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The association between clusters of chronic conditions and psychological well-being in younger and older people—A cross-sectional, population-based study from the Lolland-Falster Health Study, Denmark

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Abstract

Aim: To investigate the association between clusters of conditions and psychological well-being across age groups.

Method: This cross-sectional study used data collected in the Danish population-based Lolland-Falster Health Study. We included adults over the age of 18 years. Self-reported chronic conditions were divided into 10 groups of conditions. The primary outcome was psychological well-being (the WHO-5 Well-Being Index). Factor analysis constructed the clusters of conditions, and regression analysis investigated the association between clusters and psychological well-being.

Results: Of 10,781 participants, 31.4% were between 18 and 49 years, 35.7% were between 50 and 64 years and 32.9% were above 65 years. 35.2% had conditions represented in 1 and 32.9% in at least 2 of 10 condition groups. Across age groups, living with one or more chronic conditions was associated with poorer psychological well-being. Two chronic condition patterns were identified; one comprised cardiovascular, endocrine, kidney, musculoskeletal and cancer conditions, the second mental, lung, neurological, gastrointestinal and sensory conditions. Both patterns were associated with poorer psychological well-being (Pattern 1: $-4.5$ (95% CI: $-5.3$ to $-3.7$), Pattern 2: $-9.1$ (95% CI: $-13.8$ to $-8.2$). For pattern 2, participants above 65 years had poorer psychological well-being compared to younger ($-12.6$ (95% CI: $-14.2$ to $-11.0$) vs $-6.6$ (95% CI: $-7.8$ to $-5.4$) for 18–49 years and $-8.7$ (95% CI: $-10.1$ to $-7.3$) for 50–64 years, interaction: p $< 0.001$)

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Conclusion: Living with one or more chronic conditions is associated with poorer psychological well-being. Findings point toward a greater focus on supporting psychological well-being in older adults with both mental and somatic conditions.

Keywords
Multimorbidity, quality of life, chronic diseases, factor analysis, age-related health

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Background
A substantial, and growing, proportion of the adult population is affected by more than one chronic condition—commonly defined as multimorbidity.2 25–30% of people between the ages of 45 and 64 live with multimorbidity,3,4 and as prevalence rises with age, the majority of the elderly over the age of 85 years suffer from multimorbidity.3,5–7 Multimorbidity is associated with worse prognosis, increased health care utilization and intake of multiple medications.8–18

There are large differences in the severity and management of the individual chronic conditions; consequently, it is too simple to rely on only the number of conditions, when assessing the impact of multimorbidity.8,19,20 The Academy of Medical Sciences 2018 reports on research priorities for global health research in multimorbidity and highlights the importance of identifying clusters of chronic conditions (specific combinations of conditions).21 Furthermore, evidence on occurrence and impact of common clusters on health status is urgently needed to inform decisions on important determinants (factors that increase or decrease the risk of occurrence of health-related events),22 service provision, resource allocation and management strategies in prevention, treatment and rehabilitation of multimorbidity.21

Reduced physical and mental health can be a consequence of multimorbidity11,12,20 However, previous research regarding the association between clusters of conditions and self-perceived health has predominantly focused on aging populations,20,21,23–27 with little, if any, available evidence comparing older and younger age groups. In the older population, especially the combination of mental and somatic conditions seems to be associated with poor self-perceived health compared to combinations of somatic conditions alone.20,23,25,26 As more than half of people with multimorbidity are younger than 65 years of age,3 an understanding of the association in younger age groups is needed in order to improve knowledge about and care for younger patients.21 In addition, self-perceived health has mainly been investigated as an overall concept without exploring some of the underlying domains such as psychological well-being.28

Currently, there is no universal definition of multimorbidity nor any guidelines for how diseases and/or conditions should be grouped.29 In a study by Willadsen et al.,8 different mortality rates were reported for different groups of chronic conditions in people with multimorbidity. Conditions were grouped based on similarities in how they are treated and organized in the health care system. This definition was an attempt to provide a relatively simple and clinically relevant definition of multimorbidity, which also includes the complexity related to navigating across different medical specialties and sectors of the health care system.8

Building on a similar framework as Willadsen et al.,8 we aimed to investigate the associations between clusters of conditions and self-perceived health status, with psychological well-being as the primary outcome and overall self-rated health as the secondary outcome, in people with one or more chronic conditions compared to people without chronic conditions in younger (18–49 years), middle (50–64 years) and older (≥65 years) age groups.

Method
The study is reported according to the STROBE Statement for cross-sectional studies.30

Study design
Data for this cross-sectional study were collected in the Lolland-Falster Health Study (LOFUS). LOFUS is a household-based population study initiated to gain knowledge on determinants of health in a socio-economically disadvantaged area of Denmark using questionnaires, physical examination and biological samples. Persons aged 18 years and over were randomly sampled and invited to participate together with the rest of their households.31 Study design and methodology of LOFUS have been described in details elsewhere.31,32

Region Zealand’s Ethical Committee on Health Research has approved LOFUS (Reg: SJ-421). All data storage and management for this study were approved by the Regional Data Protection Agency of Zealand (REG-024-2019 & REG-24-2015), and the use of data was accepted by the LOFUS steering committee. LOFUS is registered in Clinicaltrials.gov (NCT02482896).

Sample
Adults aged 18 years and above, who participated in LOFUS between February 8, 2016 and March 7, 2019,
were eligible for this study. Most of the participants had completed the questionnaire electronically at home before attending the physical examination in one of three stationary sites strategically placed within the study area. Questionnaires and physical examination were typically completed within a week from each other. Only participants who had answered the items about chronic conditions and the self-perceived health items in the questionnaire were included in this study.32

Data variables

Classification of medical conditions. Participants reported their current chronic conditions from a list of 18 conditions. This list has previously been used in the Danish General Suburban Population Study33 and a national health cohort in Denmark conducted since 1987.34 The 18 conditions were; 1) acute myocardial infarction, 2) atherosclerosis in the heart, 3) angina pectoris, 4) blood clot (thrombosis) in the leg, 5) diabetes, 6) asthma, 7) allergy (not asthma), 8) kidney disease, 9) cancer, 10) anxiety, 11) depression, 12) osteoarthritis, 13) rheumatoid arthritis, 14) hypertension, 15) chronic bronchitis, emphysema, chronic obstructive pulmonary disease (COPD), 16) migraine or frequent headaches, 17) spinal hernia or other spinal diseases, 18) others. The response category “others” was left open for participants to add any other condition(s) that they had. Conditions from the response category “others” were coded based on the following inclusion and exclusion criteria; clearly named specific conditions (e.g. atrial fibrillation) and conditions that clearly indicated a medical condition and its location (e.g. gastrointestinal disease) were included. Conditions indicated as former, conditions not defined as a disease (e.g. dizziness) and risk factors (e.g. hypertension and hyperlipidemia) were excluded. The condition classification hypertension was likewise excluded. All conditions from the “others” category were assessed twice by the first author and afterward reviewed twice by a clinical assistant. Inconsistencies were debated, and a third person (STS) was consulted, if needed. In total, 74 conditions were classified from the “others” category.

The 90 conditions from LOFUS (16 condition categories and 74 from “others”) were organized in 10 groups, based on similarities in treatments, clinical manifestation or organization in the health care system and were inspired by the framework from Willadsen et al.,8 i.e. lung, musculoskeletal, endocrine, mental, cancer, neurological, gastrointestinal, cardiovascular, kidney and sensory organs. As validation, six of the authors (KL, AF, TW, AM, RJ, STK) with extensive medical knowledge peer-reviewed both the classification process and the classification of the 90 conditions into the 10 groups. Inconsistencies between the co-authors were discussed with the first author until consensus was reached. The entire classification process is outlined in Appendix 1a.

Self-perceived health. As primary outcome, we assessed the psychological aspect of health28 using The World Health Organization Well-Being Index (WHO-5), which is a generic, self-reported questionnaire assessing psychological well-being.35 It consists of five statements about people’s feelings within the last 2 weeks, which are rated according to frequency; All of the time, Most of the time, More than half of the time, Less than half of the time, Some of the time, At no time. Each answer is given a score, 0 to 5, and a total score is calculated by summing the answers from the five statements, with 0 representing worst possible and 25 representing best possible psychological well-being. To obtain a percentage score ranging from 0 to 100, the raw score is multiplied by 4.36 WHO-5 is valid in adults as a screening tool for depression and as an outcome measure in clinical trials and has successfully been used as an measure for well-being across a wide range of patient groups.35 Ten percentage points is considered a clinically relevant difference.35,36

As a secondary outcome, we assessed health as a global aspect28 using a global question measuring self-rated health. A single item question “In general, would you say your health is?” asks the participants to rate their general health on a five-point scale going from “Very poor” to “Excellent.”37 Self-rated health has been widely used in population-based investigations,37 is considered valid and is an independent predictor of mortality and other health outcomes.38–40 For the purpose of this analysis, self-rated health was dichotomized into “good” (containing responses Excellent and Good”) or “poor” (containing responses Fair, Poor and Very poor).

Covariates

Sociodemographic covariates collected in LOFUS32 were coded as; age (years), gender (female/male), education level (Less than high school, High school, Bachelor degree, Advanced degree, Other), marital status (Married, Separated/divorced, Widowed, Single) and working status (Unemployed, Out of the labor market, In labor, Studying or training, Carers or work in home, Other). For education level and working status, an “other” category was available without any further information on what this could be. In total, 612 (5.5%) responded “other” for education level and 297 (2.6%) for working status.

Statistical Analyses

Participant characteristics are presented as mean ± SD for normally distributed data, as medians and interquartile ranges for nonparametric data and as frequencies and percentages for categorical data. Linear regression analysis was used to evaluate the associations between WHO-5 and each of the 10 condition groups and to compare these associations between age groups; 18–49 years, 50–64 years and ≥65 years of age. Similarly, associations were calculated
for self-rated health using logistic regression analysis presented as odds ratios (OR). Two regression models were performed; model 1 adjusted for age (continuous variable) and gender and model 2 adjusted for age, gender, education, marital status, working status and condition groups. Tests for interaction between age groups and each of the 10 condition groups were performed in both models without inclusion of age as continuous variable. Model assumptions were evaluated from diagnostics plots.

To investigate the correlation between the 10 condition groups and identify possible patterns of chronic conditions, a principal-components analysis was performed. As all 10 condition groups in our study were coded dichotomously for each participant, we performed a polychoric correlation matrix using factor analysis. Each condition group was assigned to the pattern (a factor) where its coefficient yielded the highest factor loading.23,25 Based on a previous study, a factor loading of <0.3 was considered to be weak and a loading ≥0.3 was considered to be moderate or strong.25 Participants were assigned to the pattern that yielded the highest score after summing the individual factor loadings for each individual. After this process, the association between each identified condition pattern and psychological well-being and self-rated health, respectively, was calculated, as well as tested for interactions between age groups. As with the analysis of the 10 individual condition groups, this was done using linear regression for WHO-5 and logistic regression for self-rated health. Level of statistical significance was set as p < 0.05. All statistical analyses were performed using the software SAS Enterprise Guide 5.1 (SAS Institute Inc., Cary, NC, USA).

### Results

In total, 11,771 persons were eligible for this study. Participant characteristics are provided in Table 1.

In total, 1,563 (14% of participants provided information in the disease category “others.” All conditions in this category except three (HIV, periodontitis and alopecia) were dichotomous for each participant. We performed a polychoric correlation matrix using factor analysis. Each condition group was assigned to the pattern (a factor) where its coefficient yield the highest factor loading.23,25 Based on a previous study, a factor loading of <0.3 was considered to be weak and a loading ≥0.3 was considered to be moderate or strong.25 Participants were assigned to the pattern that yielded the highest score after summing the individual factor loadings for each individual. After this process, the association between each identified condition pattern and psychological well-being and self-rated health, respectively, was calculated, as well as tested for interactions between age groups. As with the analysis of the 10 individual condition groups, this was done using linear regression for WHO-5 and logistic regression for self-rated health. Level of statistical significance was set as p < 0.05. All statistical analyses were performed using the software SAS Enterprise Guide 5.1 (SAS Institute Inc., Cary, NC, USA).

### Table 1. Baseline characteristics of participants in total and divided into age groups.

| Demographic | In total (n = 10781) | 18–49 years of age (n = 3379) | 50–64 years of age (n = 3854) | ≥65 years of age (n = 3549) |
|-------------|---------------------|-----------------------------|-----------------------------|-----------------------------|
| Female      | 5740 (53.2%)        | 1886 (55.8%)                | 2115 (54.9%)                | 1739 (49.0%)                |
| Age (years) | 56.2 (± 15.8)       | 37.1 (± 9.1)                | 57.7 (± 4.3)                | 72.6 (± 5.6)                |
| Height (cm) | 171.1 (± 9.5)       | 173.3 (± 9.1)               | 171.5 (± 9.3)               | 168.7 (± 9.3)               |
| Weight (kg) | 79.9 (± 17.2)       | 80.3 (± 18.4)               | 81.2 (± 17.2)               | 78.1 (± 15.9)               |
| Married / Partnered | 7240 (67.7%) | 1792 (53.4%) | 2788 (72.7%) | 2660 (75.8%) |
| Employed | 5618 (51.0%) | 2484 (73.6%) | 2841 (73.8%) | 293 (8.3%) |
| Education—bachelor’s degree or higher | 2813 (26.3%) | 1001 (29.6%) | 978 (25.4%) | 834 (23.5%) |

### Number of condition groups

| Condition groups | 1 (0–2)* | 1 (0–1)* | 1 (0–2)* | 1 (1–2)* |
|------------------|----------|----------|----------|----------|
| Lung             | 957 (8.8%) | 235 (7.0%) | 338 (8.8%) | 384 (10.8%) |
| Musculoskeletal  | 4524 (42.0%) | 753 (22.3%) | 1765 (45.8%) | 2006 (56.5%) |
| Endocrine        | 735 (6.8%) | 88 (2.6%) | 284 (7.4%) | 363 (10.2%) |
| Mental           | 1167 (10.8%) | 417 (12.3%) | 448 (11.6%) | 302 (8.5%) |
| Cancer           | 396 (3.7%) | 19 (0.6%) | 104 (2.7%) | 273 (7.7%) |
| Neurological     | 1694 (15.7%) | 743 (22.0%) | 617 (16.0%) | 334 (9.4%) |
| Gastrointestinal | 165 (1.5%) | 58 (1.7%) | 62 (1.6%) | 45 (1.3%) |
| Cardiovascular   | 885 (8.2%) | 73 (2.2%) | 292 (7.6%) | 520 (14.7%) |
| Kidney           | 171 (1.6%) | 26 (0.8%) | 57 (1.5%) | 88 (2.5%) |
| Sensory organs   | 2085 (19.3%) | 746 (22.1%) | 766 (19.9%) | 573 (16.5%) |

### Self-perceived health

| Five Well-Being Index (WHO-5) (0–100) | 67.5 (± 18.2) | 63.8 (± 17.5) | 66.6 (± 18.6) | 72.0 (± 17.6) |
|--------------------------------------|---------------|---------------|---------------|---------------|
| Excellent                            | 1345 (12.5%) | 496 (14.7%) | 417 (10.8%) | 432 (12.2%) |
| Good                                 | 6126 (56.8%) | 1983 (58.7%) | 2131 (55.3%) | 2012 (56.7%) |
| Fair                                 | 2824 (26.2%) | 766 (22.7%) | 1082 (28.1%) | 976 (27.5%) |
| Poor                                 | 445 (4.1%)   | 126 (3.7%)   | 203 (5.3%)   | 116 (3.3%)   |
| Very poor                            | 41 (0.4%)    | 8 (0.2%)     | 21 (0.4%)    | 12 (0.3%)    |

*Interquartile range.

1 Wilcoxon–Mann–Whitney test.

for self-rated health using logistic regression analysis presented as odds ratios (OR). Two regression models were performed; model 1 adjusted for age (continuous variable) and gender and model 2 adjusted for age, gender, education, marital status, working status and condition groups. Tests for interaction between age groups and each of the 10 condition groups were performed in both models without inclusion of age as continuous variable. Model assumptions were evaluated from diagnostics plots.

To investigate the correlation between the 10 condition groups and identify possible patterns of chronic conditions, a principal-components analysis was performed. As all 10 condition groups in our study were coded dichotomously for each participant, we performed a polychoric correlation matrix using factor analysis. Each condition group was assigned to the pattern (a factor) where its coefficient yielded the highest factor loading. Based on a previous study, a factor loading of <0.3 was considered to be weak and a loading ≥0.3 was considered to be moderate or strong. Participants were assigned to the pattern that yielded the highest score after summing the individual factor loadings for each individual. After this process, the association between each identified condition pattern and psychological well-being and self-rated health, respectively, was calculated, as well as tested for interactions between age groups. As with the analysis of the 10 individual condition groups, this was done using linear regression for WHO-5 and logistic regression for self-rated health. Level of statistical significance was set as p < 0.05. All statistical analyses were performed using the software SAS Enterprise Guide 5.1 (SAS Institute Inc., Cary, NC, USA).
could be classified into 1 of the 10 condition groups from Willadsen et al.8 Of the 10 condition groups, musculoskeletal conditions had the highest prevalence (42.0%) and gastrointestinal the lowest (1.5%) (Table 1). A total of 3,544 (32.9%) participants had conditions represented in at least 2 of the 10 condition groups (24.5% in 18–49 years of age, 34.5% in 50–64 years of age and 39.1% in ≥65 years of age), 3,789 (35.2%) in one (33.2% in 18–49 years of age, 35.0% in 50–64 years of age and 37.2% in ≥65 years of age), and 3,448 (32.0%) reported no conditions (42.4% in 18–49 years of age, 30.5% in 50–64 years of age and 23.8% in ≥65 years of age). The prevalence of binary combinations between the 10 condition groups is illustrated in Table 2.

Having a condition in at least one of nine condition groups resulted in significantly poorer psychological well-being and self-rated health (Table 3). Compared to the rest of the study sample, having a mental disorder was associated with the lowest ratings of psychological well-being, −15.1 (95% CI −16.1 to −14.1 (fully adjusted model). For self-rated health, this was gastrointestinal (OR of 2.41 (95% CI 1.72 to 3.39) (fully adjusted model)). Model assumptions were not violated.

For psychological well-being, the fully adjusted model revealed interactions between age groups and the conditions, lung, musculoskeletal and neurological, with poorer well-being in participants ≥65 years of age (Table 3).

The factor analysis identified two patterns of chronic conditions across the 10 condition groups. Based on factor loadings (Table 4), the first pattern (pattern 1) comprised the cardiovascular, endocrine, kidney, musculoskeletal and cancer condition groups. The second pattern (pattern 2) comprised mental, lung, neurological, gastrointestinal and sensory organs condition groups (Table 4). Adjusting for the other condition pattern, both patterns were negatively associated with psychological well-being and self-rated health (fully adjusted model) (Table 5).

Interaction between age and the two multimorbidity patterns were only found for pattern 2, where participants ≥65 years of age had poorer psychological well-being than the younger age groups (fully adjusted model: −12.6 (95% CI −14.2 to −11.0) vs −6.6 (95% CI: −7.8 to −5.4) for 18–49 years of age and −8.7 (95% CI: −10.1 to −7.3) for 50–64 years of age, test for interaction: p ≤ 0.001) (Table 5).

Discussion

This is the first study investigating the association between clusters of chronic conditions and psychological well-being and self-rated health comparing different age groups. Being represented in at least one of nine groups of chronic conditions was associated with poorer psychological well-being and self-rated health. Older adults had poorer psychological well-being compared to younger adults in 3 out of the 10 condition groups. Two patterns of chronic conditions were identified that both were associated with

### Table 2. Prevalence of binary combinations between the 10 condition groups.*

| Disease group | Lung n (%) | Musculoskeletal n (%) | Endocrine n (%) | Mental n (%) | Cancer n (%) | Neurological n (%) | Gastrointestinal n (%) | Cardiovascular n (%) | Kidney n (%) | Sensory organs n (%) |
|---------------|------------|-----------------------|-----------------|--------------|--------------|---------------------|-----------------------|----------------------|-------------|----------------------|
| Lung          | 967 (8.9)  | 533 (4.9)             | 383 (3.6)       | 735 (6.8)    | 1167 (10.8) | 177 (1.6)           | 224 (2.0)             | 102 (1.0)            | 46 (0.4)    | 424 (4.2)            |
| Musculoskeletal| 4524 (42.0)| 383 (3.6)             | 224 (2.0)       | 102 (1.0)    | 46 (0.4)     | 177 (1.6)           | 224 (2.0)             | 102 (1.0)            | 46 (0.4)    | 383 (3.6)            |
| Endocrine     | 735 (6.8)  | 383 (3.6)             | 224 (2.0)       | 102 (1.0)    | 46 (0.4)     | 177 (1.6)           | 224 (2.0)             | 102 (1.0)            | 46 (0.4)    | 735 (6.8)            |
| Mental        | 1167 (10.8)| 177 (1.6)             | 224 (2.0)       | 102 (1.0)    | 46 (0.4)     | 177 (1.6)           | 224 (2.0)             | 102 (1.0)            | 46 (0.4)    | 1167 (10.8)          |
| Cancer        | 396 (3.7)  | 735 (6.8)             | 1167 (10.8)     | 46 (0.4)     | 735 (6.8)    | 1167 (10.8)         | 46 (0.4)              | 735 (6.8)            | 1167 (10.8) | 396 (3.7)            |
| Neurological  | 1694 (15.7)| 1694 (15.7)           | 1694 (15.7)     | 1694 (15.7)  | 1694 (15.7)  | 1694 (15.7)         | 1694 (15.7)           | 1694 (15.7)          | 1694 (15.7) | 1694 (15.7)          |
| Gastrointestinal | 1694 (15.7)| 1694 (15.7)           | 1694 (15.7)     | 1694 (15.7)  | 1694 (15.7)  | 1694 (15.7)         | 1694 (15.7)           | 1694 (15.7)          | 1694 (15.7) | 1694 (15.7)          |
| Cardiovascular| 396 (3.7)  | 396 (3.7)             | 396 (3.7)       | 396 (3.7)    | 396 (3.7)    | 396 (3.7)           | 396 (3.7)             | 396 (3.7)            | 396 (3.7)    | 396 (3.7)            |
| Kidney        | 171 (1.6)  | 171 (1.6)             | 171 (1.6)       | 171 (1.6)    | 171 (1.6)    | 171 (1.6)           | 171 (1.6)             | 171 (1.6)            | 171 (1.6)    | 171 (1.6)            |

*The table shows all binary combinations—all condition groups are included in the table.
| Condition group | Age/gender adjusted | Fully adjusted model | Self-rated Health item | Age/gender adjusted | Fully adjusted model |
|-----------------|---------------------|----------------------|-----------------------|---------------------|----------------------|
| Lung            |                     |                      |                       |                     |                      |
| Age groups      |                     |                      |                       |                     |                      |
| 18–49           | -6.9 (-8.0 to -5.7) | -3.6 (-4.7 to -2.5)  | 1.99 (1.74 to 2.27)   | 1.66 (1.43 to 1.92) |
| 50–64           | -7.2 (-9.4 to -4.8) | 0.12                 | 1.85 (1.41 to 2.41)   | 1.49 (1.13 to 2.00) |
| ≥65             | -5.6 (-7.6 to -3.5) | -1.7 (-3.6 to 0.2)   | 2.05 (1.63 to 2.57)   | 1.70 (1.32 to 2.20) |
| Musculoskeletal | -8.1 (-9.9 to -6.3) | -0.6 (-7.8 to -4.3)  | 2.04 (1.65 to 2.53)   | 1.79 (1.43 to 2.25) |
| Age groups      | -6.6 (-7.3 to -5.9) | -3.8 (-4.5 to -3.1)  | 1.61 (1.49 to 2.75)   | 1.33 (1.22 to 1.45) |
| 18–49           | -6.0 (-7.5 to -5.0) | 0.14                 | 1.69 (1.43 to 2.00)   | 1.31 (1.10 to 1.58) |
| 50–64           | -7.4 (-8.5 to -6.2) | -4.1 (-5.2 to -3.0)  | 1.75 (1.54 to 1.99)   | 1.36 (1.19 to 1.57) |
| ≥65             | -6.5 (-7.7 to -5.4) | -4.4 (-5.5 to -3.3)  | 1.44 (1.26 to 1.65)   | 1.28 (1.11 to 1.48) |
| Endocrine       | -4.8 (-6.1 to -3.4) | -2.6 (-3.8 to -1.4)  | 1.81 (1.56 to 2.11)   | 1.59 (1.36 to 1.87) |
| Age groups      |                     |                      |                       |                     |                      |
| 18–49           | -5.8 (-9.4 to -2.1) | 0.90                 | 2.14 (1.39 to 3.31)   | 2.05 (1.30 to 3.23) |
| 50–64           | -4.7 (-9.1 to -2.6) | -2.3 (-4.3 to -0.3)  | 2.05 (1.60 to 2.63)   | 1.74 (1.33 to 2.17) |
| ≥65             | -4.5 (-6.3 to -2.6) | -2.3 (-4.1 to -0.6)  | 1.57 (1.26 to 1.96)   | 1.39 (1.11 to 1.75) |
| Mental          | -19.6 (-20.6 to -18.6) | -151.1 (-161.1 to -141.1) | 2.63 (2.32 to 2.99) | 1.74 (1.52 to 2.00) |
| Age groups      |                     |                      |                       |                     |                      |
| 18–49           | -19.0 (-20.7 to -17.4) | 0.81            | 2.64 (2.14 to 3.28) | 1.66 (1.31 to 2.10) |
| 50–64           | -20.0 (-21.7 to -18.2) | -145.5 (-156.3 to -128) | 2.82 (2.29 to 3.47) | 1.70 (1.35 to 2.14) |
| ≥65             | -19.3 (-21.2 to -17.2) | -161.1 (-180.8 to -141.1) | 2.31 (1.81 to 2.95) | 1.86 (1.44 to 2.40) |
| Cancer          | -3.5 (-5.3 to -1.6) | -2.2 (-3.9 to -0.6)  | 1.53 (1.24 to 1.87)   | 1.39 (1.12 to 1.72) |
| Age groups      |                     |                      |                       |                     |                      |
| 18–49           | -4.1 (-11.9 to 3.7) | 0.95                 | 1.56 (0.63 to 3.86)   | 1.10 (0.42 to 2.88) |
| 50–64           | -3.8 (-7.4 to -0.2) | -0.9 (-4.2 to -2.3)  | 1.81 (1.28 to 2.85)   | 1.70 (1.10 to 2.62) |
| ≥65             | -3.6 (-5.8 to -1.4) | -2.7 (-4.7 to -0.7)  | 1.41 (1.10 to 1.81)   | 1.34 (1.04 to 1.74) |
| Neurological    | -8.9 (-9.8 to -8.0) | -5.4 (-6.2 to -4.5)  | 1.84 (1.65 to 2.05)   | 1.51 (1.35 to 1.70) |
| Age groups      |                     |                      |                       |                     |                      |
| 18–49           | -7.2 (-8.7 to -5.8) | 0.04                 | 1.68 (1.42 to 1.99)   | 1.40 (1.17 to 1.67) |
| 50–64           | -9.6 (-11.2 to -8.2) | -3.8 (-4.2 to -2.3)  | 1.99 (1.67 to 2.38)   | 1.61 (1.32 to 1.95) |
| ≥65             | -9.9 (-11.9 to -7.9) | -2.7 (-4.7 to -0.7)  | 1.90 (1.52 to 2.39)   | 1.60 (1.26 to 2.04) |
| Gastrointestinal| -6.8 (-9.6 to -4.1) | -2.7 (-4.7 to -0.7)  | 1.90 (1.52 to 2.39)   | 1.60 (1.26 to 2.04) |
| Age groups      |                     |                      |                       |                     |                      |
| 18–49           | -3.4 (-7.9 to 1.0)  | 0.23                 | 2.00 (1.18 to 3.20)   | 1.85 (1.06 to 3.23) |
| 50–64           | -7.8 (-12.4 to -3.1) | -3.4 (-7.6 to 0.7)   | 3.96 (2.21 to 7.10)   | 3.46 (1.87 to 6.40) |
| ≥65             | -9.5 (-14.6 to -4.3) | -6.7 (-11.4 to -1.9) | 2.20 (1.20 to 4.03)   | 2.21 (1.17 to 4.16) |
| Cardiovascular  | -5.7 (-6.9 to -4.4) | -2.7 (-3.8 to -1.5)  | 1.84 (1.60 to 2.13)   | 1.54 (1.32 to 1.79) |

(continued)
### Table 3. (continued)

| Condition group | WHO-5 | | Self-rated Health item | |
|-----------------|-------|-------|------------------------|-------|
|                 | Age/gender adjusted | Fully adjusted model | Age/gender adjusted | Fully adjusted model |
|                 | Mean (95% CI) | p-value* | Mean (95% CI) | p-value* | OR (95% CI) | p-value* | OR (95% CI) | p-value* |
| **Age groups**  |       |       |                       |       |       |       |       |       |
| 18–49           | −2.7 (−6.7 to 1.3) | 0.08 | 0.68 (−3.0 to 4.4) | 0.10 | 1.93 (1.21 to 3.10) | 0.01 | 1.51 (0.92 to 2.49) | 0.08 |
| 50–64           | −7.6 (−9.8 to −5.4) |     | −3.4 (−5.4 to −1.4) |     | 2.53 (1.97 to 3.25) |     | 1.94 (1.48 to 2.54) |     |
| ≥65             | −5.1 (−6.7 to −3.4) |     | −2.6 (−4.1 to −1.1) |     | 1.53 (1.27 to 1.85) |     | 1.37 (1.12 to 2.66) |     |
| **Kidney**      |       |       |                       |       |       |       |       |       |
| 18–49           | −5.1 (−7.8 to −2.4) |     | −1.9 (−4.4 to 0.5) |     | 1.80 (1.32 to 2.44) |     | 1.48 (1.07 to 2.04) |     |
| 50–64           | 7.1 (10.9 to 2.3)  |     | 3.9 (8.3 to 0.5)    |     | 2.32 (1.38 to 4.01) |     | 1.97 (1.10 to 3.54) |     |
| ≥65             | 3.6 (7.3 to 0.1)   |     | 0.4 (1.8 to 0.9)    |     | 1.89 (1.23 to 2.91) |     | 1.54 (0.98 to 2.43) |     |
| **Sensory organs** |       |       |                       |       |       |       |       |       |
| 18–49           | −3.0 (−3.9 to −2.2) | 0.54 | −3.3 (−9.4 to 2.7) | 0.43 | 0.88 (0.40 to 1.94) | 0.13 | 0.91 (0.40 to 2.07) | 0.32 |
| 50–64           | −7.1 (−11.9 to −2.3) |     | −3.9 (−8.3 to 0.5) |     | 2.32 (1.38 to 4.01) |     | 1.97 (1.10 to 3.54) |     |
| ≥65             | −3.6 (−7.3 to 0.1) |     | 0.1 (−3.4 to 3.5) |     | 1.89 (1.23 to 2.91) |     | 1.54 (0.98 to 2.43) |     |

**Age/gender adjusted model**: Adjusted for age (continuous) and gender—In the one item self-rated health item the analysis odds is for reporting “Poor health.”

**Fully adjusted model**: Adjusted for age (continuous, gender, education level, marital status, working status and the nine other conditions groups)—In the one item self-rated health item the analysis odds is for reporting “Poor health.”

*P-value for interaction between age groups and the condition groups in model 1 and model 2.

**Abbreviations**: (95% CI): 95% confidence interval, WHO-5: the WHO Five Well-Being Index, OR: Odds Ratio.
poor psychological well-being and poorer self-rated health. Age differences in the associations were related to pattern type and outcome measure.

**Self-perceived health in younger and older adults**

While growing evidence highlights high multimorbidity prevalence rates and increased mortality and readmission rates for people living with multimorbidity, little is known about clusters of conditions and self-perceived health in younger age groups compared to older. Based on our results, 9 of 10 condition groups are associated with poor psychological well-being and self-rated health across age groups. This is similar to findings in previous studies of older adults (>50 years of age), where chronic conditions, especially mental conditions, had a substantial negative impact on self-perceived health both interpreted as psychological well-being (−15.1 (95% CI: −16.1 to −14.1) and self-rated health (OR 2.63 (95% CI 2.32 to 2.99)). Being ≥65 years of age, especially in comparison to the youngest age group (18–49 years), was associated with poorer psychological well-being in 3 out of the 10 groups of conditions in our study. This is interesting as emotional well-being is relatively stable over time, but is reported to increase with age. Charles’s Strength and Vulnerability Integration model (SAVI; Charles, 2010) shows that exposure to stressors that naturally accompany the aging process helps individuals learn appropriate emotion regulation strategies that they can use to either avoid or cope with negative stimuli. The psychological well-being of the full sample of our study (including people with and without chronic conditions) aligns with this interpretation (WHO-5 score: 18–49 years of age, 63.8 (±17.5) and 50–64 years of age, 66.6 (±18.6) vs 65+ years of age, 72.0 (±17.6): p < 0.001). However, while older adults in general tend to have better psychological well-being than younger adults, having one or more chronic conditions appears to be related to a similar or poorer association to psychological well-being in older adults. Nevertheless, the differences were small and potentially not clinically relevant.

### Table 4. Factor loadings for the two identified multimorbidity patterns.

| Factors          | Patterns 1 | Pattern 2 |
|------------------|------------|-----------|
| Lung             | 0.22       | 0.44      |
| Musculoskeletal  | 0.35       | 0.27      |
| Endocrine        | 0.40       | −0.01     |
| Mental           | 0.16       | 0.44      |
| Cancer           | 0.44       | −0.04     |
| Neurological     | 0.01       | 0.38      |
| Gastrointestinal | −0.13      | 0.29      |
| Cardiovascular   | 0.47       | 0.09      |
| Kidney           | 0.49       | 0.05      |
| Sensory organs   | 0.01       | 0.46      |

Factor loading of <0.3 considered to be weak, and a loading ≥0.3 considered to be moderate or strong. Bold loadings indicate which pattern each condition group is assigned to.

### Table 5. Difference in self-perceived health (WHO-5 and the one item self-rated health) in people represented in one of two multimorbidity patterns compared to the rest of the study sample and with a further comparison across age groups.

|                  | **WHO-5** |                  | **Self-rated Health** |                  |
|------------------|-----------|------------------|-----------------------|------------------|
|                  | Age/gender adjusted | Fully adjusted | Age/gender adjusted | Fully adjusted |
|                  | Mean (95% CI) | p-value | Mean (95% CI) | p-value | OR (95% CI) | p-value | OR (95% CI) | p-value |
| Pattern 1: Cardiovascular, musculoskeletal, endocrine, kidney and cancer | | | | | | | |
| Age groups | | | | | | | |
| 18–49 | 0.12 (−0.3 to 0.5) | −1.04 (−4.5 to −7.8) | | | 1.30 (1.17 to 1.44) | | |
| 50–64 | 0.14 (−1.0 to −1.4) | 0.17 (−4.5 to −5.9) | | | 1.45 (1.22 to 1.71) | | |
| ≥65 | 0.15 (−1.0 to −1.4) | 0.92 (−0.81 to −0.5) | | | 1.25 (1.05 to 1.49) | | |
| Pattern 2: Mental, neurological, lung, gastrointestinal and sensory organs | | | | | | | |
| Age groups | | | | | | | |
| 18–49 | −8.1 (−8.8 to −7.4) | −8.1 (−13.8 to −8.2) | | | 1.52 (1.40 to 1.65) | | 1.57 (1.44 to 1.73) | | |
| 50–64 | −9.1 (−9.7 to −8.5) | −9.1 (−14.2 to −10.0) | | | 1.51 (1.30 to 1.76) | | 1.74 (1.43 to 2.11) | | |
| ≥65 | −9.5 (−10.2 to −8.8) | −9.5 (−14.2 to −9.0) | | | 1.51 (1.30 to 1.76) | | 1.74 (1.43 to 2.11) | | |

**Age/gender adjusted model:** Adjusted for age (continuous) and gender—in the one item self-rated health item the analysis odds is for reporting “Poor health.”

**Fully adjusted model:** Adjusted for age (continuous), gender, education level, marital status, working status and the other conditions pattern—in the one item self-rated health item the analysis odds is for reporting “Poor health.”

\*P-value for interaction between age groups and the pattern in model 1 and model 2.

**Abbreviations:** (95% CI): 95% confidence interval, WHO-5: the WHO Five Well-Being Index, OR: Odds Ratio.
Both condition patterns found in our study were associated with poor psychological well-being. However, pattern 2 including mental disorder, compared to pattern 1, revealed the largest negative association with the WHO-5. The fact that WHO-5 is a measure of psychological well-being and that mental disorder is included in pattern 2 is likely to explain at least part of this difference. Furthermore, in older participants, the association between pattern 2 and WHO-5 was clinically relevant (−12.6 (95% CI −14.2 to −11.0). The negative influence of mental disorder in multimorbidity patterns has previously been demonstrated in older adults.²⁰,²²,²⁵,²⁶ Also, for self-rated order in multimorbidity patterns has previously been CI/C0 SI/F36 norm score below 50.⁴⁶ Similar to our findings for line with another Danish study where participants represented in the same cluster.⁴³,⁴⁷ Also, depending on the analytic approach, osteoarthritis seems to be related to this pattern.⁴⁵ Some of the individual conditions grouped in pattern 2 have also been found in previous work.⁴⁷ It is unknown to us why diseases like mental disorders and lung condition are likely to be in the same pattern.

### Clusters of chronic conditions

Investigating clusters of conditions based on factor analysis is one of several available statistical methods to investigate combinations of conditions.⁴³ One common method is a simple prevalence analysis of combinations of conditions.²⁰,²²,⁴⁴ Clinically, prevalence analyses are easier to interpret as only highly prevalent condition combinations are included, but at the same time they are highly selective as they leave out a large variety of potential combinations of conditions. In contrast, factor analysis constructs condition patterns by factoring in all conditions without any preselection on prevalence, but it may at the same time complicate the clinical interpretation.⁴⁵ Our factor analysis approach inspired by Rivera-Almaraz et al.²³ and Jackson et al.²⁵ revealed two multimorbidity patterns, of which one was associated with poorer self-perceived health. This is in line with another Danish study where participants represented in five out of seven clusters of conditions had an SF-36 norm score below 50.⁴⁶ Similar to our findings for pattern 1, earlier studies have demonstrated that cardiovascular and metabolic diseases, e.g. diabetes, are likely to be represented in the same cluster.⁴¹,⁴⁷ Also, depending on the analytic approach, osteoarthritis seems to be related to this pattern.⁴⁵ Some of the individual conditions grouped in pattern 2 have also been found in previous work.⁴⁷ It is unknown to us why diseases like mental disorders and lung condition are likely to be in the same pattern.

Comparing our condition pattern to the previous studies using the factor analysis method that we were inspired by, Rivera-Almaraz et al.,²³ we identified three multimorbidity patterns also associated with reduced self-perceived health; 1) chronic obstructive pulmonary disease/asthma/angina, 2) diabetes/hypertension/stroke/cataracts and 3) arthritis/depression. Jackson et al.²⁵ identified three patterns labeled; 1) musculoskeletal/somatic, 2) neurological/mental health and 3) cardiovascular. These disease patterns as well as those in our study highlight that condition patterns are complex and can span across disease pathologies and body systems.²³,²⁵,⁴⁶

It is a challenge to compare existing literature on multimorbidity patterns due to the complexity and heterogeneity in the individual conditions studied, the categorization of the conditions and the analytic approach used.⁴³ In contrast to other studies, we categorized 87 individual conditions into 10 large condition groups, based on similarities in types of care services and organization of care.⁹ Such grouping embraces the complexity across organizational issues and pathophysiological challenges that occur when chronic conditions across body systems interact.²⁹ At the same time, it clearly reduced information across conditions in the same body system.⁴³ In future research, the inclusion of a certain condition categorization should be based on the research purpose; however, endorsed guidelines for disease clustering and analysis are needed to increase comparability across studies and to make the interpretation easier.

### Limitations

Although this study is strengthened by a large sample size, valid assessment tools and a well-known statistical approach, there are some methodological limitations important to consider when interpreting the results.

First, the study has a cross-sectional design and results should be interpreted as associations only.

Second, the study was conducted based on data from a large Danish population-based study (LOFUS) conducted in a socio-economically disadvantaged area of Denmark.³¹ As self-perceived health is related to external and internal resources, results may not be generalizable to the entire Danish population.³⁸,⁴⁸

Third, our primary focus was a generic measurement of psychological well-being, which means that some dimensions and variations among participants with different conditions of self-perceived health (e.g. biological and social) were not explored.²⁸,⁴⁸,⁴⁹ Also, our secondary outcome, self-rated health, is a global construct of self-perceived health, comprising all major domains of health, including psychological well-being. Taking the many dimensions of health into consideration, other variables than those adjusted for are likely to influence one’s health and potentially be confounders, including cognitive⁵⁰ and economic status.

Fourth, although research has shown that current chronic conditions can be accurately reported by patients⁵¹–⁵³ and are as likely to predict health-related quality of life as objectively assessed conditions,⁵⁵ caution is needed when interpreting findings. 14% of the participants
provided additional disease information, which was left open for interpretation by the authors. Despite our effort to strictly assess the additional condition information (the “others” category), this might have induced some interpretation bias in our classification of conditions.

Conclusions
Living with one or more chronic conditions was associated with poorer psychological well-being, especially when a mental condition was self-reported. For lung, musculoskeletal and neurological conditions, psychological well-being was poorer in older adults compared to younger adults. Our results revealed two patterns of chronic conditions, which were associated with poorer self-perceived health. For psychological well-being, the association was higher in the pattern that contained mental conditions, especially in elderly patients. Our findings point toward a greater clinical focus on poorer psychological well-being in older adults and patients with a combination of mental and somatic conditions.

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References
1. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet Lond Engl 2015; 386: 743–800.
2. Valderas JM, Starfield B, Sibbald B, et al. Defining comorbidity: implications for understanding health and health services. Ann Fam Med 2009; 7: 357–363.
3. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. Lancet Lond Engl 2012; 380: 37–43.
4. Schiotz ML, Stockmarr A, Host D, et al. Social disparities in the prevalence of multimorbidity—a register-based population study. BMC Public Health 2017; 17: 422.
5. Salive ME. Multimorbidity in older adults. Epidemiol Rev 2013; 35: 75–83.
6. Formiga F, Ferrer A, Sanz H, et al. Patterns of comorbidity and multimorbidity in the oldest old: the Octabaix study. Eur J Intern Med 2013; 24: 40–44.
7. Hvidberg MF, Johnsen SP, Davidsen M, et al. A nationwide study of prevalence rates and characteristics of 199 chronic conditions in Denmark. PharmacoEconomics Open. Epub ahead of print 24 July 2019. DOI: 10.1007/s41669-019-0167-7.
8. Willadsen TG, Siersva M, Nicolaissodttir DR, et al. Multimorbidity and mortality: a 15-year longitudinal registry-based nationwide Danish population study. J Comorbidity 2018; 8: 2235042X18804063.
9. Menotti A, Mulder I, Nissinen A, et al. Prevalence of morbidity and multimorbidity in elderly male populations and their impact on 10-year all-cause mortality: the FINE study (Finland, Italy, Netherlands, Elderly). J Clin Epidemiol 2001; 54: 680–686.
10. Nunes BP, Flores TR, Mielke GI, et al. Multimorbidity and mortality in older adults: a systematic review and meta-analysis. Arch Gerontol Geriatr 2016; 67: 130–138.
11. Fortin M, Lapointe L, Hudon C, et al. Multimorbidity and quality of life in primary care: a systematic review. Health Qual Life Outcomes 2004; 2: 51.
12. Fortin M, Bravo G, Hudon C, et al. Psychological distress and multimorbidity in primary care. Ann Fam Med 2006; 4: 417–422.
13. Bayliss EA, Bayliss MS, Ware JE, et al. Predicting declines in physical function in persons with multiple chronic medical conditions: what we can learn from the medical problem list. Health Qual Life Outcomes 2004; 2: 47.
14. Vogeli C, Shields AE, Lee TA, et al. Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. *J Gen Intern Med* 2007; 22(3): 391–395.
15. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev* 2011; 10: 430–439.
16. Townsend A, Hunt K and Wyke S. Managing multiple morbidity in mid-life: a qualitative study of attitudes to drug use. *BMJ* 2003; 327: 837.
17. Ryan A, Wallace E, O’Hara P, et al. Multimorbidity and functional decline in community-dwelling adults: a systematic review. *Health Qual Life Outcomes* 2015; 13: 168.
18. Frolich A, Ghith N, Schiøtz M, et al. Multimorbidity, health-care utilization and socioeconomic status: a register-based study in Denmark. *PLoS One* 2019; 14: e0214183.
19. Prados-Torres A, Calderón-Larrañaga A, Hanco-Saavedra J, et al. Multimorbidity patterns: a systematic review. *J Clin Epidemiol* 2014; 67: 254–266.
20. Sheridan PE, Mair CA and Quiñones AR. Associations between prevalent multimorbidity combinations and prospective disability and self-rated health among older adults in Europe. *BMC Geriatr* 2019; 19: 198.
21. The Academy of Medical Sciences. *Multimorbidity: a priority for global health research*. 2018. [https://iacmedsci.ac.uk/file-download/82222577](https://iacmedsci.ac.uk/file-download/82222577)
22. Antonisamy B, Premkumar PS and Christopher S. *Principles and practice of biostatistics*. [http://public.eblib.com/choice/publicfullrecord.aspx?p=5554141](http://public.eblib.com/choice/publicfullrecord.aspx?p=5554141) (2017, accessed 31 July 2019).
23. Rivera-Almaraz A, Manrique-Espinoza B, Ávila-Funes JA, et al. Disability, quality of life and all-cause mortality in older Mexican adults: association with multimorbidity and frailty. *BMC Geriatr* 2018; 18: 236.
24. Hunger M, Thorand B, Schunk M, et al. Multimorbidity and health-related quality of life in the older population: results from the German KORA-age study. *Health Qual Life Outcomes* 2011; 9: 53.
25. Jackson CA, Jones M, Tooth L, et al. Multimorbidity patterns are differentially associated with functional ability and decline in a longitudinal cohort of older women. *Age Ageing* 2015; 44: 810–816.
26. Quiñones AR, Markwardt S and Botoseneanu A. Multimorbidity combinations and disability in older adults. *J Gerontol A Biol Sci Med Sci* 2016; 71: 823–830.
27. Walker V, Perret-Guillaume C, Kesse-Guyot E, et al. Effect of multimorbidity on health-related quality of life in adults aged 55 years or older: results from the SU.VI.MAX 2 Cohort. *PLoS One* 2016; 11: e0169282.
28. McDowell I. Measures of self-perceived well-being. *J Psychosom Res* 2010; 69: 69–79.
29. Willadsen TG, Bebe A, Koster-Rasmussen R, et al. The role of diseases, risk factors and symptoms in the definition of multimorbidity—a systematic review. *Scand J Prim Health Care* 2016; 34: 112–121.
30. ISPM - University of Bern. *STROBE Statement*. [https://strobe-statement.org/index.php?id=strobe-home](https://strobe-statement.org/index.php?id=strobe-home) (accessed 9 March 2020).
31. Jepsen R, Egholm CL, Brodersen J, et al. Lolland-Falster Health Study: study protocol for a household-based prospective cohort study. *Scand J Public Health* 2020; 48: 382–390.
32. Egholm CL, Packness A, Stokholm J, et al. Questionnaire development for the Lolland-Falster Health Study, Denmark: an iterative and incremental process. *BMC Med Res Methodol* 2020; 20: 52.
33. Bergholdt HKM, Bathum L, Kvetny J, et al. Study design, participation and characteristics of the Danish General Suburban Population Study. *Dan Med J* 2013; 60: A4693.
34. The National Representative Health and Morbidity Studies (SUSY). [SDU/en/sif/forskning/projekter/sundheds_og_sygemedicinalundersoegelserne](http://www.psykatri-regionh.dk/who-5/Pages/default.aspx) (accessed 4 February 2020).
35. Topp CW, Østergaard SD, Sondergaard S, et al. The WHO-5 Well-Being Index: a systematic review of the literature. *Psychother Psychosom* 2015; 84: 167–176.
36. Mental Health Centre North Zealand. The WHO-5 website. [https://www.psykiatri-regionh.dk/who-5/Pages/default.aspx](https://www.psykiatri-regionh.dk/who-5/Pages/default.aspx) (accessed 30 August 2019).
37. Bowling A. Just one question: If one question works, why ask several? *J Epidemiol Community Health* 2005; 59: 342–345.
38. Benyamini Y. Why does self-rated health predict mortality? An update on current knowledge and a research agenda for psychologists. *Psychol Health* 2011; 26: 1407–1413.
39. Vie TL, Hufthammer KO, Holmen TL, et al. Is self-rated health a stable and predictive factor for allostatic load in early adulthood? Findings from the Nord Trøndelag Health Study (HUNT). *Soc Sci Med* 2014; 117: 1–9.
40. Idler EL and Benyamini Y. Self-rated health and mortality: a review of twenty-six community studies. *J Health Soc Behav* 1997; 38: 21–37.
41. Joiner RJ, Bergeman CS and Wang L. Affective experience across the adult lifespan: an accelerated longitudinal design. *Psychol Aging* 2018; 33: 399–412.
42. Charles ST. Strength and vulnerability integration (SAVI): a model of emotional well-being across adulthood. *Psychol Bull* 2010; 136: 1068–1091.
43. Sk N, Tawiah R, Sawyer M, et al. Patterns of multimorbidity health conditions: a systematic review of analytical methods and comparison analysis. *Int J Epidemiol* 2018; 47: 1687–1704.
44. Violan C, Fuguet-Boreu Q, Flores-Mateo G, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One* 2014; 9: e102149.
45. Goldberg R. *PROC FACTOR*: How to Interpret the Output of a Real-World Example. 5.
47. Bayes-Marín I, Sanchez-Niubo A, Egea-Cortés L, et al. Multimorbidity patterns in low-middle and high income regions: a multiregion latent class analysis using ATHLOS harmonised cohorts. *BMJ Open* 2020; 10: e034441.

48. Jylhä M. What is self-rated health and why does it predict mortality? Towards a unified conceptual model. *Soc Sci Med* 2009; 69: 307–316.

49. Møller A, Bissenbakker KH, Arreskov AB, et al. Specific measures of quality of life in patients with multimorbidity in primary healthcare: a systematic review on patient-reported outcome measures’ adequacy of measurement. *Patient Relat Outcome Meas* 2020; 11: 1–10.

50. Caracciolo B, Gatz M, Xu W, et al. Relationship of subjective cognitive impairment and cognitive impairment no dementia to chronic disease and multimorbidity in a nation-wide twin study. *J Alzheimers Dis* 2013; 36: 275–284.

51. Sangha O, Stucki G, Liang MH, et al. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003; 49: 156–163.

52. Katz JN, Chang LC, Sangha O, et al. Can comorbidity be measured by questionnaire rather than medical record review? *Med Care* 1996; 34: 73–84.

53. Olomu AB, Corser WD, Stommel M, et al. Do self-report and medical record comorbidity data predict longitudinal functional capacity and quality of life health outcomes similarly? *BMC Health Serv Res* 2012; 12: 398.