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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 ≥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.

Background

A substantial, and growing, proportion of the adult population is affected by more than one chronic condition[1]—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 multimorbidity[11,12,20] 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.[31] 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 Study[33] 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 health[28] 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 aspect[28] 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 LOFUS[32] 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 $\pm$ 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 $\geq$65 years of age. Similarly, associations were calculated

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

	In total (n = 10781)	18–49 years of age (n = 3379)	50–64 years of age (n = 3854)	≥65 years of age (n = 3549)
Demographic	n(%) / Mean ($\pm$SD)	n(%) / Mean ($\pm$SD)	n(%) / Mean ($\pm$SD)	n(%) / Mean ($\pm$SD)
Female	5740 (53.2%)	1886 (55.8%)	2115 (54.9%)	1739 (49.0%)
Age (years)	56.2 ($\pm$15.8)	37.1 ($\pm$9.6)	57.7 ($\pm$4.3)	72.6 ($\pm$5.6)
Height (cm)	171.1 ($\pm$9.5)	173.3 ($\pm$9.1)	171.5 ($\pm$9.3)	168.7 ($\pm$9.3)
Weight (kg)	79.9 ($\pm$17.2)	80.3 ($\pm$18.4)	81.2 ($\pm$17.2)	78.1 ($\pm$15.9)
Married / Partnered	7240 (67.7%)	1792 (53.4%)	2788 (72.7%)	2660 (75.8%)
Employed	5618 (51.0%)	2484 (73.6%)	2841 (73.8%)	293 (8.3%)
Education—bachelor's degree or higher	2813 (26.3%)	1001 (29.6%)	978 (25.4%)	834 (23.5%)
Health conditions				
Number of condition groups	1 (0–2)*	1 (0–1)*	1 (0–2)*	1 (1–2)*
Condition groups				
Lung	957 (8.8%)	235 (7.0%)	338 (8.8%)	384 (10.8%)
Musculoskeletal	4524 (42.0%)	753 (22.3%)	1765 (45.8%)	2006 (56.5%)
Endocrine	735 (6.8%)	88 (2.6%)	284 (7.4%)	363 (10.2%)
Mental	1167 (10.8%)	417 (12.3%)	448 (11.6%)	302 (8.5%)
Cancer	396 (3.7%)	19 (0.6%)	104 (2.7%)	273 (7.7%)
Neurological	1694 (15.7%)	743 (22.0%)	617 (16.0%)	334 (9.4%)
Gastrointestinal	165 (1.5%)	58 (1.7%)	62 (1.6%)	45 (1.3%)
Cardiovascular	885 (8.2%)	73 (2.2%)	292 (7.6%)	520 (14.7%)
Kidney	171 (1.6%)	26 (0.8%)	57 (1.5%)	88 (2.5%)
Sensory organs	2085 (19.3%)	746 (22.1%)	766 (19.9%)	573 (16.5%)
Self-perceived health				
Five Well-Being Index (WHO-5) (0–100)	67.5 ($\pm$18.2)	63.8 ($\pm$17.5)	66.6 ($\pm$18.6)	72.0 ($\pm$17.6)
Self-rated Health item				
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.
†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.[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%) participants provided information in the disease category "others." All conditions in this category except three (HIV, periodontitis and alopecia (n = 7))

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	957 (8.9)									
Musculoskeletal	533 (4.9)	4524 (42.0)								
Endocrine	85 (0.8)	383 (3.6)	735 (6.8)							
Mental	177 (1.6)	663 (6.2)	102 (1.0)	1167 (10.8)						
Cancer	53 (0.5)	224 (2.0)	46 (0.4)	50 (0.4)	396 (3.7)					
Neurological	178 (1.7)	839 (7.8)	114 (1.0)	362 (3.4)	50 (0.4)	1694 (15.7)				
Gastrointestinal	20 (0.2)	82 (0.8)	7 (0.0)	31 (0.2)	6 (0.0)	37 (0.4)	165 (1.5)			
Cardiovascular	123 (1.2)	525 (4.8)	124 (1.2)	144 (1.4)	72 (0.6)	142 (1.4)	12 (0.2)	885 (8.2)		
Kidney	25 (0.2)	101 (1.0)	29 (0.2)	27 (0.2)	21 (0.2)	36 (0.4)	1 (0.0)	32 (0.2)	171 (1.6)	
Sensory organs	398 (3.6)	976 (9.0)	142 (1.4)	296 (2.8)	63 (0.6)	439 (4.0)	49 (0.4)	182 (1.6)	41 (0.4)	2085 (19.3)

*The table shows all binary combinations—e.g. if a participant is represented with three condition groups all binary combinations of these have been included in the table.

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Table 3. Difference in self-perceived health (WHO-5 and the one item self-rated health) in people represented in 1 of the 10 condition groups compared to the rest of the study sample and with a further comparison across age groups.

| | WHO-5 | | | | Self-rated Health item | | | |
| | Age/gender adjusted | | Fully adjusted model | | Age/gender adjusted | | Fully adjusted model | |
Condition group	Mean (95%) CI	p-value*	Mean (95%) CI	p-value*	OR (95% CI)	p-value*	OR (95% CI)	p-value*
Lung	−6.8 (−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)	
Age groups								
18–49	−7.2 (−9.4 to −4.8)	0.12	−2.9 (−5.1 to −0.7)	<0.001	1.85 (1.41 to 2.41)	0.78	1.49 (1.13 to 2.00)	0.44
50–64	−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)	
≥65	−8.1 (−9.9 to −6.3)		−6.0 (−7.8 to −4.3)		2.04 (1.65 to 2.53)		1.79 (1.43 to 2.25)	
Musculoskeletal	−6.6 (−7.3 to −5.9)		−3.8 (−4.5 to −3.1)		1.61 (1.49 to 1.75)		1.33 (1.22 to 1.45)	
Age groups								
18–49	−6.0 (−7.5 to −5.0)	0.14	−2.6 (−4.0 to −1.2)	0.01	1.69 (1.43 to 2.00)	0.11	1.31 (1.10 to 1.58)	0.86
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	−3.8 (−7.2 to −0.5)	0.79	2.14 (1.39 to 3.31)	0.19	2.05 (1.30 to 3.23)	0.15
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 1.27)	
≥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)		−15.1 (−16.1 to −14.1)		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	−14.3 (−16.0 to −12.5)	0.11	2.64 (2.14 to 3.28)	0.51	1.66 (1.31 to 2.10)	0.75
50–64	−20.0 (−21.7 to −18.2)		−14.5 (−16.3 to −12.8)		2.82 (2.29 to 3.47)		1.70 (1.35 to 2.14)	
≥65	−19.3 (−21.2 to −17.2)		−16.1 (−18.0 to −14.1)		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	−1.0 (−8.2 to 6.1)	0.34	1.56 (0.63 to 3.86)	0.47	1.10 (0.42 to 2.88)	0.55
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	−4.0 (−5.3 to −2.6)	0.02	1.68 (1.42 to 1.99)	0.56	1.40 (1.17 to 1.67)	0.53
50–64	−9.6 (−11.2 to −8.2)		−5.8 (−7.3 to −4.4)		1.99 (1.67 to 2.38)		1.61 (1.32 to 1.95)	
≥65	−9.9 (−11.9 to −7.9)		−6.2 (−8.1 to −4.4)		1.90 (1.52 to 2.39)		1.60 (1.26 to 2.04)	
Gastrointestinal	−6.8 (−9.6 to −4.1)		−3.8 (−6.3 to −1.3)		2.61 (1.87 to 3.61)		2.41 (1.72 to 3.39)	
Age groups								
18–49	−3.4 (−7.9 to 1.0)	0.23	−1.4 (−5.5 to 2.7)	0.19	2.00 (1.18 to 3.20)	0.21	1.85 (1.06 to 3.23)	0.30
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	−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)	
Age groups								
18–49	−3.9 (−10.6 to 2.8)	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)	
Sensory organs	−3.0 (−3.9 to −2.2)		−1.2 (−2.0 to −0.4)		1.18 (1.07 to 1.30)		1.01 (0.91 to 1.12)	
Age groups								
18–49	−2.5 (−3.9 to −1.1)	0.10	−1.2 (−2.5 to 0.1)	0.06	1.11 (0.94 to 1.31)	0.19	1.00 (0.83 to 2.88)	0.17
50–64	−2.2 (−3.7 to −0.8)		−0.4 (−1.8 to −0.9)		1.11 (0.94 to 1.30)		0.93 (0.78 to 1.11)	
≥65	−4.6 (−6.2 to −3.0)		−2.2 (−3.6 to −0.7)		1.37 (1.14 to 1.64)		1.17 (0.96 to 1.41)	

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.

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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,[8–18] little is known about clusters of conditions and self-perceived health in younger age groups compared to older.[21] 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),[20,23,25,26] 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.[41,42] 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.[42] 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 ($\pm$17.5) and 50–64 years of age, 66.6 ($\pm$18.6) vs 65+ years of age, 72.0 ($\pm$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.[25]
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								
	0.2 (−0.6 to 0.9)		−4.5 (−5.3 to −3.7)		1.04 (0.95 to 1.13)		1.30 (1.17 to 1.44)	
Age groups								
18–49	1.2 (−0.5 to 2.9)		− 2.1 (−3.9 to −0.3)		1.05 (0.86 to 1.29)		1.24 (0.98 to 1.55)	
50–64	− 0.2 (−1.4 to 1.1)	0.14	− 4.5 (−5.9 to −3.1)	0.17	1.16 (1.01 to 1.33)	0.06	1.45 (1.22 to 1.71)	0.15
≥65	− 0.2 (−1.4 to 1.0)		− 6.8 (−8.2 to −5.4)		0.92 (0.81 to 1.05)		1.25 (1.05 to 1.49)	
Pattern 2: Mental, neurological, lung, gastrointestinal and sensory organs								
	−8.1 (−8.8 to −7.4)		−9.1 (−13.8 to −8.2)		1.52 (1.40 to 1.65)		1.57 (1.44 to 1.73)	
Age groups								
18–49	−7.8 (−8.9 to −6.6)		−6.6 (−7.8 to −5.4)		1.53 (1.33 to 1.76)		1.40 (1.20 to 1.64)	
50–64	−7.9 (−9.1 to −6.7)	0.99	−8.7 (−10.1 to −7.3)	<0.001	1.51 (1.32 to 1.72)	0.87	1.63 (1.38 to 1.92)	0.13
≥65	−8.2 (−9.5 to −6.9)		−12.6 (−14.2 to −11.0)		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.[20,23,25,26] Also, for self-rated health, the largest negative association was found for pattern 2, but with no difference between age groups. Hence, the poorer psychological well-being and self-rated health indicate that a greater clinical focus is needed on patients with the combination of mental and somatic conditions, in particular when it comes to elderly patients.

The fact that no interaction was found between pattern 1 and the three age groups for psychological well-being is not that surprising as all three individual conditions (lung, musculoskeletal and neurological) which showed a significantly interaction with age were represented in pattern 2.

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.[20,26,44] 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.[43,47] Also, depending on the analytic approach, osteoarthritis seems to be related to this pattern.[43] 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.[8] 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 cognitive[50] and economic status.

Fourth, although research has shown that current chronic conditions can be accurately reported by patients[51–53] and are as likely to predict health-related quality of life as objectively assessed conditions,[53] 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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