, difficulties in daily
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56 life, and the status of medical check-ups. The MHLW provided anonymised data from the
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4 CSLC for 97,345 individuals in 2013.
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7 For investigating the prevalence of multimorbidity, we excluded individuals who were
8 aged <20 years or had missing age data and those who were hospitalised, institutionalised, or
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10 had missing residence data at the time of the survey because they were not included for the
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12 questions on health conditions. In the analysis of multimorbidity patterns, we excluded those
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14 aged <65 years because we wanted to investigate multimorbidity patterns in older people.
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16 Finally, we excluded individuals with missing SRH data from the analysis of the association
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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,

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4 arthropathy, stiff neck, back pain, osteoporosis, kidney diseases, benign prostatic hyperplasia,
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7 perimenopausal or postmenopausal disorders, fracture, injury or burn other than fracture,
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10 anaemia and other blood diseases, malignancies, pregnancy or puerperium, infertility, others,
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13 and unknown. We used 34 conditions after excluding eight conditions: acute nasopharyngitis,
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16 dental diseases, fracture, injury or burn other than fracture, pregnancy or puerperium, infertility,
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19 others, and unknown, as they were not considered chronic conditions. For individuals aged ≥ 65
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22 years, 33 chronic conditions were included because none of the participants reported
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25 perimenopausal or postmenopausal disorders. To investigate multimorbidity patterns, 33
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28 chronic diseases were grouped into 13 body system-dependent clusters based on International
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31 Classification of Diseases (ICD)-10 chapters: malignancies, haematologic diseases (anaemia
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34 and other blood diseases), endocrine and metabolic diseases (diabetes mellitus, obesity,
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37 dyslipidaemia, and thyroid diseases), mental disorders (depression and other mental disorders),
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40 nervous system diseases (dementia, Parkinson's disease, and other nervous system diseases),
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43 eye diseases, ear diseases, circulatory system diseases (hypertension, stroke, angina pectoris or
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46 myocardial infarction, and other circulatory system diseases), respiratory system diseases
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49 (allergic rhinitis, chronic obstructive pulmonary disease, asthma, and other respiratory system
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52 diseases), digestive system diseases (stomach and duodenal diseases, liver and gallbladder
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55 diseases, and other digestive system diseases), skin diseases (atopic dermatitis and other skin
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58 diseases), musculoskeletal system diseases (gout, rheumatoid arthritis, arthropathy, stiff neck,
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4 back pain, and osteoporosis), and urinary system diseases (kidney diseases and benign prostatic
5 hyperplasia). The reason for this grouping was that it was difficult to treat ‘other’ diseases,
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7 such as other neurological diseases, when analysing multimorbidity patterns. Assessment of
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9 multimorbidity by grouping conditions based on body systems, such as complex
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11 multimorbidity that can identify patients needing complex healthcare interventions rather than
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13 conventional multimorbidity, could be useful.[18] In addition, since the multimorbidity
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15 patterns in the previous studies were mostly classified by organ systems,[2, 8, 19] we thought
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17 that grouping by organ system in advance would not have a significant effect on the pattern
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19 composition.
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31 We defined multimorbidity as the coexistence of ≥ 2 chronic health conditions out of 34
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33 conditions and complex multimorbidity as the presence of ≥ 3 affected body systems out of 13
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35 systems based on the ICD-10 chapters within one person.
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43 Self-rated health

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46 Data on SRH were obtained through the question ‘What is your present general health
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48 status?’ Participants chose from five options: ‘excellent’, ‘fairly good’, ‘average’, ‘not very
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50 good’, and ‘bad’. Those who chose ‘excellent’, ‘fairly good’, or ‘average’ were regarded as
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52 being in a ‘fine SRH’ condition, whereas those who chose ‘not very good’ or ‘bad’ were
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54 regarded as being in a ‘poor SRH’ condition. The distribution of responses to the five scale
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4 items differs depending on the country owing to cultural differences. When dividing the five
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7 scale items into two values, it is common in Europe and the United States to classify the middle
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10 'average' or 'good' as 'poor SRH',[20] whereas in Japan and Korea, it is common to classify
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13 'average' or 'good' as 'fine SRH'. [21, 22]
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19 Covariates

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

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58 We applied a two-step procedure to determine the extent to which multimorbidity
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4 patterns are associated with poor SRH.
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7 Identification of multimorbidity patterns: Multimorbidity patterns were determined
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10 using exploratory factor analysis based on polychoric correlations. We used 13 body system-
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13 dependent clusters grouped into 33 chronic health conditions, which were coded as
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16 dichotomous variables. We applied the maximum likelihood method and promax rotation. The
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19 number of factors was determined based on a parallel analysis. A factor loading greater than
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22 0.30 is considered meaningful and was used as the criterion for item selection. In addition,
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25 multimorbidity patterns were also determined based on clinical plausibility, as assessed by two
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28 primary care physicians (YH and TA).
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31 Associations between multimorbidity patterns and poor SRH: For each participant, a
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34 multimorbidity pattern score was calculated for each identified pattern. These scores
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37 correspond to the number of affected body system-dependent clusters in each pattern.[11]
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40 Modified Poisson regression analyses (i.e. Poisson regression with robust error variance)[29]
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43 were conducted to investigate the association between each multimorbidity pattern score and
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46 poor SRH. The following possible confounding variables were included as covariates in the
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49 analyses: age, sex, educational level, and K6 score. Each multimorbidity pattern score was
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52 individually included in the model to avoid multicollinearity. We also analysed the association
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55 between a simple count of affected body systems, regardless of multimorbidity pattern, and
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58 poor SRH. Missing values for covariates were analysed as missing categories. As a sensitivity
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4 analysis, we also performed modified Poisson regression analyses after handling missing data
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7 with multiple imputations using a fully conditional specification. We created and analysed 100
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10 multiple-imputed datasets.
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13 All P-values were two-tailed, and statistical significance was set at $P < 0.05$. We used
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16 IBM SPSS Statistics 28.0 (IBM Japan, Tokyo, Japan) and R 4.0.3 (R Foundation for Statistical
17
18
19 Computing, Vienna, Austria) for the analysis.
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25 **Ethics**

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

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46 No patients or public were involved.
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52 **RESULTS**

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

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

14 ICD, International Statistical Classification of Diseases and Related Health Problems

15 Maximum likelihood method and promax rotation are applied.

16 Loadings are bolded if they exceed 0.30.

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22 Three multimorbidity patterns were identified and labelled as follows: i)
23 degenerative/mental health (Factor 1), ii) malignant/digestive/urologic/haematologic (Factor
24 2), and iii) cardiovascular/metabolic pattern (Factor 4). Factor 3 included only nervous system
25 diseases, which was not considered a multimorbidity pattern. The respiratory system and skin
26 diseases were not classified into any factor. Two primary care clinicians (YH and TA) agreed
27 that the three multimorbidity patterns were clinically plausible.
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40 Table 2 presents the characteristics of older participants with SRH data who were not
41 hospitalised or institutionalised in care facilities (N = 23,340). Poor SRH was found in 5,554
42 participants (23.8%).
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52 Table 2. Characteristics of older participants with SRH data who were not hospitalised or institutionalised

53 Characteristic	54 All participants (N = 23,340)	55 Fine SRH (N = 17,786)	56 Poor SRH (N = 5,554)
57 Age (years)			
58 65-69	6,818	5,704 (83.6)	1,114 (16.4)
59 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,

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4 sex, and educational level as covariates is summarised in Table 3 and that adjusted for age, sex,
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7 educational level, and K6 is shown in Table 4. Multimorbidity pattern scores corresponded to
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10 the number of affected body system-dependent clusters in each pattern (e.g. the
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13 malignant/digestive/urologic/haematologic pattern score for a person with malignancy and
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16 anaemia was two). In the model with age, sex, and educational level as covariates, high
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19 malignant/digestive/urologic/haematologic, degenerative/mental health, and
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22 cardiovascular/metabolic pattern scores were significantly associated with poor SRH (adjusted
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25 risk ratio [aRR] = 1.68, 95% confidence interval [CI]: 1.60-1.76, aRR = 1.63, 95% CI: 1.58-
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28 1.69, and aRR = 1.31, 95% CI: 1.26-1.36, respectively) (Table 3). In the model with age, sex,
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31 educational level, and K6 as covariates, high malignant/digestive/urologic/haematologic,
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34 degenerative/mental health, and cardiovascular/metabolic pattern scores were significantly
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37 associated with poor SRH (aRR = 1.47, 95% CI: 1.40-1.54, aRR = 1.44, 95% CI: 1.39-1.49,
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40 and aRR = 1.24, 95% CI: 1.19-1.28, respectively) (Table 4). The association between
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43 multimorbidity pattern scores and poor SRH was reduced when K6 was added to the model as
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46 a covariate, particularly for the malignant/digestive/urologic/haematologic and
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49 degenerative/mental health patterns. Although the simple count of affected body systems,
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52 regardless of multimorbidity pattern, was also significantly associated with poor SRH when
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55 adjusted for age, sex, and educational level with and without K6 as covariates (aRR = 1.35,
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58 95% CI: 1.34-1.37 and aRR = 1.27, 95% CI: 1.25-1.29, respectively), the association was
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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

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

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19 In the present study of nationally representative data from 77,120 participants in Japan
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21 who were not hospitalised or institutionalised, we found a prevalence of multimorbidity.
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23 Analysis using data from 23,730 older participants aged ≥ 65 years revealed three
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25 multimorbidity patterns: i) degenerative/mental health, ii)
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27 malignant/digestive/urologic/haematologic, and iii) cardiovascular/metabolic. To the best of
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29 our knowledge, this is the first study to investigate the association between certain
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31 multimorbidity patterns and SRH. We found a positive association between each
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33 multimorbidity pattern score and poor SRH. This association was stringer for
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35 degenerative/mental health and malignant/digestive/urologic/haematologic patterns than for
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37 cardiovascular/metabolic patterns. Health care professionals can use the results to recognise
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39 multimorbidity in patients at high risk for poor SRH and consider possible interventions.
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52 Although the prevalence of multimorbidity in the present study was relatively lower
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54 than that reported in previous studies from Europe, North America, Australia, and Japan,[1, 2]
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57 it would considerably reflect the prevalence in the free-living general population in Japan. The
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4 prevalence of multimorbidity could have been lower in our study because the survey excluded
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7 hospitalised or institutionalised people who were expected to have more chronic conditions.
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10 The results reflect the state of the community residents who visit medical institutions and are
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13 subject to health care policies. In addition, differences in the method of ascertainment of
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16 chronic conditions could contribute to differences in the prevalence. Various methods have
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19 been used in previous studies, including self-reporting, administrative health records, and
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22 clinical assessments.[1] Moreover, within self-reports, questions about chronic conditions
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25 varied among surveys. Although the participants in this study were asked about the health
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28 conditions for which they were attending medical institutions at the time of the survey,
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31 participants in another study were asked about chronic conditions that had been reported by
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34 healthcare professionals.[2] As this study did not cover inactive conditions that were not being
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37 attended to in medical institutions at the time, it could reflect only the conditions that were
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40 currently burdening participants.
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44 Because the multimorbidity patterns in this study were plausible based on previous
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46 reports and clinical perspectives, they can be widely generalised to older people in developed
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48 countries. Mental health pattern and cardiometabolic pattern were reported as the two most
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50 replicable multimorbidity patterns in a systematic review in 2019,[8] whereas another
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53 systematic review in Asia reported the following five patterns: cardiovascular/metabolic,
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56 mental health, degenerative, pulmonary, and cancer.[19] The systematic review in Asia
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4 contained one study from Japan that reported five patterns: cardiovascular/renal/metabolic,
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7 neuropsychiatric, skeletal/articular/digestive, respiratory/dermal, and
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10 malignant/digestive/urologic.[2] We found that the cardiovascular/metabolic pattern was
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13 consistent with that reported in previous studies. The degenerative/mental health pattern in this
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16 study was close to the falls/fractures/vision disorders/cognitive impairment and falls/vision
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19 impairment/cognitive impairment/urinary incontinence/hearing impairment reported in the
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22 systematic review in 2019, and mental patterns and degenerative patterns in the systematic
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25 review in Asia. As a mechanism for the construction of this pattern, we speculate that
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28 communication disability, social isolation, functional disability, limited mobility, and poorly
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31 treated pain due to vision and hearing impairment[30] or musculoskeletal diseases led to mental
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34 disorders such as depression. The malignant/digestive/urologic/haematologic pattern in this
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37 study was similar to the pattern reported in the previous study in Japan. As a mechanism for
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40 the construction of this pattern, we speculate that digestive and urologic organs are relatively
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43 frequent as sites of primary lesions in cancer survivors.[31] Furthermore, anaemia is one of the
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46 common complications of malignancy and its treatment and can also be associated with chronic
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49 kidney disease or bleeding from gastrointestinal diseases. The multimorbidity patterns revealed
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52 by the data limited to the older population in this study may differ from those reported in
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55 previous studies involving younger generations. We believe it is valuable to report
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58 multimorbidity patterns in the older in Japan, where the population is ageing ahead of the rest
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4 of the world.
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7 The association between multimorbidity pattern scores and poor SRH was greater for
8 malignant/digestive/urologic/haematologic and degenerative/mental health patterns than for
9 cardiovascular/metabolic patterns. The strong association between
10 malignant/digestive/urologic/haematologic patterns and poor SRH in the present study is
11 consistent with the findings of a previous study that reported poorer SRH in older cancer
12 survivors than in people without cancer.[32] Symptoms of digestive or urological conditions
13 can affect eating and elimination, which may exacerbate SRH. The strong association between
14 degenerative/mental health patterns and poor SRH in this study is consistent with the findings
15 of previous studies. Rheumatic and musculoskeletal diseases have been reported to have the
16 strongest association with poor SRH among the chronic conditions.[33] SRH in older people
17 with multimorbidity is exacerbated by vision impairment, hearing impairment, depression, and
18 anxiety.[34] Mental disorders and/or musculoskeletal diseases have been reported as
19 combinations of chronic conditions associated with poor SRH.[35] Communication disability,
20 social isolation, functional disability, limited mobility, and poorly treated pain due to vision
21 and hearing impairment or musculoskeletal diseases can worsen SRH. In contrast, the
22 association between cardiovascular/metabolic patterns and poor SRH was weaker than that
23 between other patterns and poor SRH. We suspect that this is because stable conditions of
24 cardiovascular/metabolic diseases, such as diabetes or ischaemic heart disease, may not have
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4 severe symptoms and may not affect daily life significantly. However, one previous study
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7 reported that cardiometabolic diseases contribute the most to the worsening of SRH in the
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10 general population aged 30-79 years in China.[36] Differences in participants' ages across
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13 studies may affect multimorbidity patterns and the association between these patterns and SRH.
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16 The K6, a screening scale for depression and anxiety, partially mediated the association
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18 between multimorbidity pattern scores and poor SRH. Comparing the models of multivariate
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20 regression analysis that included K6 as a covariate and those that did not include it as a
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23 covariate revealed that the association between multimorbidity pattern scores and poor SRH
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26 was weaker in the model that included K6 for all three patterns. We speculate that the growing
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29 patient burden due to the increasing number of chronic conditions may have partially caused
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32 mood disorders, resulting in the worsening of SRH.
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37 The results of this study will help clinicians recognise patients with multimorbidity
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39 patterns, which are highly associated with poor SRH, and consider possible interventions.
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42 Because the multimorbidity pattern score we used was simple and easy to apply in clinical
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45 practice, clinicians could calculate the score for each patient and assess the risk of poor SRH.
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48 Given that a previous study reported that the association between multimorbidity and poor SRH
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51 could be reduced by increasing physical activity,[37] clinicians may improve SRH by
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54 prescribing exercise to patients with multimorbidity at risk for poor SRH. Further research is
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57 warranted to confirm whether such interventions can improve SRH in patients with
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4 multimorbidity.
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7 Our study has several limitations. First, because of the cross-sectional design, it was
8 impossible to determine whether there was a causal relationship between multimorbidity
9 patterns and SRH. Additional research using a longitudinal design is needed to confirm the
10 association between multimorbidity patterns and SRH. Second, because chronic diseases were
11 measured using self-report questionnaires, it is possible that the prevalence of chronic diseases
12 was underestimated or that the conditions were misclassified. However, previous studies have
13 demonstrated that assessment of morbidity using self-reported data can predict clinical
14 outcomes, including SRH, compared with measures based on administrative data.[38] Finally,
15 it is unclear whether the results of this study can be applied to older adults who require
16 hospitalisation or institutionalisation, such as those with severe chronic diseases or functional
17 decline, because the survey did not include such patients.
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43 **CONCLUSIONS**

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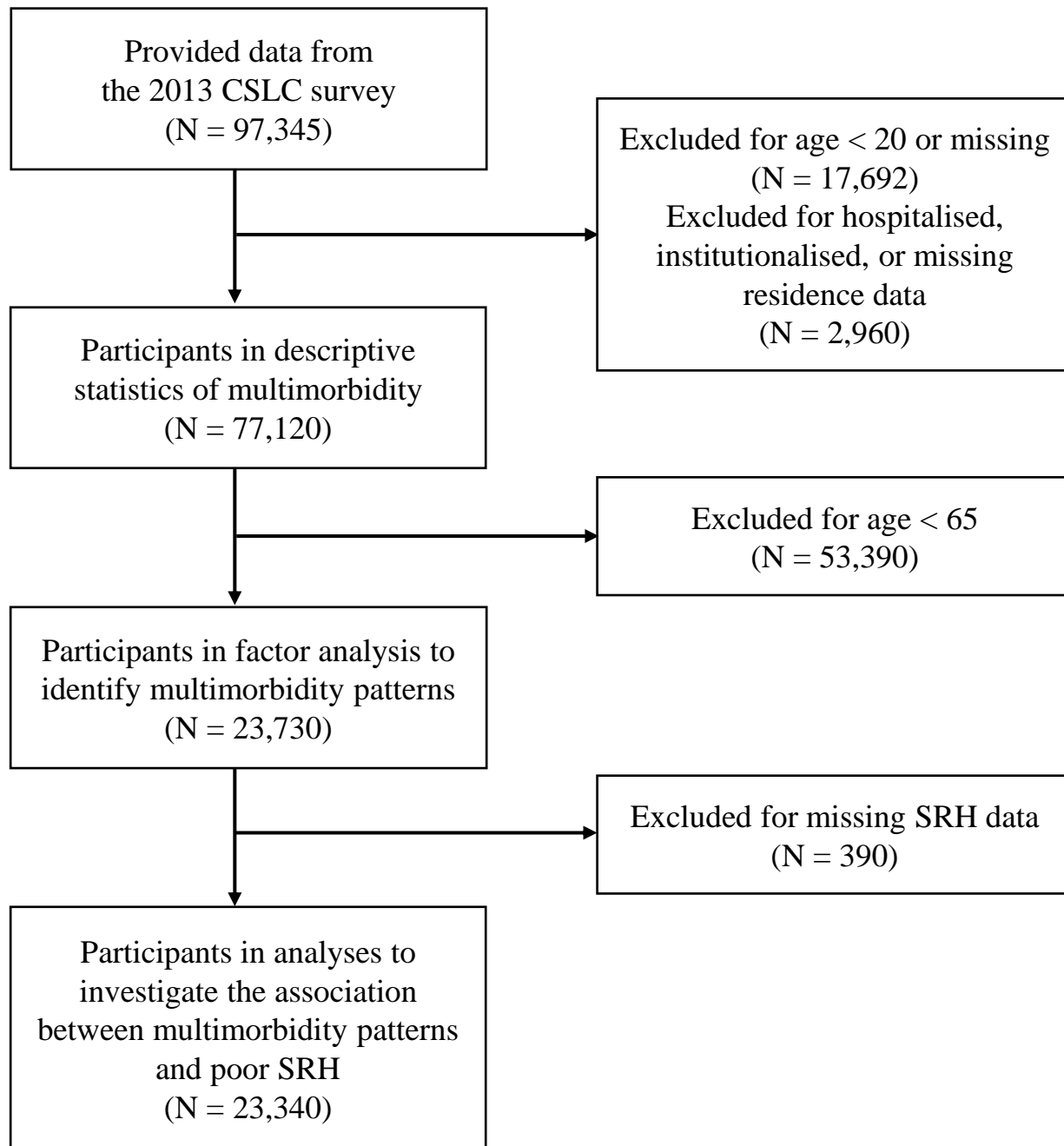
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Figure legend

Figure. Participant flow chart

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

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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	1.60 (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	1.10 (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	1.45 (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	1.80 (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	2.03 (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	2.06 (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	1.29 (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	1.15 (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	1.50 (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	1.75 (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	1.88 (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	1.88 (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	0.99 (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	0.93 (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	2.66 (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	4.55 (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.

BMJ Open

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

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Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Epidemiology, Geriatric medicine
Keywords:	EPIDEMIOLOGY, GENERAL MEDICINE (see Internal Medicine), GERIATRIC MEDICINE, PRIMARY CARE

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4 1 **Multimorbidity patterns and the relation to self-rated health among older Japanese**
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13 4 Yuki Honda,^{1, 2} MD, Mieko Nakamura,¹ MD, PhD, Takuya Aoki,³ MD, PhD, MMA, and
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55 18 **Word count:** 3991 words
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58 19 **Keywords:** multimorbidity, multimorbidity pattern, self-rated health
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4 20 **ABSTRACT**

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7 21 **Objectives:** Classifying individuals into multimorbidity patterns can be useful to identify the
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10 22 target population with poorer clinical outcomes. Self-rated health (SRH) is one of the core
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13 23 outcomes in multimorbidity patients. Although studies have reported that multimorbidity is
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16 24 associated with poor SRH, whether certain patterns have stronger associations remains
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19 25 unknown. Therefore, this study aimed to identify the prevalence and patterns of multimorbidity
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22 26 and investigate the association between multimorbidity patterns and SRH in an older Japanese
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25 27 population.

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28 28 **Design:** Cross-sectional study

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31 29 **Setting:** Data were obtained from the 2013 Comprehensive Survey of Living Conditions, a
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34 30 nationally representative survey of the general Japanese population.

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37 31 **Participants:** This study mainly examined 23,730 participants aged ≥ 65 years who were not
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40 32 hospitalised or institutionalised.

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43 33 **Primary outcome measure:** Poor SRH was defined as choosing 'not very good' or 'bad' from
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46 34 five options: 'excellent', 'fairly good', 'average', 'not very good', and 'bad'.

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49 35 **Results:** The prevalence of multimorbidity was 40.9% and that of poor SRH was 23.8%. Three
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52 36 multimorbidity patterns were identified by exploratory factor analysis: i) degenerative/mental
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55 37 health, ii) malignant/digestive/urologic/haematologic, and iii) cardiovascular/metabolic.
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58 38 Multivariable modified Poisson regression analysis revealed that high
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4 39 malignant/digestive/urologic/haematologic, degenerative/mental health, and
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7 40 cardiovascular/metabolic pattern scores, corresponding to the number of affected body systems
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11 41 in each pattern, were significantly associated with poor SRH [adjusted risk ratio (aRR) = 1.68,
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13 42 95% confidence interval (CI): 1.60-1.76, aRR = 1.63, 95% CI: 1.58-1.69; and aRR = 1.31, 95%
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16 43 CI: 1.26-1.36, respectively]. When including the Kessler 6 score, a screening scale for
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19 44 psychological distress, in the analysis, the association between each multimorbidity pattern
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22 45 score and poor SRH decreased.

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25 46 **Conclusions:** Malignant/digestive/urologic/haematologic and degenerative/mental health
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28 47 patterns may be associated with a high risk for poor SRH. Further research should focus on
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31 48 interventions to improve SRH in multimorbidity patients.

32 33 34 49 35 36 37 50 **Strengths and limitations of this study**

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40 51 • Randomly selected nationally representative data from the general population in Japan
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43 52 were used to determine the prevalence and patterns of multimorbidity in older people.
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46 53 • The modified Poisson regression model allowed for an appropriate estimate of the risk
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49 54 ratio of poor SRH to multimorbidity patterns because the incidence of the outcome was
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52 55 common.
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55 56 • The multimorbidity pattern score, which is the sum of affected conditions in each
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58 57 pattern, was easy to calculate to assess each patient's condition in the clinical practice
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7 59 • The cross-sectional design of the study limited the causality between multimorbidity
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10 60 patterns and poor SRH.

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13 61 • Self-reporting of affected conditions could cause underestimation or misclassification,
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16 62 but the influence would not differ between participants with and without poor SRH.

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20 21 22 64 **INTRODUCTION**

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25 65 Multimorbidity is defined as the co-occurrence of two or more chronic conditions
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28 66 within a person and is common in older people, requiring individualised management. In
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31 67 Europe, North America, and Australia, the prevalence of multimorbidity was reported as
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34 68 approximately 10-50% in individuals aged 20-65 years and 70-80% in those aged ≥ 65 years.[1]

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37 69 A study from Japan showed similar results, with a prevalence of multimorbidity of 29.9% for
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40 70 those aged ≥ 18 years and 62.8% for those aged ≥ 65 years.[2] However, the prevalence of

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43 71 multimorbidity varies widely from a few percent to 80% among older people in China[3] and
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46 72 is approximately 20% among adults in South Korea.[4] Multimorbidity is associated with

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49 73 several health care outcomes, including mortality, hospitalisation, functional limitations, and
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52 74 health care utilisation and costs.[5] Furthermore, the management of multimorbidity is difficult

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55 75 because applying a combination of individual clinical practice guidelines for each disease to
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58 76 multimorbidity patients may increase the treatment burden and negatively affect the

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4 77 patients.[6] Multimorbidity is highly complex and heterogeneous, with various disease
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7 78 combinations, and the guidelines for multimorbidity recommend individualised
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10 79 management.[7]
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13 80 Multimorbidity patterns and their association with health care outcomes have been the
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16 81 focus of much attention. A systematic review of 51 studies showed that mental health and
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19 82 cardiometabolic patterns were the two most replicable multimorbidity patterns based on
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22 83 specific combinations of conditions.[8] In a study of 3,256 Japanese general people, five
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25 84 multimorbidity patterns were identified: cardiovascular/renal/metabolic, neuro/psychiatric,
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28 85 skeletal/articular/digestive, respiratory/dermal, and malignant/digestive/urologic.[2]
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31 86 Furthermore, previous studies have reported associations between certain multimorbidity
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34 87 patterns and clinical outcomes, such as mortality,[9] functional ability,[10] and reduced health-
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37 88 related quality of life.[11] In caring for patients with multimorbidity, classifying individuals
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40 89 into multimorbidity patterns can be useful in identifying the target population with poorer
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43 90 clinical outcomes.
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46 91 Self-rated health (SRH), the subjective perception of an individual's overall health, is
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49 92 a simple and powerful predictor of outcomes, such as mortality[12] and health care
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52 93 expenditure.[13] SRH is also one of the core outcomes in patients with multimorbidity.[14]
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55 94 Although several studies have shown that multimorbidity is associated with poor SRH,[15,16]
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58 95 it is unknown whether certain multimorbidity patterns are associated with poor SRH.
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4 96 Therefore, the present study aimed i) to identify the prevalence of multimorbidity and
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7 97 multimorbidity patterns and ii) to investigate the association between multimorbidity patterns
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10 98 and poor SRH in the older population in Japan using large nationwide data from the 2013
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13 99 Comprehensive Survey of Living Conditions (CSLC). We focused on the older population in
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16 100 this study because stratifying multimorbidity patterns by age group is recommended to better
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19 101 understand the evolution of multimorbidity over a lifespan.[8]
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25 103 **METHODS**

28 104 **Design, setting, and participants**

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31 105 In this nationwide cross-sectional study, we used data from the CSLC conducted by
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34 106 the Ministry of Health, Labour, and Welfare (MHLW) of the Japanese government in June
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37 107 2013.[17] The CSLC is a nationwide repeated cross-sectional survey of households and
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40 108 household members. In 2013, the CSLC covered all households and household members in
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43 109 5,530 districts stratified and randomly selected from the census tracts. Trained investigators
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46 110 visited households to distribute and collect self-administered questionnaires. The survey items
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49 111 included a household-related questionnaire that inquired about sex, age, educational level, and
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52 112 work status and a health-related questionnaire that inquired about health conditions, difficulties
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55 113 in daily life, and status of medical check-ups. The MHLW provided anonymised data from the
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58 114 CSLC for 97,345 individuals in 2013.
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4 115 For investigating the prevalence of multimorbidity, we excluded individuals who were
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7 116 aged <20 years or had missing age data and those who were hospitalised, institutionalised, or
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10 117 had missing residence data at the time of the survey because they were not included for the
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13 118 questions on health conditions. In the analysis of multimorbidity patterns, we excluded those
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16 119 aged <65 years because we wanted to investigate multimorbidity patterns in older people.
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19 120 Finally, we excluded individuals with missing SRH data from the analysis of the association
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22 121 between multimorbidity patterns and poor SRH.
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123 **Measures**

124 **Chronic health conditions**

125 In the CSLC survey, participants chose from 42 options about health conditions for
126 which they were attending medical institutions. The options included diabetes mellitus, obesity,
127 dyslipidaemia, thyroid diseases, depression and other mental disorders, dementia, Parkinson's
128 disease, other nervous system diseases, eye diseases, ear diseases, hypertension, stroke, angina
129 pectoris or myocardial infarction, other circulatory system diseases, acute nasopharyngitis,
130 allergic rhinitis, chronic obstructive pulmonary disease, asthma, other respiratory system
131 diseases, stomach and duodenal diseases, liver and gallbladder diseases, other digestive system
132 diseases, dental diseases, atopic dermatitis, other skin diseases, gout, rheumatoid arthritis,
133 arthropathy, stiff neck, back pain, osteoporosis, kidney diseases, benign prostatic hyperplasia,
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4 134 perimenopausal or postmenopausal disorders, fracture, injury or burn other than fracture,
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7 135 anaemia and other blood diseases, malignancies, pregnancy or puerperium, infertility, others,
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10 136 and unknown. We included 35 conditions after excluding the following seven conditions.
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13 137 Acute nasopharyngitis, fracture, injury or burn other than fracture, pregnancy or puerperium,
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16 138 others, and unknown were excluded because they were acute conditions or conditions whose
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19 139 acute or chronic state was difficult to determine. Although there are some previous studies on
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22 140 multimorbidity treated dental diseases as one of the chronic conditions,[18,19] most studies
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25 141 did not contain dental diseases in the list of chronic conditions.[1,8,20] Therefore, we excluded
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28 142 dental diseases. For individuals aged ≥ 65 years, 33 chronic conditions were included because
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31 143 none of the participants reported perimenopausal or postmenopausal disorders and infertility.
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34 144 To investigate multimorbidity patterns, 33 chronic diseases were grouped into 13 body system-
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37 145 dependent clusters based on the International Classification of Diseases (ICD)-10 chapters
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40 146 (Table 1). The reason for this grouping was that treatment of ‘other’ diseases, such as other
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43 147 neurological diseases, was difficult when analysing multimorbidity patterns. Assessment of
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46 148 multimorbidity by grouping conditions based on body systems, such as complex
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49 149 multimorbidity that can identify patients needing complex healthcare interventions rather than
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52 150 conventional multimorbidity, could be useful.[21] Moreover, since the multimorbidity patterns
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55 151 in the previous studies were mostly classified by organ systems,[2,8,19] we thought that
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58 152 grouping by organ system in advance would not have a significant effect on the pattern
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153 composition.

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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

155

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

159

160 Self-rated health

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

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171 Covariates

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

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4 173 are associated with multimorbidity and poor SRH;[24–26] therefore, we used age, sex, and
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7 174 educational level as covariates. Data on age were provided in 5-year categories. Data regarding
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10 175 educational level were divided into three categories: less than high school, high school, and
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13 176 more than high school.

16 177 The risk of psychological distress is reportedly higher in people with
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19 178 multimorbidity,[27] and psychological distress is an independent predictor of change in
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22 179 SRH;[28] therefore, we hypothesised that psychological distress serves as a mediator between
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25 180 multimorbidity and SRH and evaluated the impact of psychological distress on the relationship
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28 181 between multimorbidity and SRH using the Kessler 6 (K6) score, a screening scale for
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31 182 psychological distress.[29,30] The Japanese version of the K6 scale is a validated scale that
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34 183 comprises six questions answered on a scale of 0-4, with a total score of 0-24.[31] We classified
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37 184 the scores into three categories: 0-4 (normal), 5-12 (psychological distress), and 13-24 (severe
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40 185 mental illness).[32]

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46 187 **Statistical analysis**

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49 188 We applied a two-step procedure to determine the extent to which multimorbidity
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52 189 patterns are associated with poor SRH.

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58 191 Identification of multimorbidity patterns (exploratory factor analysis)

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4 192 Multimorbidity patterns were determined using exploratory factor analysis based on
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7 193 polychoric correlations. We used 13 body system-dependent clusters grouped into 33 chronic
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10 194 health conditions, which were coded as dichotomous variables. We applied the maximum
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13 195 likelihood method and promax rotation. The number of factors was determined based on a
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16 196 parallel analysis. A factor loading greater than 0.30 is considered meaningful and was used as
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19 197 the criterion for item selection. Moreover, multimorbidity patterns were also determined based
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22 198 on clinical plausibility, as assessed by two primary care physicians (YH and TA).
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28 200 Investigation of the associations between multimorbidity patterns and poor SRH
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31 201 (multivariable modified Poisson regression analyses)
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34 202 For each participant, a multimorbidity pattern score was calculated for each identified
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37 203 pattern. These scores correspond to the number of affected body system-dependent clusters in
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40 204 each pattern.[11] Modified Poisson regression analyses (i.e. Poisson regression with robust
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43 205 error variance)[33] were conducted to investigate the association between each multimorbidity
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46 206 pattern score and poor SRH. We estimated the risk ratio directly using modified Poisson
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49 207 regression because the odds ratio derived from the logistic regression can no longer
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52 208 approximate the risk ratio due to the high prevalence of >10% of poor SRH.[34] The possible
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55 209 confounding variables—age, sex, and educational level—were included as covariates in the
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58 210 analyses. Each multimorbidity pattern score was individually included in the model to avoid
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4 211 multicollinearity. To evaluate the impact of the K6 score as a mediator on the relationship
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7 212 between multimorbidity and SRH, we compared the results of two multivariable models with
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10 213 and without the K6 score. We analysed the association between a simple count of affected body
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13 214 systems, regardless of multimorbidity pattern, and poor SRH. Missing values for covariates
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16 215 were analysed as missing categories. As sensitivity analyses, we performed modified Poisson
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19 216 regression analyses with complete cases and after handling missing data with multiple
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22 217 imputations using a fully conditional specification. We created and analysed 100 multiple-
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25 218 imputed datasets. Because unmeasured confounding factors, such as income,[24–26] could be
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28 219 present, we calculated the E-value, which estimates how strong unmeasured confounders
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31 220 would need to be to overturn the association between each multimorbidity pattern score and
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34 221 poor SRH.[35,36]

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40 223 All P-values were two-tailed, and statistical significance was set at $P < 0.05$. We used
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43 224 IBM SPSS Statistics 28.0 (IBM Japan, Tokyo, Japan) and R 4.0.3 (R Foundation for Statistical
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46 225 Computing, Vienna, Austria) for the analysis.

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50 51 52 227 **Ethics**

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55 228 Ethical approval was not required for this study because it involved a secondary
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58 229 analysis of the national surveillance data that did not contain any personally identifiable
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4 230 information. According to Article 36 of Japan's Statistics Act, anonymised data from the CSLC
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7 231 can be used for scientific research after approval by the MHLW of Japan.
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13 233 **Patient and public involvement**

16 234 No patients or public were involved.
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22 236 **RESULTS**

25 237 Supplemental Figure 1 shows a flowchart of the participants. The descriptive statistics
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28 238 of multimorbidity included 77,120 participants, factor analysis to identify multimorbidity
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31 239 patterns included 23,730 participants, and analyses to investigate the association between
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34 240 multimorbidity patterns and poor SRH included 23,340 participants.
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37 241 The prevalence of multimorbidity was 20% in participants aged ≥ 20 years, 41% in those
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40 242 aged ≥ 65 years, and 48% in those aged ≥ 75 years. The prevalence of complex multimorbidity
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43 243 was 6.5% in participants aged ≥ 20 years, 16% in those aged ≥ 65 years, and 20% in those aged
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46 244 ≥ 75 years.
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49 245 Table 1 shows the grouping and prevalence of chronic conditions in older participants.
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52 246 We conducted a parallel analysis to examine the maximum number of factors for exploratory
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55 247 factor analysis to identify multimorbidity patterns and a seven-factor solution was suggested.
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58 248 After factor analyses using two- to seven-factor solutions, a four-factor solution was adopted
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249 because the multimorbidity pattern was the most clinically plausible and consistent with
 250 previous reports. Table 2 shows the factor loadings for the four-factor solution following an
 251 exploratory factor analysis in older participants who were not hospitalised or institutionalised
 252 in care facilities (N = 23,730).

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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.

254

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

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4 258 diseases. There were very few participants with nervous system multimorbidity: only 37
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7 259 participants (0.16% of the total older participants) had two or more nervous system diseases.
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10 260 Therefore, we have not considered this factor as a multimorbidity pattern. The respiratory
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13 261 system and skin diseases were not classified into any factor. Two primary care clinicians (YH
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16 262 and TA) agreed that the three multimorbidity patterns were clinically plausible.

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19 263 Table 3 presents the characteristics of older participants with SRH data who were not
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22 264 hospitalised or institutionalised in care facilities (N = 23,340). Poor SRH was found in 5,554
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25 265 participants (23.8%).
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31 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.

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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

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4 276 risk ratio [aRR] = 1.68, 95% confidence interval [CI]: 1.60-1.76, aRR = 1.63, 95% CI: 1.58-
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7 277 1.69, and aRR = 1.31, 95% CI: 1.26-1.36, respectively) (Table 4). The E-value for the
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10 278 association between each multimorbidity pattern score and poor SRH was 2.75 (lower limit of
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13 279 95% CI: 2.58) for malignant/digestive/urologic/haematologic pattern, 2.64 (lower limit of 95%
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16 280 CI: 2.54) for degenerative/mental health pattern, and 1.95 (lower limit of 95% CI: 1.83) for
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19 281 cardiovascular/metabolic pattern. In the model with age, sex, educational level, and K6 as
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22 282 covariates, high malignant/digestive/urologic/haematologic, degenerative/mental health, and
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25 283 cardiovascular/metabolic pattern scores were significantly associated with poor SRH (aRR =
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28 284 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,
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31 285 respectively) (Table 5). The E-value for the association between each multimorbidity pattern
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34 286 score and poor SRH was 2.30 (lower limit of 95% CI: 2.15) for
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37 287 malignant/digestive/urologic/haematologic pattern, 2.24 (lower limit of 95% CI: 2.13) for
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40 288 degenerative/mental health pattern, and 1.79 (lower limit of 95% CI: 1.67) for
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43 289 cardiovascular/metabolic pattern. The association between multimorbidity pattern scores and
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46 290 poor SRH was reduced when K6 was added to the model as a covariate, particularly for the
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49 291 malignant/digestive/urologic/haematologic and degenerative/mental health patterns. Although
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52 292 the simple count of affected body systems, regardless of multimorbidity pattern, was also
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55 293 significantly associated with poor SRH when adjusted for age, sex, and educational level with
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58 294 and without K6 as covariates (aRR = 1.35, 95% CI: 1.34-1.37 and aRR = 1.27, 95% CI: 1.25-
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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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4 301 For sensitivity analyses, we performed modified Poisson regression analyses with
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7 302 complete cases and after handling missing data with multiple imputations (Supplemental
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10 303 Tables 1 and 2). The proportion of missing values was 14.6% for educational level and 9.0%
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13 304 for K6. In total, 4,806 of the 23,340 records (20.6%) were incomplete. The association of each
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16 305 multimorbidity pattern score and covariate with poor SRH did not differ considerably between
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19 306 the analyses using multiple imputations and the analyses on the subset of complete cases.
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308 **DISCUSSION**

28 309 In the present study of nationally representative data from 77,120 participants in Japan
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31 310 who were not hospitalised or institutionalised, we found a prevalence of multimorbidity.
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34 311 Analysis using data from 23,730 older participants aged ≥ 65 years revealed three
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37 312 multimorbidity patterns: i) degenerative/mental health, ii)
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40 313 malignant/digestive/urologic/haematologic, and iii) cardiovascular/metabolic. To the best of
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43 314 our knowledge, this is the first study to investigate the association between certain
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46 315 multimorbidity patterns and SRH. We found a positive association between each
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49 316 multimorbidity pattern score and poor SRH. This association was stronger for
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52 317 degenerative/mental health and malignant/digestive/urologic/haematologic patterns than for
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55 318 cardiovascular/metabolic patterns. Health care professionals can use the results to recognise
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58 319 multimorbidity in patients at high risk for poor SRH and consider possible interventions.
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4 320 Although the prevalence of multimorbidity in the present study was relatively lower
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7 321 than that reported in previous studies from Europe, North America, Australia, and Japan,[1,2]
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10 322 it would considerably reflect the prevalence in the free-living general population in Japan. The
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13 323 prevalence of multimorbidity could have been lower in our study because the survey excluded
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16 324 hospitalised or institutionalised people who were expected to have more chronic conditions.
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19 325 The results reflect the state of the community residents who visit medical institutions and are
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22 326 subject to health care policies. In addition, differences in the method of ascertainment of
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25 327 chronic conditions could contribute to differences in the prevalence. Various methods have
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28 328 been used in previous studies, including self-reporting, administrative health records, and
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31 329 clinical assessments.[1] Moreover, within self-reports, questions about chronic conditions
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34 330 varied among surveys. Although the participants in this study were asked about the health
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37 331 conditions for which they were attending medical institutions at the time of the survey,
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40 332 participants in another study were asked about chronic conditions that had been reported by
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43 333 healthcare professionals.[2] As this study did not cover inactive conditions that were not being
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46 334 attended to in medical institutions at the time, it could reflect only the conditions that were
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49 335 currently burdening participants.

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52 336 Because the multimorbidity patterns in this study were plausible based on previous
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55 337 reports and clinical perspectives, they can be widely generalised to older people in developed
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58 338 countries. Mental health pattern and cardiometabolic pattern were reported as the two most
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4 339 replicable multimorbidity patterns in a systematic review in 2019,[8] whereas another
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7 340 systematic review in Asia reported the following five patterns: cardiovascular/metabolic,
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10 341 mental health, degenerative, pulmonary, and cancer.[20] The systematic review in Asia
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13 342 contained one study from Japan that reported five patterns: cardiovascular/renal/metabolic,
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16 343 neuropsychiatric, skeletal/articular/digestive, respiratory/dermal, and
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19 344 malignant/digestive/urologic.[2] We found that the cardiovascular/metabolic pattern was
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22 345 consistent with that reported in previous studies. The degenerative/mental health pattern in this
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25 346 study was close to the falls/fractures/vision disorders/cognitive impairment and falls/vision
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28 347 impairment/cognitive impairment/urinary incontinence/hearing impairment reported in the
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31 348 systematic review in 2019, and mental patterns and degenerative patterns in the systematic
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34 349 review in Asia. As a mechanism for the construction of this pattern, we speculate that
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37 350 communication disability, social isolation, functional disability, limited mobility, and poorly
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40 351 treated pain due to vision and hearing impairment[37] or musculoskeletal diseases led to mental
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43 352 disorders such as depression. Moreover, patients with musculoskeletal diseases have a high
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46 353 risk of depression and anxiety, and those with both musculoskeletal diseases and anxiety or
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49 354 depression show increased pain,[38] explaining the interrelationship between musculoskeletal
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52 355 diseases and mental health disorders in degenerative/mental health patterns. The
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55 356 malignant/digestive/urologic/haematologic pattern in this study was similar to the pattern
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58 357 reported in the previous study in Japan. As a mechanism for the construction of this pattern,
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4 358 we speculate that digestive and urologic organs are relatively frequent as sites of primary
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7 359 lesions in cancer survivors.[39] Furthermore, anaemia is a common complication of
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10 360 malignancy and its treatment[40,41] and can also be associated with chronic kidney disease[42]
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13 361 or bleeding due to gastrointestinal diseases. The multimorbidity patterns revealed by the data
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16 362 limited to the older population in this study may differ from those reported in previous studies
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19 363 involving younger generations. We believe it is valuable to report multimorbidity patterns in
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22 364 the older in Japan, where the population is ageing ahead of the rest of the world.

25 365 The association between multimorbidity pattern scores and poor SRH was greater for
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28 366 malignant/digestive/urologic/haematologic and degenerative/mental health patterns than for
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31 367 cardiovascular/metabolic patterns. The strong association between
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34 368 malignant/digestive/urologic/haematologic patterns and poor SRH in the present study is
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37 369 consistent with the findings of a previous study that reported poorer SRH in older cancer
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40 370 survivors than in people without cancer.[43] Symptoms of digestive or urological conditions
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43 371 can affect eating and elimination, which may exacerbate SRH. The strong association between
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46 372 degenerative/mental health patterns and poor SRH in this study is consistent with the findings
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49 373 of previous studies. Rheumatic and musculoskeletal diseases have been reported to have the
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52 374 strongest association with poor SRH among the chronic conditions.[44] SRH in older people
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55 375 with multimorbidity is exacerbated by vision impairment, hearing impairment, depression, and
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58 376 anxiety.[45] Mental disorders and/or musculoskeletal diseases have been reported as
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4 377 combinations of chronic conditions associated with poor SRH.[46] Communication disability,
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7 378 social isolation, functional disability, limited mobility, and poorly treated pain due to vision
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10 379 and hearing impairment or musculoskeletal diseases can worsen SRH. Reportedly,
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13 380 multimorbidity, depressive symptoms, and disability synergistically exacerbate SRH.[47] The
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16 381 combined involvement of these factors in degenerative/mental health patterns could explain
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19 382 the strong association with poor SRH. In contrast, the association between
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22 383 cardiovascular/metabolic patterns and poor SRH was weaker than that between other patterns
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25 384 and poor SRH. We suspect that this is because stable conditions of cardiovascular/metabolic
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28 385 diseases, such as diabetes or ischaemic heart disease, may not have severe symptoms and may
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31 386 not affect daily life significantly. However, one previous study reported that cardiometabolic
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34 387 diseases contribute the most to the worsening of SRH in the general population aged 30-79
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37 388 years in China.[48] Differences in participants' ages across studies may affect multimorbidity
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40 389 patterns and the association between these patterns and SRH.

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43 390 The K6, a screening scale for psychological distress, partially mediated the association
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46 391 between multimorbidity pattern scores and poor SRH. Comparing the models of multivariable
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49 392 regression analysis that included K6 and those that did not include it revealed that the
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52 393 association between multimorbidity pattern scores and poor SRH was weaker in the model that
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55 394 included K6 for all three patterns. We speculate that the growing patient burden due to the
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58 395 increasing number of chronic conditions may have partially caused psychological distress,
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4 396 resulting in the worsening of SRH.[27,28] There might be a correlation between the
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7 397 degenerative/mental health pattern score and K6 conceptually. However, because the Pearson
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10 398 correlation coefficient between the degenerative/mental health pattern score and K6 was 0.053
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13 399 and the variance inflation factor of the degenerative/mental health pattern score and K6 was
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16 400 1.025 and 1.035 in the multivariable model, respectively, no significant multicollinearity was
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19 401 noted of concern in statistical analysis.

22 402 The results of this study will help clinicians recognise patients with multimorbidity
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25 403 patterns, which are highly associated with poor SRH, and consider possible interventions.
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28 404 Because the multimorbidity pattern score we used was simple and easy to apply in clinical
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31 405 practice, clinicians could calculate the score for each patient and assess the risk of poor SRH.
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34 406 Given that a previous study reported that the association between multimorbidity and poor SRH
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37 407 could be reduced by increasing physical activity,[49] clinicians may improve SRH by
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40 408 prescribing exercise to patients with multimorbidity at risk for poor SRH. Further research is
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43 409 warranted to confirm whether such interventions can improve SRH in patients with
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46 410 multimorbidity.

49 411 Our study has several limitations. First, because of the cross-sectional design, it was
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52 412 impossible to determine whether there was a causal relationship between multimorbidity
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55 413 patterns and SRH. Additional research using a longitudinal design is needed to confirm the
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58 414 association between multimorbidity patterns and SRH. Second, because chronic diseases were
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4 415 measured using self-report questionnaires, it is possible that the prevalence of chronic diseases
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7 416 was underestimated or that the conditions were misclassified. However, previous studies have
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10 417 demonstrated that assessment of morbidity using self-reported data can predict clinical
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13 418 outcomes, including SRH, compared with measures based on administrative data.[50] Third,
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16 419 there might be unmeasured confounding factors, such as income.[24–26] However, the E-
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19 420 values for the association between each multimorbidity pattern score and poor SRH were
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22 421 reasonably high, making it unlikely that unmeasured confounders would overturn the observed
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25 422 association between each multimorbidity pattern score and poor SRH. Fourth, we could not
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28 423 show the magnitude of mediation by the psychological distress of the relationship between
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31 424 multimorbidity and SRH, as it is beyond the study scope. This should be examined in future
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34 425 studies using causal mediation analysis. Finally, it is unclear whether the results of this study
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37 426 can be applied to older adults who require hospitalisation or institutionalisation, such as those
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40 427 with severe chronic diseases or functional decline, because the survey did not include such
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43 428 patients.

49 430 **CONCLUSIONS**

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52 431 We found differences in the association between multimorbidity patterns and poor SRH.
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55 432 Malignant/digestive/urologic/haematologic and degenerative/mental health patterns may be
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58 433 associated with a high risk for poor SRH. Further research should focus on interventions to
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4 434 improve SRH in patients with multimorbidity.
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10 436 **Statements**

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13 437 **Author contributions:** All authors (YH, MN, TA, and TO) contributed to the conception or
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16 438 design of the study, reviewed and edited the manuscript, contributed to the interpretation of the
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19 439 data and the analyses, performed critical review of the manuscript, and gave the final approval
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22 440 of the manuscript before submission. YH performed the statistical analyses and drafted the
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25 441 manuscript. MN, TA, and TO supervised the work.

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28 442 **Competing interest:** TA received a grant from Pfizer Health Research Foundation, Japan for
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30
31 443 another research project related to multimorbidity (Grant No. 21-E-01).

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34 444 **Funding:** This research received no specific grant from any funding agency in the public,
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37 445 commercial or not-for-profit sectors.

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40 446 **Data availability:** These data were derived from the CSLC in June 2013, which was conducted
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43 447 by the MHLW of Japan. You can use the anonymous data if you apply for and receive
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46 448 permission from the ministry. [<https://www.mhlw.go.jp/toukei/itaku/tokumei.html>]

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49 449 **Participant consent:** Not applicable.

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52 450 **Ethical approval:** Ethical approval was not required for this study because it involved a
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55 451 secondary analysis of the national surveillance data that did not contain any personally
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58 452 identifiable information. According to Article 36 of Japan's Statistics Act, anonymised data
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4 453 from the CSLC can be used for scientific research after approval by the MHLW of Japan.
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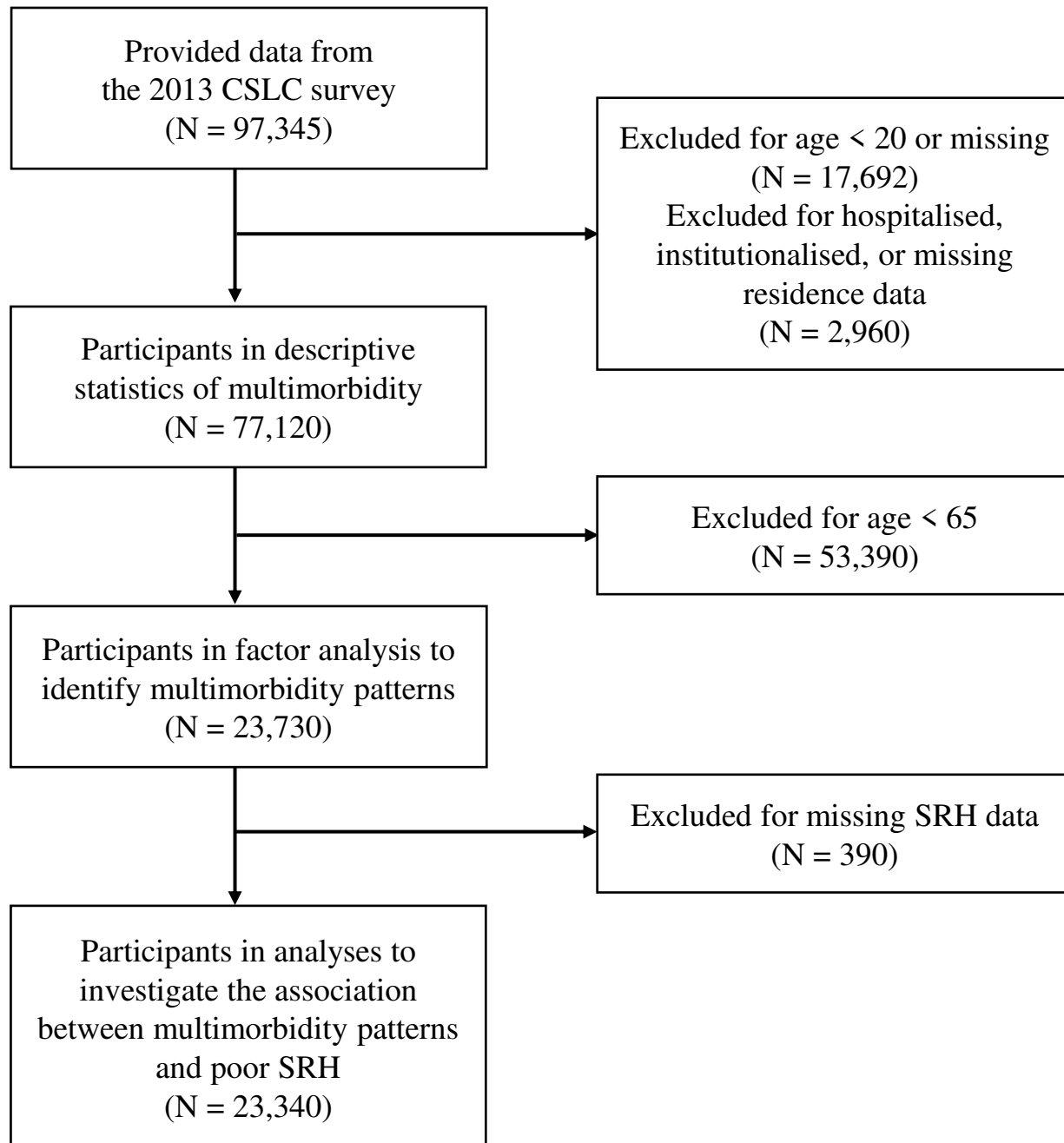
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Supplemental Figure 1. Participant flow chart.



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.