BMJ Open

Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-036851
Article Type:	Original research
Date Submitted by the Author:	07-Jan-2020
Complete List of Authors:	Vinjerui, Kristin Hestmann; Norwegian University of Science and Technology, Department of Public Health and Nursing/HUNT Research Centre; Helse Nord-Trondelag, Psychiatric Department Bjerkeset, Ottar; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Mental Health Bjorngaard, Johan; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences Krokstad, Steinar; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing/HUNT Research Centre; Helse Nord-Trondelag, Psychiatric Department Douglas, Kirsty; Australian National University, Australian National University Medical School Sund, Erik; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing/HUNT Research Centre; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences
Keywords:	SOCIAL MEDICINE, EPIDEMIOLOGY, PUBLIC HEALTH

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study

Kristin H Vinjerui,[1,2,3,*] Ottar Bjerkeset,[4,5] Johan H Bjorngaard,[4,6] Steinar Krokstad,[1,3] Kirsty Douglas,[2] Erik R Sund.[1,4]

1 HUNT Research centre, Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Levanger, Norway

2 Academic Unit of General Practice, Australian National University Medical School, Canberra, Australia

3 Psychiatric Department, Levanger Hospital, Nord-Trøndelag Hospital Trust, Norway.

4 Faculty of Nursing and Health Sciences, Nord University, Levanger, Norway

5 Department of Mental Health, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, Norway

6 Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, Norway

*Corresponding author: Kristin Hestmann Vinjerui, HUNT Research centre, Forskningsvegen 2, 7600 Levanger, Norway. E-mail: Kristin.vinjerui@ntnu.no.Tel.: 0047-90173201/74019240/74075180

WORD COUNT

Abstract: 288 words, max 300.

Text: 3457 words, max 4000.

KEYWORDS

Multimorbidity. Socioeconomic status. Occupations. Public health. Health inequality. The HUNT Study.

ABSTRACT

Objectives: Multimorbidity, the co-occurrence of multiple long-term conditions that are all equally important, is common and increasing. Definitions and assessment methods vary, yielding differences in estimates of prevalence and multimorbidity severity. Sociodemographic characteristics are associated with complicating factors of multimorbidity. We aimed to investigate complex multimorbidity (defined as chronic conditions in three or more organ systems) by sex and occupational groups throughout adulthood.

Design: Cross-sectional study

Setting: The third total county survey of The Nord-Trøndelag Health Study (HUNT), 2006-2008, Norway.

Participants: Individuals aged 25-100 years with classifiable occupational data and complete questionnaires and measurements.

Outcome measure: 51 chronic conditions were grouped in 14 *ICD-10* organ-specific chapters, and complex multimorbidity was identified as conditions in three or more organ systems.

Analysis: Logistic regression models with age and occupational group were specified for each sex separately.

Results: 38027 of 41193 adults (55% women) were included in our analyses. 54% of the participants were identified as having complex multimorbidity. Prevalence differences in percentage points (pp) of those in the low occupational group (vs the high occupation group [reference]) were 19 (95% CI,16 to 21) pp in women and 10 (8 to 13) pp in men at 30 years; 12 (10 to 14) pp in women and 13 (11 to 15) pp in men at 55 years; and 2 (-1 to 4) pp in women and 7 (4 to 10) pp in men at 75 years.

Conclusion: Complex multimorbidity is common from early adulthood, and social inequalities persist until 75 years in women and 90 years in men in the general population. These findings have policy implications for public health as well as health care, organization, treatment, education, and research, as complex multimorbidity breaks with the specialized, fragmented paradigm dominating medicine today.

ARTICLE SUMMARY

Strengths and limitations of this study

1. As a large, entire-county, general population health survey with a vast number of variables, the HUNT Study is ideal to estimate the prevalence of multimorbidity by self-reports and clinical measurements.
2. Complex multimorbidity operationalized as three or more organ systems affected is relevant in both clinic and research, with high specificity into old age, implicating need of coordinated multidisciplinary care and increasing comparability between studies.
3. Socioeconomic position operationalized as occupations allocated in the European Socio-economic Classification scheme makes international comparison of gradients possible.

4. Socioeconomic differences in association with complex multimorbidity are reported with both absolute and relative measures for women and men separately.
5. The original data lacked information of chronicity of a majority of the conditions, which may lead to overestimation of complex multimorbidity.

INTRODUCTION

Multimorbidity, the cooccurrence of multiple long-term conditions in which none is more important,[1] is common and increasing.[2 3] It challenges the individual's ability to self-manage[4 5] as well as clinical decision-making[5-7] due to complexity that conflicts with subspecialized medicine and clinical guidelines. Multimorbidity is associated with high health care utilization in both primary and specialist care,[8] including emergency department visits.[9]

Multimorbidity is heterogenous, and a mere count of conditions may not imply complexity[5 10] requiring coordinated multidisciplinary care. In attempts to detect individuals with high needs, guidelines by and large focus on combinations of conditions, such as concurrent mental and somatic conditions[5 11 12] or three or more conditions in separate organ systems,[5 13] and consequences thereof, such as polypharmacy[5 11 12] and requirements for assistance in daily living.[5 11 12] Individual factors that increase patient complexity include sociodemographic characteristics,[14] social resources,[14] and health and social experiences.[14] Recent recommendations on multimorbidity care have taken into account social networks,[12] socioeconomic positions,[12] and patient experiences, such as treatment burden.[11 12]

Research results from multimorbidity studies has been difficult to compare because of differences in definitions, methods, and the number and types of conditions included.[15 16] Still, associations with lower socioeconomic position[3 15 17], female sex,[3 15 17] and increasing age[3 15 17] persist across studies. Further, defining multimorbidity as simultaneously having three or more conditions increases the specificity of the multimorbidity measure into older age groups,[13 16] and comparability between studies increases when multimorbidity is operationalized as multiple organ systems affected.[13]

Inequalities in health according to socioeconomic position are persistent,[18] even in comparatively egalitarian Nordic societies.[19] The association of socioeconomic differences with the occurrence of multimorbidity has been explored using multiple measures, such as education,[15 20] income,[20] occupation,[3] and deprivation indexes.[15 17] In fact, any measure of socioeconomic position will detect health differences in descriptive studies, if differences exist.[21] Using an occupational classification may reflect specific work-related exposures in addition to general associations to income, material resources, and social status.[21]

In sum, multimorbidity represents a challenge both for the individual and clinician, as well as for the coordination of services within health care. Furthermore, demographic and socioeconomic gradients clearly operate. In Norway, multimorbidity prevalence and patterns have been partly explored.[22] In this study, we investigate one definition of complex multimorbidity, three or more conditions in separate organ systems, throughout the adult life span by sex and occupational groups in a general population health survey.

METHODS

Reporting statement

The STROBE cross sectional reporting guidelines[23] were used for reporting of this observational study.

Study population

The HUNT Study is a population-based health study for all adults 20 years and older living in Nord-Trøndelag County, Norway. Four surveys have been completed since the 1980s, and cohort profiles and data collection procedures have been described in detail elsewhere. [24 25] This study is a secondary analysis of data from the HUNT3 Survey (2006-2008), where 93860 citizens were invited to participate. In short, the survey consisted of a main questionnaire received with the invitation by mail and handed in when attending a screening station, where participants were interviewed and clinical measurements and biological samples were taken. A second sex- and age-specific questionnaire was handed out at the screening station and returned by mail.

A total of 50807 individuals (54% of 93860 invited) completed the main questionnaire, required to be considered an attendant of the HUNT3 Survey.[24] Sampling is described in figure 1. In this study, 41193 of 50807 participants (81%) had data on all major parts of the survey (both questionnaires, interview, measurements, and samples) and were designated as respondents. Thus, 9610 were excluded due to incomplete participation, while 4 people missed complete participation data. Under the assumption that young adults may not have obtained their highest level of occupational class at the time of participation, 1569 participants younger than 25 years were excluded, as well as 1 person with missing age data. Occupation data was missing for 1571 respondents, and 25 people were excluded due to unspecified occupation data. Finally, 38027 of 41193 (92%) respondents were eligible for data analysis, 11204 were non-eligible and 1576 had missing data. Further sociodemographic characteristics of non-eligible and missing are provided in appendix C

Figure 1. Flowchart for sample selection; inclusion and exclusion criteria, and missing data.

Outcome variable

Complex multimorbidity was defined as “the co-occurrence of three or more chronic conditions affecting three or more different body [organ] systems within one person without defining an index chronic condition”, as suggested by previous research.[5 13]

All conditions possible to generate from the HUNT3 Survey data were included to meet recommendations on deriving the best estimate of prevalence of multimorbidity.[13] In total, 51 chronic conditions, defined singly as far as original data permitted, were constructed, and details are described in appendix A. This list of 51 conditions is more comprehensive and homogenous than previous operationalizations of multimorbidity in the HUNT3 Survey.[22]

Further, the conditions were grouped according to the *ICD-10* in 13 organ-specific chapters and one chapter on symptoms, signs, and abnormal clinical and laboratory findings (table 1), using general terms of the conditions in the Norwegian Directorate of eHealth online search engine[26] on February 1 2017.

Chapters were counted once if affected by at least one chronic condition and a summary score of the chapter variables was generated. In this study, complex multimorbidity was defined as having conditions in at least 3 of 14 chapters.

Sociodemographic Characteristics

Occupation data from the HUNT3 survey were free-text answers to the interview question, "What is/was the title of your main occupation?" Answers were manually categorized corresponding to Standard Classifications of Occupations by Statistics Norway,[27] which is based on the International Standard Classification of Occupations-88 (ISCO-88).[28] Socioeconomic position was allocated according to the simplified, 3-class version European Socio-economic Classification (ESeC) scheme.[29] The simplified scheme is based solely on occupational data, classified according to ISCO-88.[28] Details are provided in appendix B. The intention of the full ESeC scheme is to measure qualitative distinctions between employment relationships and does not reflect a clear hierarchy.[29] However, income is considered more stable in the salariat class.[29] In the 3-class version, the salariat class consists of large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, and higher-grade technician and supervisory occupations. The intermediate class contains small employers, self-employed individuals, and lower-grade supervisory and technician occupations. The working class represents lower-grade service positions, sales and clerical occupations, and lower-grade technical and routine occupations. For practical reasons in this study, the terms high, middle, and low occupational group replaced the terms salariat, intermediate, and working class, respectively.

In addition, continuous age and categorical sex data, provided by the HUNT databank, were used in the analyses.

Table 1. Conditions grouped by *ICD-10* chapter

***ICD-10* chapter**	Conditions
II	**Neoplasms**
	Cancer
III	**Blood/blood-forming organs/ immune mechanism**
	Sarcoidosis
IV	**Endocrine/nutritional/metabolic**
	Obesity
	Hypercholesterolemia
	Diabetes
	Hypothyroidism
	Hyperthyroidism
V	**Mental/behavioral**
	Alcohol problem
	Depression
	Anxiety
	Insomnia
VI	**Nervous system**
	Epilepsy
	Migraine
	Chronic headache, other
VII	**Eye/adnexa**
	Cataract
	Macula degeneration
	Glaucoma
VIII	**Ear/mastoid**
	Hearing impairment
IX	**Circulatory system**
	Undetected hypertension
	Angina pectoris
	Myocardial infarction
	Heart failure
	Other heart disease[1]
	Stroke or brain haemorrhage[1]
X	**Respiratory system**
	Chronic bronchitis, emphysema, or COPD[1,2]
	Asthma
XI	**Digestive system**
	Dental health status
	Gastro-oesophageal reflux disease
	Irritable bowel syndrome
XII	**Skin/subcutaneous tissue**
	Hand eczema
	Psoriasis
XIII	**Musculoskeletal/connective tissue**
	Rheumatoid arthritis
	Osteoarthritis
	Ankylosing spondylitis
	Fibromyalgia
	Osteoporosis
	Local musculoskeletal pain/stiffness in:
	- Neck
	- Upper back
	- Lower back
	- Shoulder
	- Elbow
	- Hand
	- Hip
	- Knee
	- Foot/ankle
XIV	**Genitourinary system**
	Kidney disease
	Urine incontinence
	Prostate symptoms
	Menopausal hot flashes
XVIII	**Symptoms/signs/abnormal clinical/ laboratory findings**
	Nocturia
	Chronic widespread pain

[1] = Exception to single entity
[2]COPD = Chronic Obstructive Pulmonary Disease

Statistical analysis

Cross-tables were used to present sociodemographic characteristics of the sample by occupational group (table 2) and by complex multimorbidity, stratified by sex (table 3).

Associations between occupational group and complex multimorbidity were analyzed using logistic regression. The final models were stratified by sex, included occupational group, continuous age, and an interaction term between occupational group and age. Choice of models were guided by likelihood ratio tests.

Since complex multimorbidity was highly prevalent, odds ratios would deviate from relative risks[30] and be challenging to interpret. Thus, we used the estimates from the logistic regression models to derive prevalence differences, the difference in mean predicted probability,[31] and prevalence ratios, the ratio between the mean predicted probabilities,[31] between occupational groups, while holding other covariates constant. The high occupational group was chosen as the reference group. Prevalence differences and prevalence ratios were calculated in 5-year intervals from 25 to 100 years, with 95% confidence intervals (CIs) (appendix D) Results for the ages 30, 55, 75, and 90 years are presented in table 4 to represent adult, middle aged, aged and oldest old in the sample.

To visualize the differential association between age and complex multimorbidity in each occupational group, we specified separate models using restricted cubic splines and graphed the findings from each model into a common plot for each sex.

Sensitivity analysis was performed to investigate if the number and types of conditions showed a similar pattern with respect to the overall prevalence as well as differences between occupational groups (appendix E). The alternative complex multimorbidity measure was derived from data in the main questionnaire only (22 conditions, grouped in 12 *ICD-10* chapters)

Complete case analysis was performed, and Stata version 15.1 was used to analyze the data (StataCorp, College Station, TX, USA).

Patient and public involvement

There was a broad participant, patient, and stakeholder involvement during the planning of the HUNT3 survey. Data collection was performed in 2006-2008. Complex multimorbidity is a universal subject, not represented by any particular patient group, and thus no patient or public representative was involved in the design of this secondary analysis study.

RESULTS

38027 individuals, aged 25 to 100 years, 55% women (n=20813), who had completed all major parts of the HUNT3 Survey and had a classifiable occupation comprised the eligible sample, as fig. 1 depicts. Table 2 presents further sociodemographic characteristics.

Table 2. Sex and age distribution by occupational group. The HUNT Study (2006-08).

	Occupational group							
	High		Middle		Low		Total	
	Freq.	(%)	Freq.	(%)	Freq.	(%)	Freq.	(%)
Total	8 970	(100)	10 243	(100)	18 814	(100)	38 027	(100)
Sex								
Female	4 505	(50)	5 386	(53)	10 922	(58)	20 813	(55)
Male	4 465	(50)	4 857	(47)	7 892	(42)	17 214	(45)
Age, yr.								
25-44	2 837	(32)	2 600	(25)	4 487	(24)	9 924	(26)
45-64	4 468	(50)	4 787	(47)	8 951	(48)	18 206	(48)
65-74	1 118	(12)	1 846	(18)	3 297	(18)	6 261	(16)
75-100	547	(6)	1 010	(10)	2 079	(11)	3 636	(10)

Abbreviations: freq., frequency, yr., years.

Nearly half the sample (49%; n=18814 of 38027; of which 58% were women, n=10922), was allocated in the low occupational group. In absolute numbers, the low occupational group was the largest socioeconomic category in both sexes and all age groups. The proportion of individuals aged 25 to 44 years decreased from 32% in the high occupational group (n=2837) to 24% in the low occupational group (n=4487), while the proportion of individuals aged 75 to 100 years increased from 6% (n=547) to 11% (n=2079). Participants aged 45 to 64 years were the largest age group in total and in all occupational groups (high, n=4468; middle, n=4787; low, n=8951).

Table 3. Sociodemographic distribution of complex multimorbidity. The HUNT Study (2006-08).

	Complex multimorbidity											
	Women						Men					
	No, *n*	(%)	Yes, *n*	(%)	Total, *n*	(%)	No, *n*	(%)	Yes, *n*	(%)	Total, *n*	(%)
Total	8 505	(41)	12 308	(59)	20 813	(100)	9 137	(53)	8 077	(47)	17 214	(100)
Occupational group												
High	2 460	(55)	2 045	(45)	4 505	(100)	2 712	(61)	1 753	(39)	4 465	(100)
Middle	2 384	(44)	3 002	(56)	5 386	(100)	2 525	(52)	2 332	(48)	4 857	(100)
Low	3 661	(34)	7 261	(66)	10 922	(100)	3 900	(49)	3 992	(51)	7 892	(100)
Age, years												
25-44	3 859	(65)	2 122	(35)	5 981	(100)	2 958	(75)	985	(25)	3 943	(100)
45-64	3 668	(37)	6 172	(63)	9 840	(100)	4 621	(55)	3 745	(45)	8 366	(100)
65-74	721	(23)	2 447	(77)	3 168	(100)	1 155	(37)	1 938	(63)	3 093	(100)
75-100	257	(14)	1 567	(86)	1 824	(100)	403	(22)	1 409	(78)	1 812	(100)
Mean (SD)	48	(13)	59	(14)	54	(14)	52	(13)	62	(13)	56	(14)

Overall, a majority (54%; n=20385 of 38027) of the sample met the criteria for having complex multimorbidity, including 59% of women (n=12308) and 47% of men (n=8077; table 3). The

percentages increased from high to low occupational group in women from 45% (n=2045) to 66% (n=7261) and in men from 39% (n=1753) to 51% (n=3992). The proportions further increased by age, from 35% (n=2122) of women aged 25 to 44 years to 86% (n=1567) of women aged 75 to 100 years. In men, the increase was from 25% (n=985) to 78% (n=1409) in the same age groups. In absolute numbers, most people classified as having complex multimorbidity were aged 45 to 64 years (women, n=6172; men, n=3745).

Table 4. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational groups, stratified by sex.

Age,	Occupational	Women				Men			
years	group	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
30	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.47	(1.28, 1.68)	0.08	(0.05, 0.11)	1.28	(1.05, 1.55)	0.03	(0.01, 0.06)
	Low	2.06	(1.84, 2.32)	0.19	(0.16, 0.21)	1.92	(1.63, 2.26)	0.10	(0.08, 0.13)
55	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.08	(1.03, 1.12)	0.04	(0.02, 0.06)	1.16	(1.10, 1.23)	0.06	(0.04, 0.08)
	Low	1.22	(1.18, 1.26)	0.12	(0.10, 0.14)	1.35	(1.28, 1.41)	0.13	(0.11, 0.15)
75	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.98	(0.95, 1.02)	-0.01	(-0.04, 0.02)	1.07	(1.02, 1.12)	0.05	(0.02, 0.08)
	Low	1.02	(0.99, 1.05)	0.02	(-0.01, 0.04)	1.10	(1.06, 1.15)	0.07	(0.04, 0.10)
90	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.98	(0.96, 1.00)	-0.02	(-0.04, 0.00)	1.03	(0.99, 1.07)	0.03	(-0.01, 0.06)
	Low	0.99	(0.97, 1.01)	-0.01	(-0.03, 0.01)	1.03	(0.99, 1.07)	0.02	(-0.01, 0.05)

Table 4 shows prevalence ratios and prevalence differences between the occupational groups after adjusting for age and occupation-age interaction and thus presented at ages 30, 55, 75, and 90 years. Prevalence differences for complex multimorbidity between high and low occupational groups varied; at 30 years, 19 (16 to 21) percentage points (pp) in women and 10 (8 to 13) pp in men; at 55 years, 12 (10 to 14) pp in women and 13 (11 to 15) pp in men; at 75 years, 2 (-1 to 4) pp in women and 7 (4 to 10) pp in men; and at 90 years, -1 (-3 to 1) pp in women and 2 (-1 to 5) in men. Compared with the high occupational group, the prevalence ratios for the low occupational group for complex multimorbidity were at 30 years, 2.06 (1.84 to 2.32) in women and 1.92 (1.63 to 2.26) in men; at 55 years, 1.22 (1.18 to 1.26) in women and 1.35 (1.28 to 1.41) in men; at 75 years, 1.02 (0.99 to 1.05) in women and 1.10 (1.06 to 1.15) in men; and at 90 years, 0.99 (0.97 to 1.01) in women and 1.03 (0.99 to 1.07) in men.

In the sensitivity analyses where the complex multimorbidity measure was derived from fewer conditions (22 vs 51) and *ICD-10* chapters (12 vs 14), the total prevalence was 15% (n=5836 of 38027, appendix E). Proportions were greater in women, higher age and the low occupational group. Compared to the results from the main analysis prevalence differences between high and low occupational groups were smaller in women at all ages and in men at age 30 years and 55 years, while prevalence ratios were greater in men at all ages and in women age 30 and 55 years.

Figure 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

Figure 2 depicts estimated prevalence of complex multimorbidity by occupational group and sex individuals aged 25 to 100 years. In all occupational groups in both sexes, the predicted prevalence increased with age throughout the age span. Further, estimated prevalence differed between the occupational groups in women until age 75 years and in men until age 90 years. Women had a consistently higher prevalence for complex multimorbidity than men.

DISCUSSION

Main results

More than half (54%) of this total county adult population sample were identified with complex multimorbidity, measured as occurrence of chronic conditions in minimum three separate organ systems. Prevalence of complex multimorbidity was common from early adulthood, increased with age, and was higher in women and in the low occupational group. Occupational group prevalence differences and ratios in complex multimorbidity were present in women until age 75 years and in men until age 90 years.

Comparison with existing literature

Few, if any, studies (to our knowledge) have investigated the prevalence and determinants of complex multimorbidity in a general population. The findings are in keeping with known determinants of lower social position, female sex, and higher age for multimorbidity in both general population-[20] and primary care studies.[3 15 17] An Australian study using a comparable operationalization of complex multimorbidity identified nearly 25% of patients in general practice with complex multimorbidity and estimated a national prevalence of 17%.[32] However, higher prevalence findings from our predominantly self-reported data are compatible with studies comparing prevalence estimates from self-reports and health record data.[33 34] In absolute numbers, the incidence of individuals identified with the stricter measure of complex multimorbidity is still highest among the group younger than 64 years, as has been shown for multimorbidity.[17 20 35] The sensitivity analysis confirms how number and types of conditions influence prevalence[13 16] and effect estimates of age, sex, and socioeconomic position.[36]

Mechanisms to explain findings

The association between lower socioeconomic position and poor health is well established. In general, unequal distribution of income, power, and wealth are understood to be socially determined fundamental causes that impact conditions of everyday life and result in social health inequities.[18] In Nordic countries assumed to be egalitarian and offering universal health care, social health inequities still exists.[19] Theories put forward are the survival of individuals with greater frailty, who are more likely to obtain a lower social position.[37] The gap in health is also explained by overall morbidity and mortality decreasing faster among the higher than the lower socioeconomic groups.[37]

In this study, occupational class serves as the proxy variable for socioeconomic position. Occupation may affect health outcomes through universal and specific mechanisms. In general,

the higher occupational groups will have more secure and higher income,[29 38] as well as advantageous social networks.[38] In particular, jobs vary in psychosocial factors, such as stress, control, and autonomy and biological factors, such as physical demands or harmful and hazardous work environments.[38] Overall, the higher occupational group have greater autonomy and control,[29] while lower occupational groups are more exposed to malign work factors.[18] Generations may have different associations between a profession and health outcomes,[38] as occupations, tasks, and exposures shift over time.

The bidirectional relationship between health and occupation,[21] may partly explain the larger prevalence differences and ratios between low and high occupational groups in the younger age categories. Higher rates of multimorbidity in young individuals in lower socioeconomic positions may also be explained by detection bias[35] in which the initiation of therapy and health care follow-up increase the likelihood of diagnosing more conditions. Diminishing occupational ratios and differences among the oldest may be explained by the higher overall prevalence of complex multimorbidity[39] and also survival bias, whereby the individuals with greatest fragility have already died. While probability of complex multimorbidity increase with age, the age distribution results in a higher number of cases occurring in those younger than 64 years.

Strengths and limitations

Strengths of this study is the estimation of prevalence of complex multimorbidity from a general population survey, the most common study design in multimorbidity studies.[40] A vast number of self-reported conditions are included, almost exclusively diagnoses and symptoms.[41] Self-report is considered a valid approach when studying large samples.[16] Furthermore, using all available data will produce the most proper prevalence estimates,[13] which in this study is demonstrated by the sensitivity analysis and which seems necessary to detect occupational differences in younger age groups. The sensitivity analyses confirm that the spectrum of conditions included may affect associations with socioeconomic position, age, and sex.[36]

Our operationalization of complex multimorbidity makes the prevalence estimates comparable to other studies categorizing conditions by any organ-based system.[13] The allocation of occupations in the European Socio-economic Classification also makes international comparison of social gradients possible.[29] We presented absolute and relative differences in compliance with recommendations on measurements of socioeconomic inequalities in health.[42] Results are further stratified by age and sex, which are stated as minimum requirements for proper reporting of multimorbidity.[15]

A number of limitations should be noted. Our study is based on data collected for a general health survey, and this limits data on conditions included in the complex multimorbidity measure. In particular, we did not have explicit information on chronicity for a majority of the conditions. Thus, the prevalence of complex multimorbidity may be overestimated.

Socioeconomic position was explored using only occupation, and while social health inequalities will be detected,[21] socioeconomic measures are not interchangeable.[21 43] Different measures of socioeconomic position will act through varying mechanisms and may associate distinctively with health outcomes.[21 43] Participants in HUNT3 reported their main occupation, while current or longest-lasting occupation is more often studied.[38] Younger subjects may be misclassified in

lower socioeconomic position, which may underestimate the occupational differences in health in this age group, whereas reverse causation, whereby prior health status determines job opportunities, is unavoidable and will increase detected differences. Occupational data may misrepresent present social context[38] and thereby underestimate social inequalities. It would have been favorable if the study had included education, income or household indicators for socioeconomic position.

Participation in the HUNT3 Survey varied by age, sex, socioeconomic position, and pattern of morbidity.[44] This may weaken the effect estimates of the determinants to complex multimorbidity. A healthy elders bias is likely, since participation required attendance at a screening station. Overall, prevalence of individual conditions have shown only slight differences between participants and nonparticipants.[44] The HUNT study is considered fairly representative for Norway,[25] and the health development in the material follows western high-income country trends closely.[45-47]

Implications for clinical practice and policy makers

Our study confirms that complex multimorbidity, a suggested measure to identify multimorbid individuals with high need for coordinated multidisciplinary care,[13] is highly prevalent in the general population, where social differences are evident from young to old adulthood. This is in line with international studies, and at policy level, an emphasis on public health intervention to prevent complex multimorbidity and social differences seems necessary. As proposed elsewhere, this will likely require a proportionate universalism life-cycle approach.[48] To improve and secure health care for this large patient group, clinical guidelines and the organization of health care is suggested to adapt to a person-centered, generalist approach.[5 11 49]

Future research

Complex multimorbidity is common in this general population sample, with a clear social gradient throughout adulthood. Careful interpretation is necessary, since there are possible biases in measures of multimorbidity and occupation. However, the HUNT3 Survey data covers a broad spectrum of conditions and gives a unique opportunity to create several measures of multimorbidity in the same sample, with directly comparable prevalence estimates and gradients. On this background, we recommend exploring alternative measures suggested to detect individuals with high needs and multimorbidity and investigate differences in patterns, and consequences of such measures by social health determinants. Since multimorbidity is the norm and represents a large challenge to health care across levels, research on overall health care utilization and organization should be a priority, as well as studying competing measures as prognostic factors for mortality. Studies on social differences in use of health care may identify vulnerable subgroups, where any specific organization of treatment later on could be evaluated.

Conclusion

Complex multimorbidity, defined as occurrence of chronic conditions in three separate organ systems, is common, and occupational differences exists throughout adulthood in both sexes. The magnitude of complex multimorbidity in all age groups implies the need for public health management to universally improve, targeted proportionate to need and disadvantage in

subpopulations, social health determinants throughout the lifespan. Complex multimorbidity, indicating the accumulation of conditions of different etiology requiring coordinated multidisciplinary care, should inspire health caregivers, health care organizations, educational institutions, and researchers to take on a generalist and person-centered focus. Studying alternative multimorbidity measures, including health care utilization and mortality according to social background, as well as multimorbidity management, should be prioritized in future research.

FIGURES

Fig. 1. Flowchart for sample selection; inclusion and exclusion criteria and missing data

Fig 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

ACKNOWLEDGEMENTS

L Getz, J Sigurdsson and C Harrison for through discussions on measures of multimorbidity.
E Solheim for guidance in the use of the European Socio-economic Classification scheme.
MS Newman for writing assistance.
The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between HUNT Research Centre (Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU), Nord-Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health.

COMPETING INTERESTS

None declared.

FUNDING STATEMENT

This study was funded by the Faculty of Medicine and Health Science at the Norwegian University of Science and Technology through the PhD program in Behavior and Health (KHV). The funding source has partly funded the HUNT3 Survey and have funded open access for this article.

The PhD program in Behavior and Health is a joint program with the Australian National University (ANU). The Liaison Committee for Education, Research and Innovation in Central Norway (Samarbeidsorganet), awarded a mobility grant to KHV (ref. 17/38297) for her research stay at ANU July 2018 – Feb 2019.

The funding sources have had no role in conceptualization this study, its design and methods, analysis and interpretation of data, writing of the article or the decision to submit the article for publication.

AUTHOR CONTRIBUTIONS

KHV, ERS, SK and JHB conceptualized the study and all authors contributed to its design. KHV has analysed the data under supervision of ERS and all authors have contributed to interpreting the data. KHV wrote the original draft, which has been revised critically by all authors. All authors have read and approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

PATIENT CONSENT

Written informed consent was obtained from all participants in the HUNT3 Survey and all participation was voluntary.

ETHICS APPROVAL

The Regional Committee for Medical and Health Research Ethics in Norway approved the current study (project no. 2014/2265).

DATA SHARING STATEMENT

To protect participants' privacy, HUNT Research Centre aims to limit storage of data outside HUNT databank and cannot deposit data in open repositories. HUNT databank has precise information on all data exported to different projects and are able to reproduce these on request. There are no restrictions regarding data export given approval of applications to HUNT Research Centre. For more information see: http://www.ntnu.edu/hunt/data

SUPPLEMENTARY FILES

Appendix A: Construction of chronic, single entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Appendix B: Operationalizing socioeconomic position using occupation.

Appendix C: Distribution of occupational groups, sex and age by participation status and missing.

Appendix D: Prevalence ratios and differences with 95% CI in complex multimorbidity between occupational groups in 5-year intervals (25 to 100 years), stratified by sex.

Appendix E: Sensitivity analyses, sociodemographic characteristics and prevalence ratios and differences with 95% CI.

REFERENCES

1. Boyd CM, Fortin M. Future of Multimorbidity Research: How Should Understanding of Multimorbidity Inform Health System Design? *Public Health Rev* 2010;32(2):451-74. doi: 10.1007/bf03391611
2. van Oostrom SH, Gijsen R, Stirbu I, et al. Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. *PLoS One* 2016;11(8):e0160264. doi: 10.1371/journal.pone.0160264 [published Online First: 2016/08/03]
3. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008;14 Suppl 1(sup1):28-32. doi: 10.1080/13814780802436093 [published Online First: 2008/10/31]
4. Coventry PA, Fisher L, Kenning C, et al. Capacity, responsibility, and motivation: a critical qualitative evaluation of patient and practitioner views about barriers to self-management in people with multimorbidity. *BMC Health Serv Res* 2014;14(1):536. doi: 10.1186/s12913-014-0536-y [published Online First: 2014/11/05]
5. Wallace E, Salisbury C, Guthrie B, et al. Managing patients with multimorbidity in primary care. *BMJ* 2015;350:h176. doi: 10.1136/bmj.h176 [published Online First: 2015/02/04]
6. Sondergaard E, Willadsen TG, Guassora AD, et al. Problems and challenges in relation to the treatment of patients with multimorbidity: General practitioners' views and attitudes. *Scand J Prim Health Care* 2015;33(2):121-6. doi: 10.3109/02813432.2015.1041828 [published Online First: 2015/07/15]
7. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. *BMJ* 2012;345:e6341. doi: 10.1136/bmj.e6341 [published Online First: 2012/10/06]
8. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract* 2011;28(5):516-23. doi: 10.1093/fampra/cmr013 [published Online First: 2011/03/26]
9. Agborsangaya CB, Lau D, Lahtinen M, et al. Health-related quality of life and healthcare utilization in multimorbidity: results of a cross-sectional survey. *Qual Life Res* 2013;22(4):791-9. doi: 10.1007/s11136-012-0214-7 [published Online First: 2012/06/12]
10. Nicholson K, Makovski TT, Griffith LE, et al. Multimorbidity and comorbidity revisited: refining the concepts for international health research. *J Clin Epidemiol* 2019;105:142-46. doi: 10.1016/j.jclinepi.2018.09.008 [published Online First: 2018/09/27]
11. National Institute for Health and Care Excellence. Multimorbidity: clinical assessment and management. NICE guideline [NG56]. https://www.nice.org.uk/guidance/ng56: National Institute for Health and Care Excellence, 2016.
12. Palmer K, Marengoni A, Forjaz MJ, et al. Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS). *Health Policy* 2018;122(1):4-11. doi: 10.1016/j.healthpol.2017.09.006 [published Online First: 2017/10/03]
13. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. *BMJ Open* 2014;4(7):e004694. doi: 10.1136/bmjopen-2013-004694 [published Online First: 2014/07/13]
14. Schaink AK, Kuluski K, Lyons RF, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. *Journal of comorbidity* 2012;2:1-9. doi: 10.15256/joc.2012.2.15 [published Online First: 2012/10/10]
15. Violan C, Foguet-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(7):e102149. doi: 10.1371/journal.pone.0102149 [published Online First: 2014/07/23]

16. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10(2):142-51. doi: 10.1370/afm.1337 [published Online First: 2012/03/14]
17. 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* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2 [published Online First: 2012/05/15]
18. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health. Geneva2008:9.
19. Mackenbach JP, Stirbu I, Roskam AJ, et al. Socioeconomic inequalities in health in 22 European countries. *N Engl J Med* 2008;358(23):2468-81. doi: 10.1056/NEJMsa0707519 [published Online First: 2008/06/06]
20. Agborsangaya CB, Lau D, Lahtinen M, et al. Multimorbidity prevalence and patterns across socioeconomic determinants: a cross-sectional survey. *BMC Public Health* 2012;12:201. doi: 10.1186/1471-2458-12-201 [published Online First: 2012/03/21]
21. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. *Br Med Bull* 2007;81-82(1):21-37. doi: 10.1093/bmb/ldm001 [published Online First: 2007/02/08]
22. Tomasdottir MO, Getz L, Sigurdsson JA, et al. Co-and multimorbidity patterns in an unselected Norwegian population: Cross-sectional analysis based on the HUNT Study and theoretical reflections concerning basic medical models. *European Journal for Person Centered Healthcare* 2014;2(3):335-45.
23. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014;12(12):1495-9. doi: 10.1016/j.ijsu.2014.07.013 [published Online First: 2014/07/22]
24. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: the HUNT Study, Norway. *Int J Epidemiol* 2013;42(4):968-77. doi: 10.1093/ije/dys095 [published Online First: 2012/08/11]
25. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. *Norsk epidemiologi* 2003;13(1):19-32.
26. Direktoratet for e-helse. FinnKode - Helsedirektoratet medisinske kodeverk [Available from: https://finnkode.ehelse.no/#icpc/0/0/0/-1 accessed 1 Feb 2017.
27. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
28. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
29. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518
30. Sedgwick P. Relative risks versus odds ratios. *Bmj-British Medical Journal* 2014;348(feb07 2):g1407-g07. doi: ARTN g1407 10.1136/bmj.g1407
31. Norton EC, Miller MM, Kleinman LC. Computing Adjusted Risk Ratios and Risk Differences in Stata. *The Stata Journal: Promoting communications on statistics and Stata* 2018;13(3):492-509. doi: 10.1177/1536867x1301300304
32. Harrison C, Henderson J, Miller G, et al. The prevalence of complex multimorbidity in Australia. *Aust N Z J Public Health* 2016;40(3):239-44. doi: 10.1111/1753-6405.12509 [published Online First: 2016/03/31]
33. Cricelli C, Mazzaglia G, Samani F, et al. Prevalence estimates for chronic diseases in Italy: exploring the differences between self-report and primary care databases. *J Public Health Med* 2003;25(3):254-7. doi: 10.1093/pubmed/fdg060 [published Online First: 2003/10/25]

34. Fortin M, Haggerty J, Sanche S, et al. Self-reported versus health administrative data: implications for assessing chronic illness burden in populations. A cross-sectional study. *CMAJ Open* 2017;5(3):E729-E33. doi: 10.9778/cmajo.20170029 [published Online First: 2017/09/28]
35. van den Akker M, Buntinx F, Metsemakers JF, et al. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol* 1998;51(5):367-75. doi: 10.1016/s0895-4356(97)00306-5 [published Online First: 1998/06/10]
36. Schafer I, Hansen H, Schon G, et al. The influence of age, gender and socio-economic status on multimorbidity patterns in primary care. First results from the multicare cohort study. *BMC Health Serv Res* 2012;12:89. doi: 10.1186/1472-6963-12-89 [published Online First: 2012/04/05]
37. Huijts T, Eikemo TA. Causality, social selectivity or artefacts? Why socioeconomic inequalities in health are not smallest in the Nordic countries. *Eur J Public Health* 2009;19(5):452-3. doi: 10.1093/eurpub/ckp103 [published Online First: 2009/07/10]
38. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60(1):7-12. doi: 10.1136/jech.2004.023531 [published Online First: 2005/12/20]
39. Scanlan JP. Guest Editorial. *Chance* 2013;19(2):47-51. doi: 10.1080/09332480.2006.10722787 [published Online First: 02 Aug 2013]
40. 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(2):112-21. doi: 10.3109/02813432.2016.1153242 [published Online First: 2016/03/10]
41. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing research reviews* 2011;10(4):430-9. doi: 10.1016/j.arr.2011.03.003 [published Online First: 2011/03/16]
42. Mackenbach JP, Kunst AE. Measuring the magnitude of socio-economic inequalities in health: an overview of available measures illustrated with two examples from Europe. *Soc Sci Med* 1997;44(6):757-71. doi: 10.1016/s0277-9536(96)00073-1 [published Online First: 1997/03/01]
43. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: one size does not fit all. *JAMA* 2005;294(22):2879-88.
44. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol* 2012;12:143. doi: 10.1186/1471-2288-12-143 [published Online First: 2012/09/18]
45. Collaboration NCDRF. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature* 2019;569(7755):260-64. doi: 10.1038/s41586-019-1171-x [published Online First: 2019/05/10]
46. Collaboration NCDRF. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet* 2017;389(10064):37-55. doi: 10.1016/S0140-6736(16)31919-5 [published Online First: 2016/11/20]
47. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017;390(10113):2627-42. doi: 10.1016/S0140-6736(17)32129-3 [published Online First: 2017/10/17]
48. Marmot M, Goldblatt P, Allen J, et al. Fair Society, Healthy Lives.: The Marmot Review 2010.
49. World Health Organization. Multimorbidity: Technical Series on Safer Primary Care. In: Organization WH, ed. Licence: CC BY-NC-SA 3.0 IGO. ed. Geneva.: World Health Organization, 2016:p. 4-5.

Fig. 1. Flowchart sample selection: inclusion and exclusion criteria and missing data.

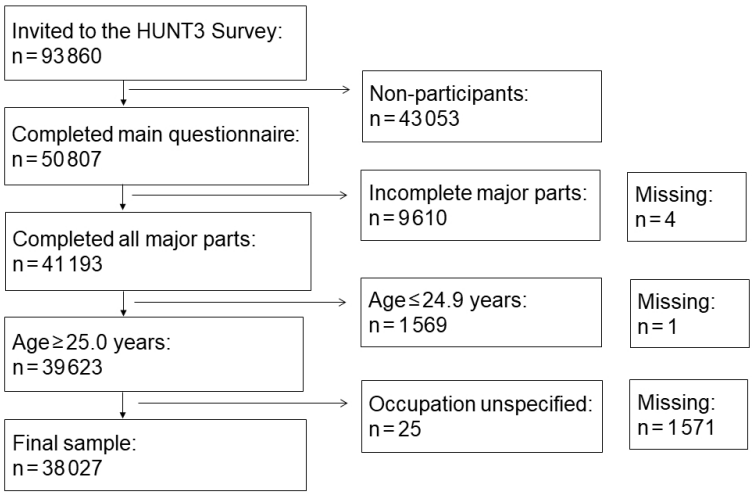

Figure 1. Flowchart for sample selection; inclusion and exclusion criteria, and missing data

338x190mm (96 x 96 DPI)

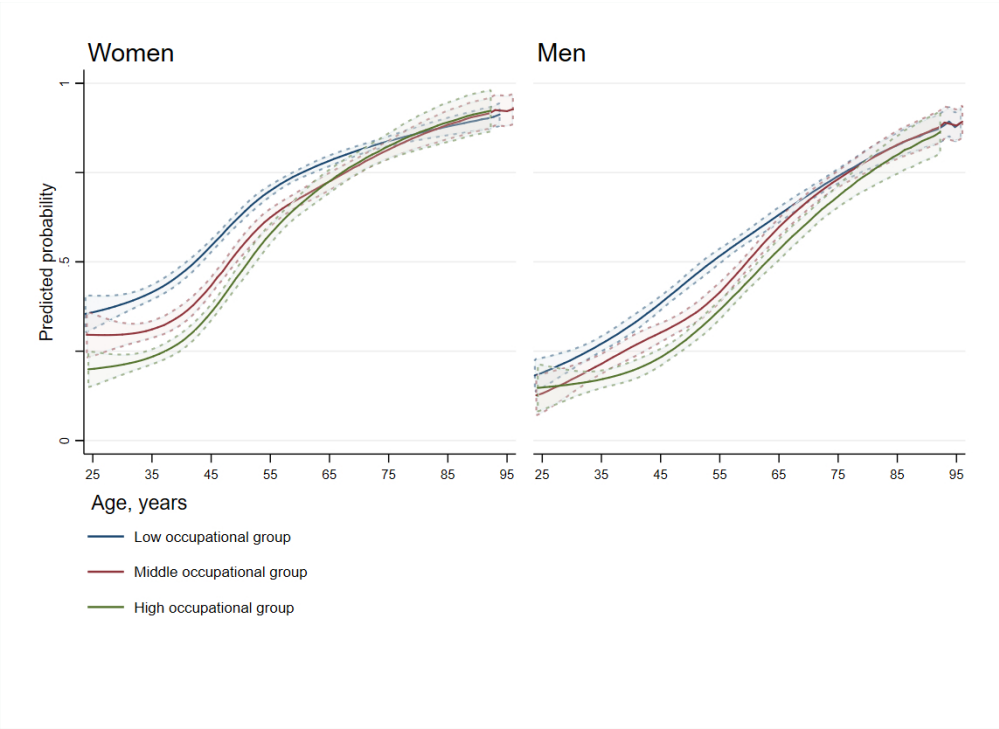

Figure 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

403x293mm (72 x 72 DPI)

Appendix A

CONSTRUCTION OF CHRONIC, SINGLE ENTITIES CONDITIONS FROM DATA IN THE HUNT3 SURVEY, BY QUESTIONNAIRES AND MEASUREMENTS.

Original questionnaires, English version.

The main questionnaire (Questionnaire 1).
https://www.ntnu.edu/c/document_library/get_file?uuid=129b68c3-520c-457f-8b98-02c49219b2ee&groupId=140075

The age- and sex-specific questionnaire (Questionnaire 2).
https://www.ntnu.edu/c/document_library/get_file?uuid=35ae2816-4155-4b64-a259-770946fa46d4&groupId=140075

Chronicity.

Chronicity was defined by either 1: duration (3 months or longer), 2: causing functional limitation (physical, mental, social) or 3: requiring health care management (pharmacological or not, primary or specialist care), [1] or 4: chronicity was assumed based on medical knowledge and clinical experience.

Missing.

In variables with index questions and cluster text, missing was in general corrected for affirmed index question and regarded as “no” if replied to any alternative to any of the other questions in the block. Information on missing is also collected from the HUNT Databank.

Main questionnaire.

Hearing impairment.
Index question: “Do you suffer from longstanding (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” Yes, no.
Options on follow-up question combined condition type (motor, vision, hearing, somatic, and psychiatric) and severity (slight, moderate, and severe).
Included with hearing impairment were those who reported chronic disease and moderate to severe hearing impairment.

“20 Diseases”: Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis.
Cluster text: “Have you had or do you have any of the following:
Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis?”

Separate tick boxes for each diagnosis: Yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis. Chronicity is assumed based on medical knowledge and clinical experience.

Sex- and age-differentiated questionnaire.

Headache.

Seven questions in one block. Question 1: “Have you had headaches in the last year?” Yes/no.

Migraine without aura.

Of those who affirmed headache last year, migraine without aura was constructed from three of seven questions:
“What is the average strength of your headaches?” 1=Mild, 2=Moderate, 3=Strong.Recoded to dichotomous variable, where 1=Moderate/Strong.
“How long does the headache usually last?” 1=Less than 4 hours, 2=4 hours - 1 day, 3=1 - 3 days, 4= More than 3 days. Recoded to dichotomous variable, where 1= Less than 4 hours – 3 days.
Cluster text: “Are the headaches usually characterized or accompanied by
Throbbing/thumping pain?” Yes, no.
Pain on one side of the head?” Yes, no.
Worsening with physical activity?” Yes, no.
Nausea and/or vomiting?” Yes, no.
Hypersensitivity to light and/or noise?” Yes, no.

Included with migraine: were those who affirmed to headache lasting 0 to 72 hours and at least two of four characteristics (pulsating quality, unilateral location, moderate/severe pain intensity, or aggravation by physical activity) and during headache having at least one of two accompanying symptoms (nausea and/or vomiting or increased sensitivity to light and/or noise).[2] Chronicity is assumed based on medical knowledge and clinical experience.

Chronic headache.

Of those who affirmed headache last year, chronic headache was constructed from two of seven questions:
“If yes (headache in the last year): What type of headache? Migraine, other.”
The HUNT Databank created two variables with range 1: 1) migraine and 2) other headache.
“Average number of days a month with headaches?:” 1=Less than 1 day, 2=1-6 days, 3=7-14 days, 4=More than 14 days. Recoded to dichotomous variable, where 1= More than 14 days.

Included as case with chronic headache were those reporting “other” type of headache and an average frequency of more than 14 days per month. Chronicity is assumed based on medical knowledge and clinical experience.

Pain.

Index question: “In the last year, have you had pain or stiffness in muscles or joints that has lasted at least 3 consecutive months?” Yes, no.
The follow-up question “If yes: Where have you had this pain or stiffness?” was combined with a figure with arrows and tick boxes at nine locations (neck, upper back, lower back, shoulder, elbow, hand, hip, knee and ankle/foot).

Chronic widespread pain.

Dichotomous variables were made for each major body area: 1) Trunk (neck, upper and lower back),

2) Upper limb (shoulder, elbow, hand), and 3) Lower limb (hip, knee, foot/ancle), where 1=At least one painful location. A sum (row total) score variable was made for the major body areas and dichotomized, where 1=3, that is one pain in each major body area.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic widespread pain was defined as pain at more than three sites in all major body areas (trunk, upper and lower limbs) for more than three months in the last year.[3]

Chronic, local pain.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic, local pain was defined as pain in the neck or upper back or lower back or shoulder or elbow or hand or hip or knee or ancle/foot, excluding presence of chronic widespread pain, generating nine dichotomous variables.

Thyroidal disease.
Cluster text: “Has it ever been verified that you have/have had hypothyroidism or hyperthyroidism?” Separate tick boxes for each condition (yes, no), generating two dichotomous variables, 1=Yes.
For each diagnosis, included were those who affirmed to have or have had the diagnosis. Chronicity is assumed based on medical knowledge and clinical experience.

Irritable bowel syndrome.
Index question: “Have you had stomach pain or discomfort in the last 12 months?” Answers: Yes, much; yes, a little; no. Irritable bowel syndrome was further constructed from four of six follow-up questions: “If yes:
“In the last 3 months, have you had this as often as 1 day a week for at least 3 weeks?” Yes, no.
“Is the pain/discomfort relieved by having a bowel movement?” Yes, no.
“Is the pain/discomfort related to more frequent or less frequent bowel movements than normal?” Yes,no.
“Is the pain/discomfort related to the stool being softer or harder than usual?” Yes, no.

Included with irritable bowel syndrome were those who affirmed little or much stomach pain or discomfort in the last year, who for as often as 1 day a week for at least 3 weeks in the last 3 months have had at least two of the following: pain/discomfort relieved by having a bowel movement, related to altered frequency of bowel movements, or related to altered stool appearance, resembling a modified version of the Rome criteria. [4 5]

Gastro-oesophageal reflux disease.
Cluster text: “To what degree have you had the following problems in the last 12 months?” Options combined type (nausea, heartburn/acid regurgitation, diarrhea, constipation, alternating constipation and diarrhea, and bloating) and frequency (never, a little, or much).
Generated one dichotomous variable, heartburn, where 1=Much.
Gastro-oesophageal reflux disease is defined as much heartburn/acid regurgitation in the last 12 months. [6]

Anxiety.
Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed a total score for anxiety (HADS-A), if all 7 anxiety items were answered. Anxiety was defined as HADS-A score >=8/21, indicating mild or possible anxiety. [8-10] Chronicity is assumed based on medical knowledge and clinical experience.

Depression.

Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed total score depression (HADS-D), if all 7 depression items were answered.
Depression was defined as HADS-D score >=8/21, indicating mild or possible depression. [8-10]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic insomnia.

There were nine questions on sleeping pattern in one cluster, including three concerning insomnia. Initial text: "How often in the last 3 months have you
"Had difficulty falling asleep at night?" Never/seldom, sometimes, several times a week.
"Woken up repeatedly during the night?" Never/seldom, sometimes, several times a week.
"Woken too early and couldn't get back to sleep?" Never/seldom, sometimes, several times a week.
Chronic insomnia was defined as in the last 3 months, several times a week, having difficulty falling asleep at night and waking up repeatedly during the night, and waking up too early. A modified version of the diagnostic criteria for insomnia in the International Classification of Sleep Disorders.[11]

Alcohol use disorder.

Instrument variable: Cut down/Annoyed/Guilty/Eye-opener, also known as the CAGE questionnaire.[12] The CAGE questionnaire is a 4-item scale with scores of 0-1. A summary variable was created and dichotomized in which a score of 1 indicates >=2 positive answers.
Alcohol use disorder was defined as CAGE score greater than 2.[13]
Chronicity is assumed based on medical knowledge and clinical experience.

Dental health problem.

"How would you say your dental health is?" Very, bad, ok, good, very good.
Dental health problems were defined as self-reported bad or very bad dental health. Chronicity is assumed based on medical knowledge and clinical experience.

Menopausal hot flashes.

Asked to women older than 30 years only.
Two questions were used to define menopausal illness:
"Do you have/have you had hot flashes due to menopause?" During the day, during the night, day and night, haven't had any.
"If you have had hot flashes, how would you describe them?" Very intense, moderately intense, hardly noticeable.
Included with menopausal hot flashes were those who reported hot flashes occurring daily and/or nightly and of at least moderate severity. Chronicity is assumed based on medical knowledge and clinical experience.

Nocturia.

Age group 20-29 years were excluded.
One question on nocturia, identical to that of the International Prostate Symptom Scale (IPSS), was asked to men and women older than 30 years.

"How many times do you get up during the night to urinate?" None, 1 time, 2 times, 3 times, 4 times, 5 times or more.
Nocturia was defined as two or more voids per night.[14] Chronicity is assumed based on medical knowledge and clinical experience.

Urine incontinence.

Men 20-29 years were excluded.
Instrument variable: The Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) questionnaire.[15]
Index question: Do you have involuntary loss of urine? Yes, no.
Urine incontinence was constructed from two of six follow up questions. "If yes":
"How often do you have involuntary loss of urine?" Less than once a month, once or more per month, once or more per week, every day and/or night
"How much urine do you leak each time?" Drops or little, small amount, large amounts.

Self-reported frequency and volume of leakage were multiplied to obtain the validated 4-level Sandvik Severity Index, categorizing incontinence as slight, moderate, severe, and very severe.[15]
Urine incontinence were included if severe to very severe. Chronicity is assumed based on medical knowledge and clinical experience.

Prostate symptoms.

Asked of men older than 30 years only.
Instrument variable: The International Prostate Symptom Scale [16] was slightly modified in HUNT3,[17] becoming a 7-item scale with scores of 0-5 per question.
Included were prostate symptoms of at least moderate severity, i.e. summary score >= 8 points.[16] Chronicity is assumed based on medical knowledge and clinical experience.

Eye diseases.

The age group 20-29 years were excluded.
Cluster text: "Do you have any of the following eye conditions?" Cataract, glaucoma, and macula degeneration. Separate tick boxes, yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.

Measurements.

Obesity.

HUNT Databank constructed the BMI variable, defined as (weight in kg)/(height in m2).
Obesity was defined as either BMI>=35 or a BMI 25-34.9 and an increased waist circumference (>= 88 cm for females; >= 102 cm for males).[18 19] Chronicity is assumed based on medical knowledge and clinical experience.

Hypertension.

Blood pressure in HUNT3 is measured three times at one consultation. The mean of measurement 2 and 3 is calculated by HUNT Databank.
Hypertension was defined as measured mean systolic BP>= 180 mmHg or diastolic BP >= 110 mmHg or reporting use of antihypertensive medications, excluding self-reported cardiovascular disease, diabetes, or kidney disease, and excluding extreme measures. Chronicity is assumed based on medical knowledge and clinical experience.

Hypercholesterolemia
Hypercholesterolemia was defined as total-cholesterol >= 8 mmol/L.[20]
Chronicity is assumed based on medical knowledge and clinical experience.

References

1. Goodman RA, Posner SF, Huang ES, et al. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. *Prev Chronic Dis* 2013;10:E66. doi: 10.5888/pcd10.120239 [published Online First: 2013/04/27]
2. Hagen K, Zwart JA, Aamodt AH, et al. The validity of questionnaire-based diagnoses: the third Nord-Trondelag Health Study 2006-2008. *J Headache Pain* 2010;11(1):67-73. doi: 10.1007/s10194-009-0174-7 [published Online First: 2009/12/01]
3. Mundal I, Grawe RW, Bjorngaard JH, et al. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. *BMC Musculoskelet Disord* 2014;15:213. doi: 10.1186/1471-2474-15-213 [published Online First: 2014/06/22]
4. Hammer J, Talley NJ. Diagnostic criteria for the irritable bowel syndrome. *Am J Med* 1999;107(5A):5S-11S. doi: 10.1016/s0002-9343(99)00276-4 [published Online First: 1999/12/10]
5. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480-91. doi: 10.1053/j.gastro.2005.11.061 [published Online First: 2006/05/09]
6. Ness-Jensen E, Lindam A, Lagergren J, et al. Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study. *Gut* 2012;61(10):1390-7. doi: 10.1136/gutjnl-2011-300715 [published Online First: 2011/12/23]
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(6):361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x [published Online First: 1983/06/01]
8. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *Br J Psychiatry* 2001;179:540-4. doi: 10.1192/bjp.179.6.540 [published Online First: 2001/12/04]
9. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
10. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res* 1997;42(1):17-41. [published Online First: 1997/01/01]
11. Medicine AAoS. The international classification of sleep disorders: diagnostic and coding manual: American Acad. of Sleep Medicine 2005.
12. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984;252(14):1905-7. doi: 10.1001/jama.252.14.1905 [published Online First: 1984/10/12]
13. Skogen JC, Overland S, Knudsen AK, et al. Concurrent validity of the CAGE questionnaire. The Nord-Trondelag Health Study. *Addict Behav* 2011;36(4):302-7. doi: 10.1016/j.addbeh.2010.11.010 [published Online First: 2010/12/21]
14. Tikkinen KA, Johnson TM, 2nd, Tammela TL, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. *Eur Urol* 2010;57(3):488-96. doi: 10.1016/j.eururo.2009.03.080 [published Online First: 2009/04/14]
15. Sandvik H, Seim A, Vanvik A, et al. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. *Neurourol Urodyn* 2000;19(2):137-45. [published Online First: 2000/02/19]
16. Barry MJ, Fowler FJ, Jr., O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148(5):1549-57; discussion 64. doi: 10.1016/s0022-5347(17)36966-5 [published Online First: 1992/11/11]
17. HUNT Databank. International Prostate Symptom Scale in HUNT3 Questionnaire 2 [Webpage]. Levanger: HUNT Databank; 2019 [cited 2019 05.20.]. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#/instrumentpart/45_11 2019.
18. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79(3):379-84. doi: 10.1093/ajcn/79.3.379 [published Online First: 2004/02/27]
19. Perreault L. Obesity in adults: Prevalence, screening, and evaluation. Waltham, MA: UpToDate 2018.
20. Helsedirektoratet. Nasjonal faglig retningslinje for individuell primærforebygging av hjerte-og karsykdommer, kortversjon, IS-1675. In: Helsedirektoratet, ed., 2009.

Appendix B

OPERATIONALIZING SOCIOECONOMIC POSITION USING OCCUPATION.

In the HUNT3 Survey interview, all participants were asked: "What is/was the title of your main occupation?" Free-text answers were manually classified according to the *Standard Classifications of Occupations* by Statistics Norway,[1] which is based on the European Union's version of the *International Standard Classification of Occupations-88.*[2]

The standard categorize occupations according to skill level and specialization, degree of independence, and manual labor but not social position.[1] Occupations are coded with up to four digits, with increasing detail. One digit indicates major groups; two digits, submajor groups; three digits, minor groups; and four digits, unit groups. The minor occupational group was the highest level of detail available in the HUNT3 Survey.

Occupational socioeconomic position was operationalized using the European Socio-economic Classification scheme.[3] The full version of the scheme requires employment status and size of organization in addition to occupation to assign a class position. We used the simplified class scheme, based on minor occupational group only[3], as the HUNT3 Survey did not have data corresponding to employment status and size of organization. It is shown that the agreement between three-digit full and simplified version of this scheme is 79.7% for the total workforce.[3]

The syntax is available from https://www.iser.essex.ac.uk/archives/esec/matrices-and-syntax. It was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA).

Table 1 gives details of transformation of data, discrepancies between the Norwegian and European Union standard and the allocated position in the full classification scheme. 2179 individuals had alterations to their occupational data to fit the syntax, 5.7% (2179/38027) of the total sample.

In the HUNT3 Survey data, the minor occupational group was a string variable. To perform the syntax, it had to be altered to a numeric variable. The string "011" changed to numeric value "11," which was manually corrected in the syntax. In the 3-digit variable, some participants were classified with 1 digit and 2 digits only. These were transformed to the corresponding 3-digit minor group, at the lowest level of detail, by manually adding suffix digits 0 or 00. This is in line with operationalizing of European Socio-economic Classification (see footnote table 1).[3]

Norwegian minor groups, which were not found in the European Union standard, were altered to the level of detail in which corresponding groups could be identified. These were *Standard Classifications of Occupations* by Statistics Norway codes: 112 (corresponding to 2 digits), 25 (corresponding to 1 digit), 251-6 (corresponding to 1 digit), 349 (corresponding to 2 digits), 631 (corresponding to 1 digit), 641 (corresponding to 1 digit), 735 (corresponding to 2 digits), and 745 (corresponding to 2 digits). See table 1.

In total, 9 classes were created. To increase power and simplify interpretation, the full scheme was collapsed into a 3-class version, with “high” combining class 1 and 2, “middle” combining 3 to 6, and “low” combining 7 to 9. [3] The high occupational class represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, higher-grade technician occupations, and supervisory occupations. The middle occupational class consist of small employers, self-employed individuals, lower supervisory occupations, and lower technician occupations. The low occupational class contain lower services, sales and clerical occupations, lower technical occupations, and routine occupations.

Table 1. The distribution of transformed occupational data and discrepancies between the Norwegian and International Standard Classifications of Occupations, and allocation in the European Socio-economic Classification scheme.

Standard Classifications of Occupations		European Socio-economic		
Norwegian	**International**	**Classification scheme**	***n***	**%**
1	100	1	262	(0.69)
011 (=num 11)	011=11	3	134	(0.35)
112*	→ 11=110	1	31	(0.08)
12	120	1	73	(0.19)
13	130	4	20	(0.05)
2	200	1	10	(0.03)
21	210	1	10	(0.03)
22	220	1	1	(0.00)
23	230	2	27	(0.07)
24	240	1	9	(0.02)
25	→ 2=200	1	4	(0.01)
251*	→ 2=200	1	296	(0.78)
252*	→ 2=200	1	48	(0.13)
253*	→ 2=200	1	20	(0.05)
254*	→ 2=200	1	138	(0.36)
255*	→ 2=200	1	64	(0.17)
256*	→ 2=200	1	46	(0.12)
3	300	3	39	(0.10)
31	310	2	37	(0.10)
33	330	3	241	(0.63)
34	340	3	45	(0.12)
349*	→34=340	3	160	(0.42)
4	400	3	1	(0.00)
41	410	3	1	(0.00)
42	420	3	1	(0.00)
5	500	7	1	(0.00)
51	510	7	8	(0.02)
61	610	5	4	(0.01)
631*	→6=600	5	93	(0.24)
641*	→6=600	5	99	(0.26)
7	700	8	20	(0.05)
71	710	8	1	(0.00)
72	720	8	6	(0.02)
73	730	6	1	(0.00)
735*	→73=730	6	38	(0.10)
74	740	8	1	(0.00)
745*	→74=740	8	46	(0.12)
8	800	9	62	(0.16)
81	810	9	38	(0.10)
82	820	9	35	(0.09)
83	830	9	6	(0.02)
9	900	9	1	(0.00)
93	930	9	1	(0.00)
Sum			2179	(5.73)

Bold* = Divergence of *Standard Classifications of Occupations* by Statistics Norway from the European Union's version of *The International Standard Classification of Occupations-88*.

References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
2. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
3. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518

Appendix C

Table C1. Distribution of occupational groups, sex and age by participation status and missing.

	Sample		Non-eligible		Missing		Total	
	Frequency	**(%)**	**Frequency**	**(%)**	**Frequency**	**(%)**	**Frequency**	**(%)**
Total	38027	(100)	11203	(100)	1576	(100)	50806	(100)
Occupational group								
High	8970	(24)	1926	(17)	0	(0)	10896	(21)
Middle	10243	(27)	2281	(20)	0	(0)	12524	(25)
Low	18814	(49)	5807	(52)	1	(0)	24622	(48)
Sex								
Women	20813	(55)	5662	(51)	1281	(81)	27756	(55)
Men	17214	(45)	5541	(49)	294	(19)	23049	(45)
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**		
Age	55	(14)	44	(18)	66	(18)		

Appendix D

Table D1 Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational groups in 5-year intervals (25 to 100 years), stratified by sex.

Age,	Occup.*	Women						Men					
years	group	PR	95% CI		PD	95% CI		PR	95% CI		PD	95% CI	
25	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.58	1.34	1.88	0.08	0.05	0.10	1.30	1.03	1.63	0.03	0.00	0.05
	Low	2.34	2.02	2.72	0.18	0.15	0.20	2.06	1.69	2.50	0.09	0.07	0.11
30	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.47	1.28	1.68	0.08	0.05	0.11	1.28	1.05	1.55	0.03	0.01	0.06
	Low	2.06	1.84	2.32	0.19	0.16	0.21	1.92	1.63	2.26	0.10	0.08	0.13
35	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.36	1.23	1.51	0.08	0.06	0.11	1.26	1.07	1.47	0.04	0.01	0.06
	Low	1.82	1.67	2.00	0.19	0.16	0.22	1.79	1.56	2.04	0.12	0.09	0.14
40	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.27	1.18	1.37	0.08	0.05	0.11	1.24	1.09	1.40	0.04	0.02	0.07
	Low	1.62	1.52	1.73	0.19	0.16	0.21	1.66	1.50	1.84	0.13	0.10	0.15
45	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.19	1.13	1.26	0.07	0.05	0.09	1.21	1.10	1.33	0.05	0.03	0.08
	Low	1.45	1.39	1.53	0.17	0.15	0.19	1.55	1.43	1.67	0.13	0.11	0.15
50	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.13	1.08	1.18	0.06	0.04	0.08	1.19	1.11	1.27	0.06	0.03	0.08
	Low	1.32	1.27	1.37	0.15	0.13	0.17	1.44	1.36	1.53	0.13	0.11	0.15
55	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.08	1.03	1.12	0.04	0.02	0.06	1.16	1.10	1.23	0.06	0.04	0.08
	Low	1.22	1.18	1.26	0.12	0.10	0.14	1.35	1.28	1.41	0.13	0.11	0.15
60	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.04	1.00	1.08	0.02	0.00	0.05	1.14	1.08	1.19	0.06	0.04	0.08
	Low	1.14	1.10	1.18	0.09	0.07	0.11	1.27	1.21	1.32	0.12	0.10	0.14
65	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.01	0.97	1.05	0.01	-0.02	0.04	1.11	1.06	1.17	0.06	0.03	0.08
	Low	1.08	1.05	1.12	0.06	0.04	0.08	1.20	1.15	1.25	0.10	0.08	0.13
70	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.99	0.96	1.03	0.00	-0.03	0.02	1.09	1.04	1.14	0.05	0.03	0.08
	Low	1.05	1.01	1.08	0.04	0.01	0.06	1.15	1.10	1.20	0.09	0.06	0.11
75	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.02	-0.01	-0.04	0.02	1.07	1.02	1.12	0.05	0.02	0.08
	Low	1.02	0.99	1.05	0.02	-0.01	0.04	1.10	1.06	1.15	0.07	0.04	0.10

80	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.01	-0.02	-0.04	0.01	1.06	1.01	1.11	0.04	0.01	0.08
	Low	1.00	0.98	1.03	0.00	-0.02	0.02	1.07	1.02	1.12	0.05	0.02	0.08
85	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.00	-0.02	-0.04	0.00	1.04	1.00	1.09	0.03	0.00	0.07
	Low	0.99	0.97	1.02	-0.01	-0.03	0.01	1.05	1.00	1.09	0.04	0.00	0.07
90	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.96	1.00	-0.02	-0.04	0.00	1.03	0.99	1.07	0.03	-0.01	0.06
	Low	0.99	0.97	1.01	-0.01	-0.03	0.01	1.03	0.99	1.07	0.02	-0.01	0.05
95	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.96	1.00	-0.02	-0.04	0.00	1.02	0.99	1.06	0.02	-0.01	0.05
	Low	0.99	0.97	1.00	-0.01	-0.03	0.00	1.02	0.98	1.05	0.01	-0.02	0.04
100	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.97	1.00	-0.02	-0.03	0.00	1.02	0.99	1.05	0.02	-0.01	0.04
	Low	0.98	0.97	1.00	-0.01	-0.03	0.00	1.01	0.98	1.04	0.01	-0.02	0.03

*Occup. = occupational

Appendix E – Sensitivity analysis

In the sensitivity analysis the outcome complex multimorbidity was created from available conditions in the main questionnaire only. In total 22 conditions, grouped in 12 *ICD-10* chapters were included vs 51 conditions, grouped in *14 ICD-10* chapters in the original measure.

The sensitivity analysis was performed to investigate if fewer number and types of conditions included in the complex multimorbidity measure, produced a similar pattern with respect to the overall prevalence as well as differences between occupational groups.

Total prevalences and prevalences by occupational group and age, stratified by sex (table E1), were obtained by cross tables.

Table E1. Sociodemographic distribution of complex multimorbidity

	Women						Men					
	No, *n*	**(%)**	**Yes, *n***	**(%)**	**Total, *n***	**(%)**	**No, *n***	**(%)**	**Yes, *n***	**(%)**	**Total, *n***	**(%)**
Total	17376	(83)	3437	(17)	20813	(100)	14815	(86)	2399	(14)	17214	(100)
Occupational group												
High	4032	(90)	473	(11)	4505	(100)	4026	(90)	439	(10)	4465	(100)
Middle	4612	(86)	774	(14)	5386	(100)	4147	(85)	710	(15)	4857	(100)
Low	8732	(80)	2190	(20)	10922	(100)	6642	(84)	1250	(16)	7892	(100)
Age, years												
25-44	5610	(94)	371	(6)	5981	(100)	3776	(96)	167	(4)	3943	(100)
45-64	8233	(84)	1607	(16)	9840	(100)	7381	(88)	985	(12)	8366	(100)
65-74	2331	(74)	837	(26)	3168	(100)	2417	(78)	676	(22)	3093	(100)
75-100	1202	(66)	622	(34)	1824	(100)	1241	(68)	571	(32)	1812	(100)
Mean, (SD)	53	(14)	62	(13)	54	(14)	55	(14)	65	(12)	56	(14)

Prevalence ratios and differences between occupational groups at ages 30, 55, 75 and 90 years were derived from logistic regression estimates (table E2).

Table E2. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational classes, stratified by sex.

Age, years	Occupational group	Women				Men			
		PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
30	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.91	(1.41, 2.57)	0.02	(0.01, 0.03)	1.28	(0.88, 1.86)	0.01	(0.00, 0.01)
	Low	3.47	(2.68, 4.49)	0.05	(0.04, 0.06)	1.96	(1.42, 2.71)	0.02	(0.01, 0.03)
55	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.18	(1.05, 1.33)	0.02	(0.01, 0.03)	1.31	(1.13, 1.52)	0.02	(0.01, 0.04)
	Low	1.59	(1.44, 1.76)	0.07	(0.05, 0.08)	1.68	(1.48, 1.91)	0.05	(0.04, 0.06)
75	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.88	(0.77, 1.01)	-0.04	(-0.08, 0.00)	1.28	(1.12, 1.47)	0.06	(0.03, 0.09)
	Low	0.96	(0.85, 1.08)	-0.01	(-0.05, 0.02)	1.44	(1.27, 1.64)	0.09	(0.06, 0.12)
90	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.80	(0.69, 0.93)	-0.12	(-0.20, -0.04)	1.23	(1.03, 1.46)	0.09	(0.01, 0.16)
	Low	0.78	(0.69, 0.88)	-0.13	(-0.20, -0.06)	1.27	(1.08, 1.50)	0.10	(0.04, 0.17)

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 (Title page)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6, tab. 1
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	Appendix A
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	8
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	5, 8
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2, p.9
		(b) Indicate number of participants with missing data for each variable of interest	5
Outcome data	15*	Report numbers of outcome events or summary measures	Table 3, pp. 9-10
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	Table 4, p 10. 8
		(*b*) Report category boundaries when continuous variables were categorized	5
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk ~~for a meaningful time period~~	8, table 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10, appendix E
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	14

*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

Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-036851.R1
Article Type:	Original research
Date Submitted by the Author:	13-Mar-2020
Complete List of Authors:	Vinjerui, Kristin Hestmann; Norwegian University of Science and Technology, Department of Public Health and Nursing/HUNT Research Centre; Helse Nord-Trondelag, Psychiatric Department Bjerkeset, Ottar; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Mental Health Bjorngaard, Johan; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences Krokstad, Steinar; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing/HUNT Research Centre; Helse Nord-Trondelag, Psychiatric Department Douglas, Kirsty; Australian National University, Australian National University Medical School Sund, Erik; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing/HUNT Research Centre; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Epidemiology, General practice / Family practice, Medical management, Patient-centred medicine
Keywords:	SOCIAL MEDICINE, EPIDEMIOLOGY, PUBLIC HEALTH

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study

Kristin H Vinjerui,[1,2,3,*] Ottar Bjerkeset,[4,5] Johan H Bjorngaard,[4,6] Steinar Krokstad,[1,3] Kirsty Douglas,[2] Erik R Sund.[1,4]

1 HUNT Research centre, Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Levanger, Norway

2 Academic Unit of General Practice, Australian National University Medical School, Canberra, Australia

3 Psychiatric Department, Levanger Hospital, Nord-Trøndelag Hospital Trust, Norway.

4 Faculty of Nursing and Health Sciences, Nord University, Levanger, Norway

5 Department of Mental Health, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, Norway

6 Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, Norway

*Corresponding author: Kristin Hestmann Vinjerui, HUNT Research centre, Forskningsvegen 2, 7600 Levanger, Norway. E-mail: Kristin.vinjerui@ntnu.no.Tel.: 0047-90173201/74019240/74075180

WORD COUNT

Abstract: 285 words.

Text: 3593 words.

KEYWORDS

Multimorbidity. Socioeconomic status. Occupations. Public health. Health inequality. The HUNT Study.

ABSTRACT

Objectives: Multimorbidity, the co-occurrence of multiple long-term conditions, none in priority, is common and increasing. Definitions and assessment methods vary, yielding differences in estimates of prevalence and multimorbidity severity. Sociodemographic characteristics are associated with complicating factors of multimorbidity. We aimed to investigate the prevalence of complex multimorbidity by sex and occupational groups throughout adulthood.

Design: Cross-sectional study

Setting: The third total county survey of The Nord-Trøndelag Health Study (HUNT), 2006-2008, Norway.

Participants: Individuals aged 25-100 years with classifiable occupational data and complete questionnaires and measurements.

Outcome measure: Complex multimorbidity defined as “the co-occurrence of three or more chronic conditions affecting three or more different body [organ] systems within one person without defining an index chronic condition”.

Analysis: Logistic regression models with age and occupational group were specified for each sex separately.

Results: 38027 of 41193 adults (55% women) were included in our analyses. 54% of the participants were identified as having complex multimorbidity. Prevalence differences in percentage points (pp) of those in the low occupational group (vs the high occupation group [reference]) were 19 (95% CI,16 to 21) pp in women and 10 (8 to 13) pp in men at 30 years; 12 (10 to 14) pp in women and 13 (11 to 15) pp in men at 55 years; and 2 (-1 to 4) pp in women and 7 (4 to 10) pp in men at 75 years.

Conclusion: Complex multimorbidity is common from early adulthood, and social inequalities persist until 75 years in women and 90 years in men in the general population. These findings have policy implications for public health as well as health care, organization, treatment, education, and research, as complex multimorbidity breaks with the specialized, fragmented paradigm dominating medicine today.

ARTICLE SUMMARY

Strengths and limitations of this study

1. As a large, entire-county, general population health survey with a vast number of variables, the HUNT Study is ideal to estimate the prevalence of multimorbidity by self-reports and clinical measurements.
2. Complex multimorbidity operationalized as three or more organ systems affected is relevant in both clinic and research, with high specificity into old age, implicating need of coordinated multidisciplinary care and increasing comparability between studies.
3. Socioeconomic position operationalized as occupations allocated in the European Socio-economic Classification scheme makes international comparison of gradients possible.
4. Non-participants have lower socioeconomic position and higher mortality, thus the social gradients in prevalence of complex multimorbidity detected are likely conservative.
5. The original data lacked information of chronicity of a majority of the conditions, which may lead to overestimation of complex multimorbidity.

INTRODUCTION

Multimorbidity, the cooccurrence of multiple long-term conditions in which none holds priority[1] is common and increasing.[2, 3] It challenges the individual's ability to self-manage[4, 5] as well as clinical decision-making[5-7] due to complexity that conflicts with subspecialized medicine and clinical guidelines. Multimorbidity is associated with high health care utilization in both primary and specialist care,[8] including emergency department visits.[9]

Multimorbidity is heterogenous, and a mere count of conditions may not imply complexity[1, 5] requiring coordinated multidisciplinary care. In attempts to detect individuals with high needs, guidelines by and large focus on combinations of conditions, such as concurrent mental and somatic conditions[5, 10, 11] or three or more conditions in separate organ systems,[5, 12] and consequences thereof, such as polypharmacy[5, 10, 11] and requirements for assistance in daily living.[5, 10, 11] Individual factors that increase patient complexity include sociodemographic characteristics,[13] social resources,[13] and health and social experiences.[13] Recent recommendations on multimorbidity care have taken into account social networks,[11] socioeconomic positions,[11] and patient experiences, such as treatment burden.[10, 11]

Research results from cross-sectional studies on multimorbidity prevalence have been difficult to compare because of differences in definitions, methods, and the number and types of conditions included.[14, 15] Still, associations with lower socioeconomic position,[3, 14, 16] female sex,[3, 14, 16] and increasing age[3, 14, 16] persist across studies. Further, defining multimorbidity as simultaneously having three or more conditions increases the specificity of the multimorbidity measure into older age groups,[12, 15] and comparability between studies increases when multimorbidity is operationalized as multiple organ systems affected.[12]

Inequalities in health according to socioeconomic position are persistent,[17] even in comparatively egalitarian Nordic societies.[18] The association of socioeconomic differences with the occurrence of multimorbidity has been explored using multiple measures, such as education,[14, 19] income,[19] occupation,[3] and deprivation indexes.[14, 16] In fact, any measure of socioeconomic position will detect health differences in descriptive studies, if differences exist.[20] Using an occupational classification may reflect specific work-related exposures in addition to general associations to income, material resources, and social status.[20]

In sum, multimorbidity represents a challenge both for the individual and clinician, as well as for the coordination of health care. Previous multimorbidity prevalence research suggests that demographic and socioeconomic gradients operate. In Norway, multimorbidity prevalence and patterns have been partly explored.[21] Studies on complex multimorbidity is lacking, and no studies have investigated sociodemographic differences. Such data, can strengthen health care planning and clinical management of multimorbidity, as well as guide public health interventions.

Our aim is to add to former knowledge by assessing the prevalence of complex multimorbidity, defined as three or more conditions in separate organ systems, by age, sex and occupational groups, in a general population health survey.

METHODS

Reporting statement

The STROBE cross sectional reporting guidelines[22] were used for reporting of this observational study.

Study population

The HUNT Study is a population-based health study for all adults 20 years and older living in Nord-Trøndelag County, Norway. Four surveys have been completed since the 1980s, and cohort profiles and data collection procedures have been described in detail elsewhere.[23, 24] This study is a secondary analysis of data from the HUNT3 Survey (2006-2008), where 93860 citizens were invited to participate. In short, the survey consisted of a main questionnaire received with the invitation by mail and handed in when attending a screening station, where participants were interviewed and clinical measurements and biological samples were taken. A second sex- and age-specific questionnaire was handed out at the screening station and returned by mail.

A total of 50807 individuals (54% of 93860 invited) completed the main questionnaire, required to be considered an attendant of the HUNT3 Survey.[23] Sampling is described in figure 1. In this study, 41193 of 50807 participants (81%) had data on all major parts of the survey (both questionnaires, interview, measurements, and samples) and were designated as respondents. Thus, 9610 were excluded due to incomplete participation, while 4 people missed complete participation data. Under the assumption that young adults may not have obtained their highest level of occupational class at the time of participation, 1569 participants younger than 25 years were excluded, as well as 1 person with missing age data. Occupation data was missing for 1571 respondents, and 25 people were excluded due to unspecified occupation data. Finally, 38027 of 41193 (92%) respondents were eligible for data analysis, 11204 were non-eligible and 1576 had missing data.

Participation in the HUNT3 Survey vary with socioeconomic position, age and sex.[25] The distribution of occupational groups among the sample were; 24% (high), 27% (middle) and 49% (low) and in non-eligible; 17% (high), 20% (middle), 52% (low) and 11% (missing). The average (SD) age in the sample was 55 (14) years, in the non-eligible group 44 (18) years and among missing 66 (18) years. Women constituted 55% (n=20813 of 38027) of the sample, 51% (n=5662 of 11203) of the non-eligible and 81% of the missing (n=1281 of 1576).

Figure 1. Flowchart for sample selection; inclusion and exclusion criteria, and missing data.

Outcome variable

Complex multimorbidity was defined as “the co-occurrence of three or more chronic conditions affecting three or more different body [organ] systems within one person without defining an index chronic condition”, as suggested by previous research.[5, 12]

All conditions possible to generate from the HUNT3 Survey data were included to meet recommendations on deriving the best estimate of prevalence of multimorbidity.[12] In total, 51 chronic conditions, defined singly as far as original data permitted, were constructed, and details are described in appendix A. This list of 51 conditions is more comprehensive and homogenous than previous operationalizations of multimorbidity in the HUNT3 Survey.[21]

Further, the conditions were grouped according to the *ICD-10* in 13 organ-specific chapters and one chapter on symptoms, signs, and abnormal clinical and laboratory findings (table 1), using general terms of the conditions in the Norwegian Directorate of eHealth online search engine[26] on February 1 2017.

Chapters were counted once if affected by at least one chronic condition and a summary score of the chapter variables was generated. In this study, complex multimorbidity was defined as having conditions in at least 3 of 14 chapters.

Sociodemographic Characteristics

Occupation data from the HUNT3 survey were free-text answers to the interview question, "What is/was the title of your main occupation?" Answers were manually categorized corresponding to Standard Classifications of Occupations by Statistics Norway,[27] which is based on the International Standard Classification of Occupations-88 (ISCO-88).[28] Socioeconomic position was allocated according to the simplified, 3-class version European Socio-economic Classification (ESeC) scheme.[29] The simplified scheme is based solely on occupational data, classified according to ISCO-88.[28] Details are provided in appendix B. The intention of the full ESeC scheme is to measure qualitative distinctions between employment relationships and does not reflect a clear hierarchy.[29] However, income is considered more stable in the salariat class.[29] In the 3-class version, the salariat class consists of large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, and higher-grade technician and supervisory occupations. The intermediate class contains small employers, self-employed individuals, and lower-grade supervisory and technician occupations. The working class represents lower-grade service positions, sales and clerical occupations, and lower-grade technical and routine occupations. For practical reasons in this study, the terms high, middle, and low occupational group replaced the terms salariat, intermediate, and working class, respectively.

In addition, continuous age and categorical sex data, provided by the HUNT databank, were used in the analyses.

Table 1. Conditions grouped by *ICD-10* chapter

***ICD-10* chapter**	Conditions
II	**Neoplasms**
	Cancer
III	**Blood/blood-forming organs/ immune mechanism**
	Sarcoidosis
IV	**Endocrine/nutritional/metabolic**
	Obesity
	Hypercholesterolemia
	Diabetes
	Hypothyroidism
	Hyperthyroidism
V	**Mental/behavioral**
	Alcohol problem
	Depression
	Anxiety
	Insomnia
VI	**Nervous system**
	Epilepsy
	Migraine
	Chronic headache, other
VII	**Eye/adnexa**
	Cataract
	Macula degeneration
	Glaucoma
VIII	**Ear/mastoid**
	Hearing impairment
IX	**Circulatory system**
	Hypertension
	Angina pectoris
	Myocardial infarction
	Heart failure
	Other heart disease[1]
	Stroke or brain haemorrhage[1]
X	**Respiratory system**
	Chronic bronchitis, emphysema, or COPD[1,2]
	Asthma
XI	**Digestive system**
	Dental health status
	Gastro-oesophageal reflux disease
	Irritable bowel syndrome
XII	**Skin/subcutaneous tissue**
	Hand eczema
	Psoriasis
XIII	**Musculoskeletal/connective tissue**
	Rheumatoid arthritis
	Osteoarthritis
	Ankylosing spondylitis
	Fibromyalgia
	Osteoporosis
	Local musculoskeletal pain/stiffness in:
	- Neck
	- Upper back
	- Lower back
	- Shoulder
	- Elbow
	- Hand
	- Hip
	- Knee
	- Foot/ankle
XIV	**Genitourinary system**
	Kidney disease
	Urine incontinence
	Prostate symptoms
	Menopausal hot flashes
XVIII	**Symptoms/signs/abnormal clinical/ laboratory findings**
	Nocturia
	Chronic widespread pain

[1] = Exception to single entity
[2]COPD = Chronic Obstructive Pulmonary Disease

Statistical analysis

Cross-tables were used to present sociodemographic characteristics of the sample by occupational group (table 2) and by complex multimorbidity, stratified by sex (table 3).

Associations between occupational group and complex multimorbidity were analyzed using logistic regression. The final models were stratified by sex, included occupational group, continuous age, and an interaction term between occupational group and age. Choice of models were guided by likelihood ratio tests.

Since complex multimorbidity was highly prevalent, odds ratios would deviate from relative risks[30] and be challenging to interpret. Thus, we used the estimates from the logistic regression models to derive prevalence differences, the difference in mean predicted probability,[31] and prevalence ratios, the ratio between the mean predicted probabilities,[31] between occupational groups, while holding other covariates constant. The high occupational group was chosen as the reference group. Prevalence differences and prevalence ratios were calculated in 5-year intervals from 25 to 100 years, with 95% confidence intervals (CIs) (appendix C) Results for the ages 30, 55, 75, and 90 years are presented in table 4 to represent adult, middle aged, aged and oldest old in the sample.

To visualize the differential association between age and complex multimorbidity in each occupational group, we specified separate models using restricted cubic splines and graphed the findings from each model into a common plot for each sex.

Sensitivity analysis was performed to investigate if the number and types of conditions showed a similar pattern with respect to the overall prevalence as well as differences between occupational groups (appendix D). The alternative complex multimorbidity measure was derived from data in the main questionnaire only (22 conditions, grouped in 12 *ICD-10* chapters)

Complete case analysis was performed, and Stata version 15.1 was used to analyze the data (StataCorp, College Station, TX, USA).

Patient and public involvement

There was a broad participant, patient, and stakeholder involvement during the planning of the HUNT3 survey. Data collection was performed in 2006-2008. Complex multimorbidity is a universal subject, not represented by any particular patient group, and thus no patient or public representative was involved in the design of this secondary analysis study.

RESULTS

38027 individuals, aged 25 to 100 years, 55% women (n=20813), who had completed all major parts of the HUNT3 Survey and had a classifiable occupation comprised the eligible sample, as fig. 1 depicts. Table 2 presents further sociodemographic characteristics.

Table 2. Sex and age distribution by occupational group. The HUNT Study (2006-08).

	Occupational group							
	High		Middle		Low		Total	
	Freq.	(%)	Freq.	(%)	Freq.	(%)	Freq.	(%)
Total	8 970	(100)	10 243	(100)	18 814	(100)	38 027	(100)
Sex								
Women	4 505	(50)	5 386	(53)	10 922	(58)	20 813	(55)
~~Male~~ Men	4 465	(50)	4 857	(47)	7 892	(42)	17 214	(45)
Age, yr.								
25-44	2 837	(32)	2 600	(25)	4 487	(24)	9 924	(26)
45-64	4 468	(50)	4 787	(47)	8 951	(48)	18 206	(48)
65-74	1 118	(12)	1 846	(18)	3 297	(18)	6 261	(16)
75-100	547	(6)	1 010	(10)	2 079	(11)	3 636	(10)

Abbreviations: freq., frequency, yr., years.

Nearly half the sample (49%; n=18814 of 38027; of which 58% were women, n=10922), was allocated in the low occupational group. In absolute numbers, the low occupational group was the largest socioeconomic category in both sexes and all age groups. The proportion of individuals aged 25 to 44 years decreased from 32% in the high occupational group (n=2837) to 24% in the low occupational group (n=4487), while the proportion of individuals aged 75 to 100 years increased from 6% (n=547) to 11% (n=2079). Participants aged 45 to 64 years were the largest age group in total and in all occupational groups (high, n=4468; middle, n=4787; low, n=8951).

Table 3. Sociodemographic distribution of complex multimorbidity. The HUNT Study (2006-08).

	Complex multimorbidity											
	Women						Men					
	No, *n*	(%)	Yes, *n*	(%)	Total, *n*	(%)	No, *n*	(%)	Yes, *n*	(%)	Total, *n*	(%)
Total	8 505	(41)	12 308	(59)	20 813	(100)	9 137	(53)	8 077	(47)	17 214	(100)
Occupational group												
High	2 460	(55)	2 045	(45)	4 505	(100)	2 712	(61)	1 753	(39)	4 465	(100)
Middle	2 384	(44)	3 002	(56)	5 386	(100)	2 525	(52)	2 332	(48)	4 857	(100)
Low	3 661	(34)	7 261	(66)	10 922	(100)	3 900	(49)	3 992	(51)	7 892	(100)
Age, years												
25-44	3 859	(65)	2 122	(35)	5 981	(100)	2 958	(75)	985	(25)	3 943	(100)
45-64	3 668	(37)	6 172	(63)	9 840	(100)	4 621	(55)	3 745	(45)	8 366	(100)
65-74	721	(23)	2 447	(77)	3 168	(100)	1 155	(37)	1 938	(63)	3 093	(100)
75-100	257	(14)	1 567	(86)	1 824	(100)	403	(22)	1 409	(78)	1 812	(100)
Mean (SD)	48	(13)	59	(14)	54	(14)	52	(13)	62	(13)	56	(14)

Overall, a majority (54%; n=20385 of 38027) of the sample met the criteria for having complex multimorbidity, including 59% of women (n=12308) and 47% of men (n=8077; table 3). The percentages increased from high to low occupational group in women from 45% (n=2045) to 66% (n=7261) and in men from 39% (n=1753) to 51% (n=3992). The

proportions further increased by age, from 35% (n=2122) of women aged 25 to 44 years to 86% (n=1567) of women aged 75 to 100 years. In men, the increase was from 25% (n=985) to 78% (n=1409) in the same age groups. In absolute numbers, most people classified as having complex multimorbidity were aged 45 to 64 years (women, n=6172; men, n=3745).

Table 4. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational groups, stratified by sex.

Age,	Occupational	Women				Men			
years	group	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
30	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.47	(1.28, 1.68)	0.08	(0.05, 0.11)	1.28	(1.05, 1.55)	0.03	(0.01, 0.06)
	Low	2.06	(1.84, 2.32)	0.19	(0.16, 0.21)	1.92	(1.63, 2.26)	0.10	(0.08, 0.13)
55	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.08	(1.03, 1.12)	0.04	(0.02, 0.06)	1.16	(1.10, 1.23)	0.06	(0.04, 0.08)
	Low	1.22	(1.18, 1.26)	0.12	(0.10, 0.14)	1.35	(1.28, 1.41)	0.13	(0.11, 0.15)
75	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.98	(0.95, 1.02)	-0.01	(-0.04, 0.02)	1.07	(1.02, 1.12)	0.05	(0.02, 0.08)
	Low	1.02	(0.99, 1.05)	0.02	(-0.01, 0.04)	1.10	(1.06, 1.15)	0.07	(0.04, 0.10)
90	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.98	(0.96, 1.00)	-0.02	(-0.04, 0.00)	1.03	(0.99, 1.07)	0.03	(-0.01, 0.06)
	Low	0.99	(0.97, 1.01)	-0.01	(-0.03, 0.01)	1.03	(0.99, 1.07)	0.02	(-0.01, 0.05)

Table 4 shows prevalence ratios and prevalence differences between the occupational groups after adjusting for age and occupation-age interaction and thus presented at ages 30, 55, 75, and 90 years. Prevalence differences for complex multimorbidity between high and low occupational groups varied; at 30 years, 19 (16 to 21) percentage points (pp) in women and 10 (8 to 13) pp in men; at 55 years, 12 (10 to 14) pp in women and 13 (11 to 15) pp in men; at 75 years, 2 (-1 to 4) pp in women and 7 (4 to 10) pp in men; and at 90 years, -1 (-3 to 1) pp in women and 2 (-1 to 5) in men. Compared with the high occupational group, the prevalence ratios for the low occupational group for complex multimorbidity were at 30 years, 2.06 (1.84 to 2.32) in women and 1.92 (1.63 to 2.26) in men; at 55 years, 1.22 (1.18 to 1.26) in women and 1.35 (1.28 to 1.41) in men; at 75 years, 1.02 (0.99 to 1.05) in women and 1.10 (1.06 to 1.15) in men; and at 90 years, 0.99 (0.97 to 1.01) in women and 1.03 (0.99 to 1.07) in men.

In the sensitivity analyses where the complex multimorbidity measure was derived from fewer conditions (22 vs 51) and *ICD-10* chapters (12 vs 14), the total prevalence was 15% (n=5836 of 38027, appendix D). Proportions were greater in women, higher age and the low occupational group. Compared to the results from the main analysis prevalence differences between high and low occupational groups were smaller in women at all ages and in men at age 30 years and 55 years, while prevalence ratios were greater in men at all ages and in women age 30 and 55 years.

Figure 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

Figure 2 depicts estimated prevalence of complex multimorbidity by occupational group and sex individuals aged 25 to 100 years. In all occupational groups in both sexes, the predicted prevalence increased with age throughout the age span. Further, estimated prevalence differed between the occupational groups in women until age 75 years and in men until age 90 years. Women had a consistently higher prevalence for complex multimorbidity than men.

DISCUSSION

Main results

More than half (54%) of this total county adult population sample were identified with complex multimorbidity, measured as occurrence of chronic conditions in minimum three separate organ systems. Prevalence of complex multimorbidity was common from early adulthood, increased with age, and was higher in women and in the low occupational group. Occupational group prevalence differences and ratios in complex multimorbidity were diminishing in women, while still present in men at age 75 years.

Comparison with existing literature

Few, if any, studies (to our knowledge) have investigated the prevalence and determinants of complex multimorbidity in a general population. The findings are in keeping with known determinants of lower social position, female sex, and higher age for multimorbidity in both general population-[19] and primary care studies.[3, 14, 16] An Australian study using a comparable operationalization of complex multimorbidity identified nearly 25% of patients in general practice with complex multimorbidity and estimated a national prevalence of 17%.[32] However, higher prevalence findings from our predominantly self-reported data are compatible with studies comparing prevalence estimates from self-reports and health record data.[33, 34] In absolute numbers, the incidence of individuals identified with the stricter measure of complex multimorbidity is still highest among the group younger than 64 years, as has been shown for multimorbidity.[16, 19, 35] The sensitivity analysis confirms how number and types of conditions influence prevalence[12, 15] and effect estimates of age, sex, and socioeconomic position.[36]

Mechanisms to explain findings

The association between lower socioeconomic position and poor health is well established. In general, unequal distribution of income, power, and wealth are understood to be socially determined fundamental causes that impact conditions of everyday life and result in social health inequities.[17] In Nordic countries assumed to be egalitarian and offering universal health care, social health inequities still exists.[18] Theories put forward are the survival of individuals with greater frailty, who are more likely to obtain a lower social position.[37] The gap in health is also explained by overall morbidity and mortality decreasing faster among the higher than the lower socioeconomic groups.[37]

In this study, occupational group serves as the proxy variable for socioeconomic position. Occupation may affect health outcomes through universal and specific mechanisms. In general, the higher occupational groups will have more secure and higher income,[29, 38] as well as advantageous social networks.[38] In particular, jobs vary in psychosocial factors, such

as stress, control, and autonomy and biological factors, such as physical demands or harmful and hazardous work environments.[38] Overall, the higher occupational group have greater autonomy and control,[29] while lower occupational groups are more exposed to malign work factors.[17] Generations may have different associations between a profession and health outcomes,[38] as occupations, tasks, and exposures shift over time.

The bidirectional relationship between health and occupation,[20] may partly explain the larger prevalence differences and ratios between low and high occupational groups in the younger age categories. Higher rates of multimorbidity in young individuals in lower socioeconomic positions may also be explained by detection bias[35] in which the initiation of therapy and health care follow-up increase the likelihood of diagnosing more conditions. Diminishing occupational ratios and differences among the oldest may be explained by the higher overall prevalence of complex multimorbidity[39] and also survival bias, whereby the individuals with greatest fragility have already died. While probability of complex multimorbidity increase with age, the age distribution results in a higher number of cases occurring in those younger than 64 years.

Strengths and limitations

Strengths of this study is the estimation of prevalence of complex multimorbidity from a general population survey, the most common study design in multimorbidity studies.[40] A vast number of self-reported conditions are included, almost exclusively diagnoses and symptoms.[41] Self-report is considered a valid approach when studying large samples.[15] Furthermore, using all available data will produce the most proper prevalence estimates,[12] which in this study is demonstrated by the sensitivity analysis and which seems necessary to detect occupational differences in younger age groups. The sensitivity analyses confirm that the spectrum of conditions included may affect associations with socioeconomic position, age, and sex.[36]

Our operationalization of complex multimorbidity makes the prevalence estimates comparable to other studies categorizing conditions by any organ-based system.[12] The occurrence of conditions in separate organ, and number of organ systems, could have been explored as a continuous measure with assumed increasing severity, however this was beyond the scope of this study.

The allocation of occupations in the European Socio-economic Classification also makes international comparison of social gradients possible.[29] We presented absolute and relative differences in compliance with recommendations on measurements of socioeconomic inequalities in health.[42] Results are further stratified by age and sex, which are stated as minimum requirements for proper reporting of multimorbidity.[14]

A number of limitations should be noted. Our study is based on data collected for a general health survey, and this limits data on conditions included in the complex multimorbidity measure. In particular, we did not have explicit information on chronicity for a majority of the conditions. Thus, the prevalence of complex multimorbidity may be overestimated.

Socioeconomic position was explored using only occupation, and while social health inequalities will be detected,[20] socioeconomic measures are not interchangeable.[20, 43] Different measures of socioeconomic position will act through varying mechanisms and may associate distinctively with health outcomes.[20, 43] Participants in HUNT3 reported their main occupation, while current or longest-lasting occupation is more often studied.[38] Younger

subjects may be misclassified in lower socioeconomic position, which may underestimate the occupational differences in health in this age group, whereas reverse causation, whereby prior health status determines job opportunities, is unavoidable and will increase detected differences. This study excludes those never having worked, which will underestimate social gradients in complex comorbidity.[44] Further, missing due to unclassifiable occupation, more common in elderly women than other participants, were excluded. Occupational data may misrepresent present social context[38] and thereby underestimate social inequalities. It would have been favorable if the study had included education, income or household indicators for socioeconomic position.

Participation in the HUNT3 Survey varied by age, sex, socioeconomic position, and pattern of morbidity.[25] This may weaken the effect estimates of the determinants to complex multimorbidity. A healthy elders bias is likely, since participation required attendance at a screening station. Overall, prevalence of individual conditions have shown only slight differences between participants and nonparticipants.[25] The HUNT study is considered fairly representative for Norway,[24] and the health development in the material follows western high-income country trends closely.[45-47]

Implications for clinical practice and policy makers

Our study confirms that complex multimorbidity, a suggested measure to identify multimorbid individuals with high need for coordinated multidisciplinary care,[12] is highly prevalent in the general population, where social differences are evident from young to old adulthood. This is in line with international studies, and at policy level, an emphasis on public health intervention to prevent complex multimorbidity and social differences seems necessary. As proposed elsewhere, this will likely require a proportionate universalism life-cycle approach.[48] To improve and secure health care for this large patient group, clinical guidelines and the organization of health care is suggested to adapt to a person-centered, generalist approach.[5, 10, 49]

Future research

Complex multimorbidity is common in this general population sample, with a clear social gradient throughout adulthood. Careful interpretation is necessary, since there are possible biases in measures of multimorbidity and occupation. However, the HUNT3 Survey data covers a broad spectrum of conditions and gives a unique opportunity to create several measures of multimorbidity in the same sample, with directly comparable prevalence estimates and gradients. On this background, we recommend exploring alternative measures suggested to detect individuals with high needs and multimorbidity and investigate differences in patterns, and consequences of such measures by social health determinants. Since multimorbidity is the norm and represents a large challenge to health care across levels, research on overall health care utilization and organization should be a priority, as well as studying competing measures as prognostic factors for mortality. Studies on social differences in use of health care may identify vulnerable subgroups, where any specific organization of treatment later on could be evaluated.

Conclusion

Complex multimorbidity, defined as occurrence of chronic conditions in three separate organ systems, is common, and occupational differences exists throughout adulthood in both sexes. The magnitude of complex multimorbidity in all age groups implies the need for public

health management to universally improve, targeted proportionate to need and disadvantage in subpopulations, social health determinants throughout the lifespan. Complex multimorbidity, indicating the accumulation of conditions of different etiology requiring coordinated multidisciplinary care, should inspire health caregivers, health care organizations, educational institutions, and researchers to take on a generalist and person-centered focus. Studying alternative multimorbidity measures, including health care utilization and mortality according to social background, as well as multimorbidity management, should be prioritized in future research.

FIGURES

Fig. 1. Flowchart for sample selection: inclusion and exclusion criteria and missing data.

Fig 2. Estimated prevalence of complex multimorbidity with 95 per cent confidence intervals (95% CI) by age and occupational group for women and men.

ACKNOWLEDGEMENTS

L Getz, J Sigurdsson and C Harrison for through discussions on measures of multimorbidity.
E Solheim for guidance in the use of the European Socio-economic Classification scheme.
MS Newman for writing assistance.
The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between HUNT Research Centre (Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU), Nord-Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health.

COMPETING INTERESTS

None declared.

FUNDING STATEMENT

Funding source: This study was funded by the Faculty of Medicine and Health Science at the Norwegian University of Science and Technology (NTNU) through the PhD program in Behavior and Health (KHV). NTNU has partly funded the HUNT3 Survey and have funded open access for this article. The Liaison Committee for Education, Research and Innovation in Central Norway (17/38297) supported a research stay at the Australian National University, Canberra. The funding sources have had no role in conceptualization this study, its design and methods, analysis and interpretation of data, writing of the article or the decision to submit the article for publication.

AUTHOR CONTRIBUTIONS

KHV, ERS, SK and JHB conceptualized the study and KHV, ERS, SK, JHB, OB and KD contributed to its design. KHV has analysed the data under supervision of ERS and KHV, ERS, SK, JHB, OB and KD have contributed to interpreting the data. KHV wrote the original draft, which has been revised critically by ERS, SK, JHB, OB and KD. KHV, ERS, SK, JHB,

OB and KD have read and approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

PATIENT CONSENT

Written informed consent was obtained from all participants in the HUNT3 Survey and all participation was voluntary.

ETHICS APPROVAL

The Regional Committee for Medical and Health Research Ethics in Norway approved the current study (project no. 2014/2265).

DATA SHARING STATEMENT

To protect participants' privacy, HUNT Research Centre aims to limit storage of data outside HUNT databank and cannot deposit data in open repositories. HUNT databank has precise information on all data exported to different projects and are able to reproduce these on request. There are no restrictions regarding data export given approval of applications to HUNT Research Centre. For more information see: http://www.ntnu.edu/hunt/data

SUPPLEMENTARY FILES

Appendix A: Construction of chronic, single entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Appendix B: Operationalizing socioeconomic position using occupation.

Appendix C: Prevalence ratios and differences with 95% CI in complex multimorbidity between occupational groups in 5-year intervals (25 to 100 years), stratified by sex.

Appendix D: Sensitivity analyses, sociodemographic characteristics and prevalence ratios and differences with 95% CI.

REFERENCES

1. Nicholson K, Makovski TT, Griffith LE, et al. Multimorbidity and comorbidity revisited: refining the concepts for international health research. *J Clin Epidemiol* 2019; 105: 142-146. 2018/09/27. DOI: 10.1016/j.jclinepi.2018.09.008.
2. van Oostrom SH, Gijsen R, Stirbu I, et al. Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. *PLoS One* 2016; 11: e0160264. 2016/08/03. DOI: 10.1371/journal.pone.0160264.
3. Uijen AA and van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008; 14 Suppl 1: 28-32. 2008/10/31. DOI: 10.1080/13814780802436093.
4. Coventry PA, Fisher L, Kenning C, et al. Capacity, responsibility, and motivation: a critical qualitative evaluation of patient and practitioner views about barriers to self-management in people with multimorbidity. *BMC Health Serv Res* 2014; 14: 536. 2014/11/05. DOI: 10.1186/s12913-014-0536-y.
5. Wallace E, Salisbury C, Guthrie B, et al. Managing patients with multimorbidity in primary care. *BMJ* 2015; 350: h176. Journal Article 2015/02/04. DOI: 10.1136/bmj.h176.
6. Sondergaard E, Willadsen TG, Guassora AD, et al. Problems and challenges in relation to the treatment of patients with multimorbidity: General practitioners' views and attitudes. *Scand J Prim Health Care* 2015; 33: 121-126. 2015/07/15. DOI: 10.3109/02813432.2015.1041828.
7. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. *BMJ* 2012; 345: e6341. Journal Article 2012/10/06. DOI: 10.1136/bmj.e6341.
8. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract* 2011; 28: 516-523. 2011/03/26. DOI: 10.1093/fampra/cmr013.
9. Agborsangaya CB, Lau D, Lahtinen M, et al. Health-related quality of life and healthcare utilization in multimorbidity: results of a cross-sectional survey. *Qual Life Res* 2013; 22: 791-799. 2012/06/12. DOI: 10.1007/s11136-012-0214-7.
10. National Institute for Health and Care Excellence. *Multimorbidity: clinical assessment and management. NICE guideline [NG56]*. https://www.nice.org.uk/guidance/ng56: National Institute for Health and Care Excellence,, 2016.
11. Palmer K, Marengoni A, Forjaz MJ, et al. Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS). *Health Policy* 2018; 122: 4-11. 2017/10/03. DOI: 10.1016/j.healthpol.2017.09.006.
12. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. *BMJ Open* 2014; 4: e004694. 2014/07/13. DOI: 10.1136/bmjopen-2013-004694.
13. Schaink AK, Kuluski K, Lyons RF, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. *Journal of comorbidity* 2012; 2: 1-9. 2012/10/10. DOI: 10.15256/joc.2012.2.15.
14. Violan C, Foguet-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. 2014/07/23. DOI: 10.1371/journal.pone.0102149.
15. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012; 10: 142-151. 2012/03/14. DOI: 10.1370/afm.1337.
16. 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* 2012; 380: 37-43. 2012/05/15. DOI: 10.1016/S0140-6736(12)60240-2.

17. Commission on Social Determinants of Health. *Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health*. Geneva 2008, p.256.
18. Mackenbach JP, Stirbu I, Roskam AJ, et al. Socioeconomic inequalities in health in 22 European countries. *N Engl J Med* 2008; 358: 2468-2481. 2008/06/06. DOI: 10.1056/NEJMsa0707519.
19. Agborsangaya CB, Lau D, Lahtinen M, et al. Multimorbidity prevalence and patterns across socioeconomic determinants: a cross-sectional survey. *BMC Public Health* 2012; 12: 201. 2012/03/21. DOI: 10.1186/1471-2458-12-201.
20. Galobardes B, Lynch J and Smith GD. Measuring socioeconomic position in health research. *Br Med Bull* 2007; 81-82: 21-37. 2007/02/08. DOI: 10.1093/bmb/ldm001.
21. Tomasdottir MO, Getz L, Sigurdsson JA, et al. Co-and multimorbidity patterns in an unselected Norwegian population: Cross-sectional analysis based on the HUNT Study and theoretical reflections concerning basic medical models. *European Journal for Person Centered Healthcare* 2014; 2: 335-345.
22. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014; 12: 1495-1499. 2014/07/22. DOI: 10.1016/j.ijsu.2014.07.013.
23. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: the HUNT Study, Norway. *Int J Epidemiol* 2013; 42: 968-977. 2012/08/11. DOI: 10.1093/ije/dys095.
24. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. *Norsk epidemiologi* 2003; 13: 19-32.
25. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol* 2012; 12: 143. 2012/09/18. DOI: 10.1186/1471-2288-12-143.
26. Direktoratet for e-helse. FinnKode - Helsedirektoratet medisinske kodeverk, https://finnkode.ehelse.no/#icpc/0/0/0/-1 (accessed 1 Feb 2017).
27. Statistics Norway. *Standard Classification of Occupations*. Oslo/Kongsvinger: Statistics Norway, 1998.
28. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88, https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm (1988, accessed 24.05. 2019).
29. Rose D and Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007; 9: 459-490. DOI: 10.1080/14616690701336518.
30. Sedgwick P. Relative risks versus odds ratios. *Bmj-British Medical Journal* 2014; 348: g1407-g1407. DOI: ARTN g1407

10.1136/bmj.g1407.
31. Norton EC, Miller MM and Kleinman LC. Computing Adjusted Risk Ratios and Risk Differences in Stata. *The Stata Journal: Promoting communications on statistics and Stata* 2018; 13: 492-509. DOI: 10.1177/1536867x1301300304.
32. Harrison C, Henderson J, Miller G, et al. The prevalence of complex multimorbidity in Australia. *Aust N Z J Public Health* 2016; 40: 239-244. 2016/03/31. DOI: 10.1111/1753-6405.12509.
33. Cricelli C, Mazzaglia G, Samani F, et al. Prevalence estimates for chronic diseases in Italy: exploring the differences between self-report and primary care databases. *J Public Health Med* 2003; 25: 254-257. 2003/10/25. DOI: 10.1093/pubmed/fdg060.
34. Fortin M, Haggerty J, Sanche S, et al. Self-reported versus health administrative data: implications for assessing chronic illness burden in populations. A cross-sectional study. *CMAJ Open* 2017; 5: E729-E733. 2017/09/28. DOI: 10.9778/cmajo.20170029.

35. van den Akker M, Buntinx F, Metsemakers JF, et al. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol* 1998; 51: 367-375. 1998/06/10. DOI: 10.1016/s0895-4356(97)00306-5.
36. Schafer I, Hansen H, Schon G, et al. The influence of age, gender and socio-economic status on multimorbidity patterns in primary care. First results from the multicare cohort study. *BMC Health Serv Res* 2012; 12: 89. 2012/04/05. DOI: 10.1186/1472-6963-12-89.
37. Huijts T and Eikemo TA. Causality, social selectivity or artefacts? Why socioeconomic inequalities in health are not smallest in the Nordic countries. *Eur J Public Health* 2009; 19: 452-453. 2009/07/10. DOI: 10.1093/eurpub/ckp103.
38. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006; 60: 7-12. 2005/12/20. DOI: 10.1136/jech.2004.023531.
39. Scanlan JP. Guest Editorial. *Chance* 2013; 19: 47-51. Guest editorial 02 Aug 2013. DOI: 10.1080/09332480.2006.10722787.
40. 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. 2016/03/10. DOI: 10.3109/02813432.2016.1153242.
41. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing research reviews* 2011; 10: 430-439. 2011/03/16. DOI: 10.1016/j.arr.2011.03.003.
42. Mackenbach JP and Kunst AE. Measuring the magnitude of socio-economic inequalities in health: an overview of available measures illustrated with two examples from Europe. *Soc Sci Med* 1997; 44: 757-771. 1997/03/01. DOI: 10.1016/s0277-9536(96)00073-1.
43. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: one size does not fit all. *JAMA* 2005; 294: 2879-2888.
44. Martikainen P and Valkonen T. Bias related to the exclusion of the economically inactive in studies on social class differences in mortality. *Int J Epidemiol* 1999; 28: 899-904. 1999/12/22. DOI: 10.1093/ije/28.5.899.
45. Collaboration NCDRF. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature* 2019; 569: 260-264. 2019/05/10. DOI: 10.1038/s41586-019-1171-x.
46. Collaboration NCDRF. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet* 2017; 389: 37-55. 2016/11/20. DOI: 10.1016/S0140-6736(16)31919-5.
47. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017; 390: 2627-2642. 2017/10/17. DOI: 10.1016/S0140-6736(17)32129-3.
48. Marmot M, Goldblatt P, Allen J, et al. *Fair Society, Healthy Lives.*: The Marmot Review, 2010, p.242.
49. World Health Organization. Multimorbidity: Technical Series on Safer Primary Care. Geneva.: World Health Organization, 2016.

Fig. 1. Flowchart sample selection: inclusion and exclusion criteria and missing data.

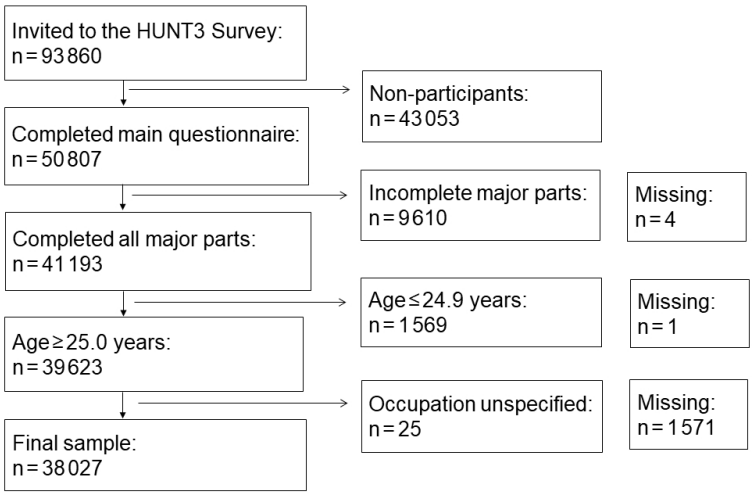

Figure 1. Flowchart for sample selection; inclusion and exclusion criteria, and missing data

338x190mm (96 x 96 DPI)

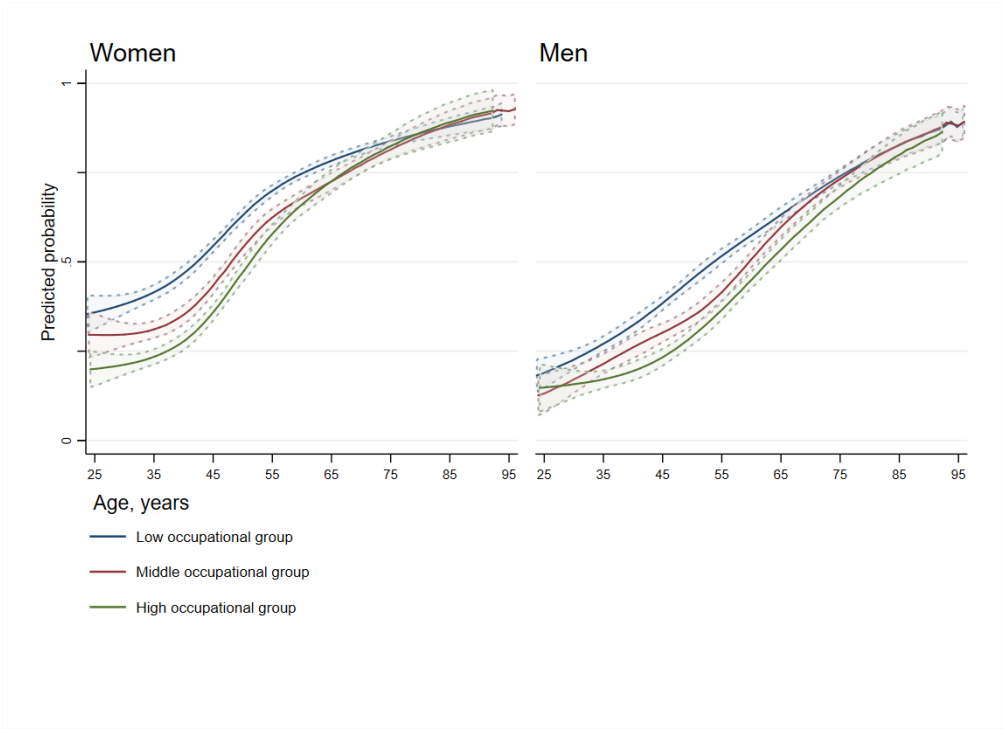

Figure 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

403x293mm (72 x 72 DPI)

Appendix A

CONSTRUCTION OF CHRONIC, SINGLE ENTITIES CONDITIONS FROM DATA IN THE HUNT3 SURVEY, BY QUESTIONNAIRES AND MEASUREMENTS.

Original questionnaires, English version.

The main questionnaire (Questionnaire 1).
https://www.ntnu.edu/c/document_library/get_file?uuid=129b68c3-520c-457f-8b98-02c49219b2ee&groupId=140075

The age- and sex-specific questionnaire (Questionnaire 2).
https://www.ntnu.edu/c/document_library/get_file?uuid=35ae2816-4155-4b64-a259-770946fa46d4&groupId=140075

Chronicity.

Chronicity was defined by either 1: duration (3 months or longer), 2: causing functional limitation (physical, mental, social) or 3: requiring health care management (pharmacological or not, primary or specialist care), [1] or 4: chronicity was assumed based on medical knowledge and clinical experience.

Missing.

In variables with index questions and cluster text, missing was in general corrected for affirmed index question and regarded as “no” if replied to any alternative to any of the other questions in the block. Information on missing is also collected from the HUNT Databank.

Main questionnaire.

Hearing impairment.
Index question: “Do you suffer from longstanding (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” Yes, no.
Options on follow-up question combined condition type (motor, vision, hearing, somatic, and psychiatric) and severity (slight, moderate, and severe).
Included with hearing impairment were those who reported chronic disease and moderate to severe hearing impairment.

“20 Diseases”: Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis.
Cluster text: “Have you had or do you have any of the following:
Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis?”

Separate tick boxes for each diagnosis: Yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis. Chronicity is assumed based on medical knowledge and clinical experience.

Sex- and age-differentiated questionnaire.

Headache.

Seven questions in one block. Question 1: “Have you had headaches in the last year?” Yes/no.

Migraine without aura.

Of those who affirmed headache last year, migraine without aura was constructed from three of seven questions:
“What is the average strength of your headaches?” 1=Mild, 2=Moderate, 3=Strong.Recoded to dichotomous variable, where 1=Moderate/Strong.
“How long does the headache usually last?” 1=Less than 4 hours, 2=4 hours - 1 day, 3=1 - 3 days, 4= More than 3 days. Recoded to dichotomous variable, where 1= Less than 4 hours – 3 days.
Cluster text: “Are the headaches usually characterized or accompanied by
Throbbing/thumping pain?” Yes, no.
Pain on one side of the head?” Yes, no.
Worsening with physical activity?” Yes, no.
Nausea and/or vomiting?” Yes, no.
Hypersensitivity to light and/or noise?” Yes, no.

Included with migraine: were those who affirmed to headache lasting 0 to 72 hours and at least two of four characteristics (pulsating quality, unilateral location, moderate/severe pain intensity, or aggravation by physical activity) and during headache having at least one of two accompanying symptoms (nausea and/or vomiting or increased sensitivity to light and/or noise).[2] Chronicity is assumed based on medical knowledge and clinical experience.

Chronic headache.

Of those who affirmed headache last year, chronic headache was constructed from two of seven questions:
“If yes (headache in the last year): What type of headache? Migraine, other.”
The HUNT Databank created two variables with range 1: 1) migraine and 2) other headache.
“Average number of days a month with headaches?:” 1=Less than 1 day, 2=1-6 days, 3=7-14 days, 4=More than 14 days. Recoded to dichotomous variable, where 1= More than 14 days.

Included as case with chronic headache were those reporting “other” type of headache and an average frequency of more than 14 days per month. Chronicity is assumed based on medical knowledge and clinical experience.

Pain.

Index question: “In the last year, have you had pain or stiffness in muscles or joints that has lasted at least 3 consecutive months?” Yes, no.
The follow-up question “If yes: Where have you had this pain or stiffness?” was combined with a figure with arrows and tick boxes at nine locations (neck, upper back, lower back, shoulder, elbow, hand, hip, knee and ankle/foot).

Chronic widespread pain.

Dichotomous variables were made for each major body area: 1) Trunk (neck, upper and lower back),

2) Upper limb (shoulder, elbow, hand), and 3) Lower limb (hip, knee, foot/ancle), where 1=At least one painful location. A sum (row total) score variable was made for the major body areas and dichotomized, where 1=3, that is one pain in each major body area.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic widespread pain was defined as pain at more than three sites in all major body areas (trunk, upper and lower limbs) for more than three months in the last year.[3]

Chronic, local pain.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic, local pain was defined as pain in the neck or upper back or lower back or shoulder or elbow or hand or hip or knee or ancle/foot, excluding presence of chronic widespread pain, generating nine dichotomous variables.

Thyroidal disease.
Cluster text: “Has it ever been verified that you have/have had hypothyroidism or hyperthyroidism?” Separate tick boxes for each condition (yes, no), generating two dichotomous variables, 1=Yes.
For each diagnosis, included were those who affirmed to have or have had the diagnosis. Chronicity is assumed based on medical knowledge and clinical experience.

Irritable bowel syndrome.
Index question: “Have you had stomach pain or discomfort in the last 12 months?” Answers: Yes, much; yes, a little; no. Irritable bowel syndrome was further constructed from four of six follow-up questions: “If yes:
“In the last 3 months, have you had this as often as 1 day a week for at least 3 weeks?” Yes, no.
“Is the pain/discomfort relieved by having a bowel movement?” Yes, no.
“Is the pain/discomfort related to more frequent or less frequent bowel movements than normal?” Yes,no.
“Is the pain/discomfort related to the stool being softer or harder than usual?” Yes, no.

Included with irritable bowel syndrome were those who affirmed little or much stomach pain or discomfort in the last year, who for as often as 1 day a week for at least 3 weeks in the last 3 months have had at least two of the following: pain/discomfort relieved by having a bowel movement, related to altered frequency of bowel movements, or related to altered stool appearance, resembling a modified version of the Rome criteria. [4 5]

Gastro-oesophageal reflux disease.
Cluster text: “To what degree have you had the following problems in the last 12 months?” Options combined type (nausea, heartburn/acid regurgitation, diarrhea, constipation, alternating constipation and diarrhea, and bloating) and frequency (never, a little, or much).
Generated one dichotomous variable, heartburn, where 1=Much.
Gastro-oesophageal reflux disease is defined as much heartburn/acid regurgitation in the last 12 months. [6]

Anxiety.
Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed a total score for anxiety (HADS-A), if all 7 anxiety items were answered. Anxiety was defined as HADS-A score >=8/21, indicating mild or possible anxiety. [8-10] Chronicity is assumed based on medical knowledge and clinical experience.

Depression.

Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed total score depression (HADS-D), if all 7 depression items were answered.
Depression was defined as HADS-D score >=8/21, indicating mild or possible depression. [8-10]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic insomnia.

There were nine questions on sleeping pattern in one cluster, including three concerning insomnia. Initial text: "How often in the last 3 months have you
"Had difficulty falling asleep at night?" Never/seldom, sometimes, several times a week.
"Woken up repeatedly during the night?" Never/seldom, sometimes, several times a week.
"Woken too early and couldn't get back to sleep?" Never/seldom, sometimes, several times a week.
Chronic insomnia was defined as in the last 3 months, several times a week, having difficulty falling asleep at night and waking up repeatedly during the night, and waking up too early. A modified version of the diagnostic criteria for insomnia in the International Classification of Sleep Disorders.[11]

Alcohol use disorder.

Instrument variable: Cut down/Annoyed/Guilty/Eye-opener, also known as the CAGE questionnaire.[12] The CAGE questionnaire is a 4-item scale with scores of 0-1. A summary variable was created and dichotomized in which a score of 1 indicates >=2 positive answers.
Alcohol use disorder was defined as CAGE score greater than 2.[13]
Chronicity is assumed based on medical knowledge and clinical experience.

Dental health problem.

"How would you say your dental health is?" Very, bad, ok, good, very good.
Dental health problems were defined as self-reported bad or very bad dental health. Chronicity is assumed based on medical knowledge and clinical experience.

Menopausal hot flashes.

Asked to women older than 30 years only.
Two questions were used to define menopausal illness:
"Do you have/have you had hot flashes due to menopause?" During the day, during the night, day and night, haven't had any.
"If you have had hot flashes, how would you describe them?" Very intense, moderately intense, hardly noticeable.
Included with menopausal hot flashes were those who reported hot flashes occurring daily and/or nightly and of at least moderate severity. Chronicity is assumed based on medical knowledge and clinical experience.

Nocturia.

Age group 20-29 years were excluded.
One question on nocturia, identical to that of the International Prostate Symptom Scale (IPSS), was asked to men and women older than 30 years.

"How many times do you get up during the night to urinate?" None, 1 time, 2 times, 3 times, 4 times, 5 times or more.
Nocturia was defined as two or more voids per night.[14] Chronicity is assumed based on medical knowledge and clinical experience.

Urine incontinence.

Men 20-29 years were excluded.
Instrument variable: The Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) questionnaire.[15]
Index question: Do you have involuntary loss of urine? Yes, no.
Urine incontinence was constructed from two of six follow up questions. "If yes":
"How often do you have involuntary loss of urine?" Less than once a month, once or more per month, once or more per week, every day and/or night
"How much urine do you leak each time?" Drops or little, small amount, large amounts.

Self-reported frequency and volume of leakage were multiplied to obtain the validated 4-level Sandvik Severity Index, categorizing incontinence as slight, moderate, severe, and very severe.[15]
Urine incontinence were included if severe to very severe. Chronicity is assumed based on medical knowledge and clinical experience.

Prostate symptoms.

Asked of men older than 30 years only.
Instrument variable: The International Prostate Symptom Scale [16] was slightly modified in HUNT3,[17] becoming a 7-item scale with scores of 0-5 per question.
Included were prostate symptoms of at least moderate severity, i.e. summary score >= 8 points.[16] Chronicity is assumed based on medical knowledge and clinical experience.

Eye diseases.

The age group 20-29 years were excluded.
Cluster text: "Do you have any of the following eye conditions?" Cataract, glaucoma, and macula degeneration. Separate tick boxes, yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.

Measurements.

Obesity.

HUNT Databank constructed the BMI variable, defined as (weight in kg)/(height in m2).
Obesity was defined as either BMI>=35 or a BMI 25-34.9 and an increased waist circumference (>= 88 cm for females; >= 102 cm for males).[18 19] Chronicity is assumed based on medical knowledge and clinical experience.

Hypertension.

Blood pressure in HUNT3 is measured three times at one consultation. The mean of measurement 2 and 3 is calculated by HUNT Databank.
Hypertension was defined as measured mean systolic BP>= 180 mmHg or diastolic BP >= 110 mmHg or reporting use of antihypertensive medications, excluding self-reported cardiovascular disease, diabetes, or kidney disease, and excluding extreme measures. Chronicity is assumed based on medical knowledge and clinical experience.

Hypercholesterolemia

Hypercholesterolemia was defined as total-cholesterol >= 8 mmol/L.[20]

Chronicity is assumed based on medical knowledge and clinical experience.

References

1. Goodman RA, Posner SF, Huang ES, et al. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. *Prev Chronic Dis* 2013;10:E66. doi: 10.5888/pcd10.120239 [published Online First: 2013/04/27]
2. Hagen K, Zwart JA, Aamodt AH, et al. The validity of questionnaire-based diagnoses: the third Nord-Trondelag Health Study 2006-2008. *J Headache Pain* 2010;11(1):67-73. doi: 10.1007/s10194-009-0174-7 [published Online First: 2009/12/01]
3. Mundal I, Grawe RW, Bjorngaard JH, et al. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. *BMC Musculoskelet Disord* 2014;15:213. doi: 10.1186/1471-2474-15-213 [published Online First: 2014/06/22]
4. Hammer J, Talley NJ. Diagnostic criteria for the irritable bowel syndrome. *Am J Med* 1999;107(5A):5S-11S. doi: 10.1016/s0002-9343(99)00276-4 [published Online First: 1999/12/10]
5. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480-91. doi: 10.1053/j.gastro.2005.11.061 [published Online First: 2006/05/09]
6. Ness-Jensen E, Lindam A, Lagergren J, et al. Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study. *Gut* 2012;61(10):1390-7. doi: 10.1136/gutjnl-2011-300715 [published Online First: 2011/12/23]
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(6):361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x [published Online First: 1983/06/01]
8. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *Br J Psychiatry* 2001;179:540-4. doi: 10.1192/bjp.179.6.540 [published Online First: 2001/12/04]
9. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
10. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res* 1997;42(1):17-41. [published Online First: 1997/01/01]
11. Medicine AAoS. The international classification of sleep disorders: diagnostic and coding manual: American Acad. of Sleep Medicine 2005.
12. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984;252(14):1905-7. doi: 10.1001/jama.252.14.1905 [published Online First: 1984/10/12]
13. Skogen JC, Overland S, Knudsen AK, et al. Concurrent validity of the CAGE questionnaire. The Nord-Trondelag Health Study. *Addict Behav* 2011;36(4):302-7. doi: 10.1016/j.addbeh.2010.11.010 [published Online First: 2010/12/21]
14. Tikkinen KA, Johnson TM, 2nd, Tammela TL, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. *Eur Urol* 2010;57(3):488-96. doi: 10.1016/j.eururo.2009.03.080 [published Online First: 2009/04/14]
15. Sandvik H, Seim A, Vanvik A, et al. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. *Neurourol Urodyn* 2000;19(2):137-45. [published Online First: 2000/02/19]
16. Barry MJ, Fowler FJ, Jr., O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148(5):1549-57; discussion 64. doi: 10.1016/s0022-5347(17)36966-5 [published Online First: 1992/11/11]
17. HUNT Databank. International Prostate Symptom Scale in HUNT3 Questionnaire 2 [Webpage]. Levanger: HUNT Databank; 2019 [cited 2019 05.20.]. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#/instrumentpart/45_11 2019.
18. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79(3):379-84. doi: 10.1093/ajcn/79.3.379 [published Online First: 2004/02/27]
19. Perreault L. Obesity in adults: Prevalence, screening, and evaluation. Waltham, MA: UpToDate 2018.
20. Helsedirektoratet. Nasjonal faglig retningslinje for individuell primærforebygging av hjerte-og karsykdommer, kortversjon, IS-1675. In: Helsedirektoratet, ed., 2009.

Appendix B

OPERATIONALIZING SOCIOECONOMIC POSITION USING OCCUPATION.

In the HUNT3 Survey interview, all participants were asked: "What is/was the title of your main occupation?" Free-text answers were manually classified according to the *Standard Classifications of Occupations* by Statistics Norway,[1] which is based on the European Union's version of the *International Standard Classification of Occupations-88.*[2]

The standard categorize occupations according to skill level and specialization, degree of independence, and manual labor but not social position.[1] Occupations are coded with up to four digits, with increasing detail. One digit indicates major groups; two digits, submajor groups; three digits, minor groups; and four digits, unit groups. The minor occupational group was the highest level of detail available in the HUNT3 Survey.

Occupational socioeconomic position was operationalized using the European Socio-economic Classification scheme.[3] The full version of the scheme requires employment status and size of organization in addition to occupation to assign a class position. We used the simplified class scheme, based on minor occupational group only[3], as the HUNT3 Survey did not have data corresponding to employment status and size of organization. It is shown that the agreement between three-digit full and simplified version of this scheme is 79.7% for the total workforce.[3]

The syntax is available from https://www.iser.essex.ac.uk/archives/esec/matrices-and-syntax. It was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA).

Table 1 gives details of transformation of data, discrepancies between the Norwegian and European Union standard and the allocated position in the full classification scheme. 2179 individuals had alterations to their occupational data to fit the syntax, 5.7% (2179/38027) of the total sample.

In the HUNT3 Survey data, the minor occupational group was a string variable. To perform the syntax, it had to be altered to a numeric variable. The string "011" changed to numeric value "11," which was manually corrected in the syntax. In the 3-digit variable, some participants were classified with 1 digit and 2 digits only. These were transformed to the corresponding 3-digit minor group, at the lowest level of detail, by manually adding suffix digits 0 or 00. This is in line with operationalizing of European Socio-economic Classification (see footnote table 1).[3]

Norwegian minor groups, which were not found in the European Union standard, were altered to the level of detail in which corresponding groups could be identified. These were *Standard Classifications of Occupations* by Statistics Norway codes: 112 (corresponding to 2 digits), 25 (corresponding to 1 digit), 251-6 (corresponding to 1 digit), 349 (corresponding to 2 digits), 631 (corresponding to 1 digit), 641 (corresponding to 1 digit), 735 (corresponding to 2 digits), and 745 (corresponding to 2 digits). See table 1.

In total, 9 classes were created. To increase power and simplify interpretation, the full scheme was collapsed into a 3-class version, with “high” combining class 1 and 2, “middle” combining 3 to 6, and “low” combining 7 to 9. [3] The high occupational class represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, higher-grade technician occupations, and supervisory occupations. The middle occupational class consist of small employers, self-employed individuals, lower supervisory occupations, and lower technician occupations. The low occupational class contain lower services, sales and clerical occupations, lower technical occupations, and routine occupations.

Table 1. The distribution of transformed occupational data and discrepancies between the Norwegian and International Standard Classifications of Occupations, and allocation in the European Socio-economic Classification scheme.

Standard Classifications of Occupations		European Socio-economic		
Norwegian	**International**	**Classification scheme**	***n***	**%**
1	100	1	262	(0.69)
011 (=num 11)	011=11	3	134	(0.35)
112*	→ 11=110	1	31	(0.08)
12	120	1	73	(0.19)
13	130	4	20	(0.05)
2	200	1	10	(0.03)
21	210	1	10	(0.03)
22	220	1	1	(0.00)
23	230	2	27	(0.07)
24	240	1	9	(0.02)
25	→ 2=200	1	4	(0.01)
251*	→ 2=200	1	296	(0.78)
252*	→ 2=200	1	48	(0.13)
253*	→ 2=200	1	20	(0.05)
254*	→ 2=200	1	138	(0.36)
255*	→ 2=200	1	64	(0.17)
256*	→ 2=200	1	46	(0.12)
3	300	3	39	(0.10)
31	310	2	37	(0.10)
33	330	3	241	(0.63)
34	340	3	45	(0.12)
349*	→34=340	3	160	(0.42)
4	400	3	1	(0.00)
41	410	3	1	(0.00)
42	420	3	1	(0.00)
5	500	7	1	(0.00)
51	510	7	8	(0.02)
61	610	5	4	(0.01)
631*	→6=600	5	93	(0.24)
641*	→6=600	5	99	(0.26)
7	700	8	20	(0.05)
71	710	8	1	(0.00)
72	720	8	6	(0.02)
73	730	6	1	(0.00)
735*	→73=730	6	38	(0.10)
74	740	8	1	(0.00)
745*	→74=740	8	46	(0.12)
8	800	9	62	(0.16)
81	810	9	38	(0.10)
82	820	9	35	(0.09)
83	830	9	6	(0.02)
9	900	9	1	(0.00)
93	930	9	1	(0.00)
Sum			2179	(5.73)

Bold* = Divergence of *Standard Classifications of Occupations* by Statistics Norway from the European Union's version of *The International Standard Classification of Occupations-88*.

References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
2. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
3. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518

Appendix C

Table C1 Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational groups in 5-year intervals (25 to 100 years), stratified by sex.

Age,	Occup.*	Women						Men					
years	group	PR	95% CI		PD	95% CI		PR	95% CI		PD	95% CI	
25	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.58	1.34	1.88	0.08	0.05	0.10	1.30	1.03	1.63	0.03	0.00	0.05
	Low	2.34	2.02	2.72	0.18	0.15	0.20	2.06	1.69	2.50	0.09	0.07	0.11
30	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.47	1.28	1.68	0.08	0.05	0.11	1.28	1.05	1.55	0.03	0.01	0.06
	Low	2.06	1.84	2.32	0.19	0.16	0.21	1.92	1.63	2.26	0.10	0.08	0.13
35	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.36	1.23	1.51	0.08	0.06	0.11	1.26	1.07	1.47	0.04	0.01	0.06
	Low	1.82	1.67	2.00	0.19	0.16	0.22	1.79	1.56	2.04	0.12	0.09	0.14
40	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.27	1.18	1.37	0.08	0.05	0.11	1.24	1.09	1.40	0.04	0.02	0.07
	Low	1.62	1.52	1.73	0.19	0.16	0.21	1.66	1.50	1.84	0.13	0.10	0.15
45	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.19	1.13	1.26	0.07	0.05	0.09	1.21	1.10	1.33	0.05	0.03	0.08
	Low	1.45	1.39	1.53	0.17	0.15	0.19	1.55	1.43	1.67	0.13	0.11	0.15
50	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.13	1.08	1.18	0.06	0.04	0.08	1.19	1.11	1.27	0.06	0.03	0.08
	Low	1.32	1.27	1.37	0.15	0.13	0.17	1.44	1.36	1.53	0.13	0.11	0.15
55	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.08	1.03	1.12	0.04	0.02	0.06	1.16	1.10	1.23	0.06	0.04	0.08
	Low	1.22	1.18	1.26	0.12	0.10	0.14	1.35	1.28	1.41	0.13	0.11	0.15
60	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.04	1.00	1.08	0.02	0.00	0.05	1.14	1.08	1.19	0.06	0.04	0.08
	Low	1.14	1.10	1.18	0.09	0.07	0.11	1.27	1.21	1.32	0.12	0.10	0.14
65	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.01	0.97	1.05	0.01	-0.02	0.04	1.11	1.06	1.17	0.06	0.03	0.08
	Low	1.08	1.05	1.12	0.06	0.04	0.08	1.20	1.15	1.25	0.10	0.08	0.13
70	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.99	0.96	1.03	0.00	-0.03	0.02	1.09	1.04	1.14	0.05	0.03	0.08
	Low	1.05	1.01	1.08	0.04	0.01	0.06	1.15	1.10	1.20	0.09	0.06	0.11
75	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.02	-0.01	-0.04	0.02	1.07	1.02	1.12	0.05	0.02	0.08
	Low	1.02	0.99	1.05	0.02	-0.01	0.04	1.10	1.06	1.15	0.07	0.04	0.10

80	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.01	-0.02	-0.04	0.01	1.06	1.01	1.11	0.04	0.01	0.08
	Low	1.00	0.98	1.03	0.00	-0.02	0.02	1.07	1.02	1.12	0.05	0.02	0.08
85	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.00	-0.02	-0.04	0.00	1.04	1.00	1.09	0.03	0.00	0.07
	Low	0.99	0.97	1.02	-0.01	-0.03	0.01	1.05	1.00	1.09	0.04	0.00	0.07
90	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.96	1.00	-0.02	-0.04	0.00	1.03	0.99	1.07	0.03	-0.01	0.06
	Low	0.99	0.97	1.01	-0.01	-0.03	0.01	1.03	0.99	1.07	0.02	-0.01	0.05
95	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.96	1.00	-0.02	-0.04	0.00	1.02	0.99	1.06	0.02	-0.01	0.05
	Low	0.99	0.97	1.00	-0.01	-0.03	0.00	1.02	0.98	1.05	0.01	-0.02	0.04
100	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.97	1.00	-0.02	-0.03	0.00	1.02	0.99	1.05	0.02	-0.01	0.04
	Low	0.98	0.97	1.00	-0.01	-0.03	0.00	1.01	0.98	1.04	0.01	-0.02	0.03

*Occup. = occupational

Appendix D – Sensitivity analysis

In the sensitivity analysis the outcome complex multimorbidity was created from available conditions in the main questionnaire only. In total 22 conditions, grouped in 12 *ICD-10* chapters were included vs 51 conditions, grouped in *14 ICD-10* chapters in the original measure.

The sensitivity analysis was performed to investigate if fewer number and types of conditions included in the complex multimorbidity measure, produced a similar pattern with respect to the overall prevalence as well as differences between occupational groups.

Total prevalences and prevalences by occupational group and age, stratified by sex (table D1), were obtained by cross tables.

Table D1. Sociodemographic distribution of complex multimorbidity

	Women						Men					
	No, *n*	**(%)**	**Yes, *n***	**(%)**	**Total, *n***	**(%)**	**No, *n***	**(%)**	**Yes, *n***	**(%)**	**Total, *n***	**(%)**
Total	17376	(83)	3437	(17)	20813	(100)	14815	(86)	2399	(14)	17214	(100)
Occupational group												
High	4032	(90)	473	(11)	4505	(100)	4026	(90)	439	(10)	4465	(100)
Middle	4612	(86)	774	(14)	5386	(100)	4147	(85)	710	(15)	4857	(100)
Low	8732	(80)	2190	(20)	10922	(100)	6642	(84)	1250	(16)	7892	(100)
Age, years												
25-44	5610	(94)	371	(6)	5981	(100)	3776	(96)	167	(4)	3943	(100)
45-64	8233	(84)	1607	(16)	9840	(100)	7381	(88)	985	(12)	8366	(100)
65-74	2331	(74)	837	(26)	3168	(100)	2417	(78)	676	(22)	3093	(100)
75-100	1202	(66)	622	(34)	1824	(100)	1241	(68)	571	(32)	1812	(100)
Mean, (SD)	53	(14)	62	(13)	54	(14)	55	(14)	65	(12)	56	(14)

Prevalence ratios and differences between occupational groups at ages 30, 55, 75 and 90 years were derived from logistic regression estimates (table D2).

Table D2. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational classes, stratified by sex.

Age, years	Occupational group	Women				Men			
		PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
30	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.91	(1.41, 2.57)	0.02	(0.01, 0.03)	1.28	(0.88, 1.86)	0.01	(0.00, 0.01)
	Low	3.47	(2.68, 4.49)	0.05	(0.04, 0.06)	1.96	(1.42, 2.71)	0.02	(0.01, 0.03)
55	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.18	(1.05, 1.33)	0.02	(0.01, 0.03)	1.31	(1.13, 1.52)	0.02	(0.01, 0.04)
	Low	1.59	(1.44, 1.76)	0.07	(0.05, 0.08)	1.68	(1.48, 1.91)	0.05	(0.04, 0.06)
75	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.88	(0.77, 1.01)	-0.04	(-0.08, 0.00)	1.28	(1.12, 1.47)	0.06	(0.03, 0.09)
	Low	0.96	(0.85, 1.08)	-0.01	(-0.05, 0.02)	1.44	(1.27, 1.64)	0.09	(0.06, 0.12)
90	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.80	(0.69, 0.93)	-0.12	(-0.20, -0.04)	1.23	(1.03, 1.46)	0.09	(0.01, 0.16)
	Low	0.78	(0.69, 0.88)	-0.13	(-0.20, -0.06)	1.27	(1.08, 1.50)	0.10	(0.04, 0.17)

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 (Title page)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6, tab. 1
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	Appendix A
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	8
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	5, 8
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2, p.9
		(b) Indicate number of participants with missing data for each variable of interest	5
Outcome data	15*	Report numbers of outcome events or summary measures	Table 3, pp. 9-10
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	Table 4, p 10. 8
		(*b*) Report category boundaries when continuous variables were categorized	5
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk ~~for a meaningful time period~~	8, table 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10, appendix E
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	14

*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

Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-036851.R2
Article Type:	Original research
Date Submitted by the Author:	31-Mar-2020
Complete List of Authors:	Vinjerui, Kristin Hestmann; Norwegian University of Science and Technology, Department of Public Health and Nursing/HUNT Research Centre; Helse Nord-Trondelag, Psychiatric Department Bjerkeset, Ottar; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Mental Health Bjorngaard, Johan; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences Krokstad, Steinar; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing/HUNT Research Centre; Helse Nord-Trondelag, Psychiatric Department Douglas, Kirsty; Australian National University, Australian National University Medical School Sund, Erik; Norwegian University of Science and Technology Faculty of Medicine and Health Sciences, Department of Public Health and Nursing/HUNT Research Centre; Nord Universitet - Levanger Campus, Faculty of Nursing and Health Sciences
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health, Epidemiology, General practice / Family practice, Medical management, Patient-centred medicine
Keywords:	SOCIAL MEDICINE, EPIDEMIOLOGY, PUBLIC HEALTH

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Socioeconomic Inequalities in the Prevalence of Complex Multimorbidity in a Norwegian Population: Findings from the Cross-sectional HUNT Study

Kristin H Vinjerui,[1,2,3,*] Ottar Bjerkeset,[4,5] Johan H Bjorngaard,[4,6] Steinar Krokstad,[1,3] Kirsty Douglas,[2] Erik R Sund.[1,4]

1 HUNT Research centre, Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Levanger, Norway

2 Academic Unit of General Practice, Australian National University Medical School, Canberra, Australia

3 Psychiatric Department, Levanger Hospital, Nord-Trøndelag Hospital Trust, Norway.

4 Faculty of Nursing and Health Sciences, Nord University, Levanger, Norway

5 Department of Mental Health, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, Norway

6 Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, NTNU - Norwegian University of Science and Technology, Trondheim, Norway

*Corresponding author: Kristin Hestmann Vinjerui, HUNT Research centre, Forskningsvegen 2, 7600 Levanger, Norway. E-mail: Kristin.vinjerui@ntnu.no.Tel.: 0047-90173201/74019240/74075180

WORD COUNT

Abstract: 282 words.

Text: 3593 words.

KEYWORDS

Multimorbidity. Socioeconomic status. Occupations. Public health. Health inequality. The HUNT Study.

ABSTRACT

Objectives: Multimorbidity, the co-occurrence of multiple long-term conditions, is common and increasing. Definitions and assessment methods vary, yielding differences in estimates of prevalence and multimorbidity severity. Sociodemographic characteristics are associated with complicating factors of multimorbidity. We aimed to investigate the prevalence of complex multimorbidity by sex and occupational groups throughout adulthood.

Design: Cross-sectional study

Setting: The third total county survey of The Nord-Trøndelag Health Study (HUNT), 2006-2008, Norway.

Participants: Individuals aged 25-100 years with classifiable occupational data and complete questionnaires and measurements.

Outcome measure: Complex multimorbidity defined as “the co-occurrence of three or more chronic conditions affecting three or more different body [organ] systems within one person without defining an index chronic condition”.

Analysis: Logistic regression models with age and occupational group were specified for each sex separately.

Results: 38027 of 41193 adults (55% women) were included in our analyses. 54% of the participants were identified as having complex multimorbidity. Prevalence differences in percentage points (pp) of those in the low occupational group (vs the high occupational group [reference]) were 19 (95% CI,16 to 21) pp in women and 10 (8 to 13) pp in men at 30 years; 12 (10 to 14) pp in women and 13 (11 to 15) pp in men at 55 years; and 2 (-1 to 4) pp in women and 7 (4 to 10) pp in men at 75 years.

Conclusion: Complex multimorbidity is common from early adulthood, and social inequalities persist until 75 years in women and 90 years in men in the general population. These findings have policy implications for public health as well as health care, organization, treatment, education, and research, as complex multimorbidity breaks with the specialized, fragmented paradigm dominating medicine today.

ARTICLE SUMMARY

Strengths and limitations of this study

1. As a large, entire-county, general population health survey with a vast number of variables, the HUNT Study is ideal to estimate the prevalence of multimorbidity by self-reports and clinical measurements.
2. Complex multimorbidity operationalized as three or more organ systems affected is relevant in both clinic and research, with high specificity into old age, implicating need of coordinated multidisciplinary care and increasing comparability between studies.
3. Socioeconomic position operationalized as occupations allocated in the European Socio-economic Classification scheme makes international comparison of gradients possible.
4. Non-participants have lower socioeconomic position and higher mortality, thus the social gradients in prevalence of complex multimorbidity detected are likely conservative.
5. The original data lacked information of chronicity of a majority of the conditions, which may lead to overestimation of complex multimorbidity.

INTRODUCTION

Multimorbidity, the cooccurrence of multiple long-term conditions in which none holds priority(1) is common and increasing.(2, 3) It challenges the individual's ability to self-manage(4, 5) as well as clinical decision-making(5-7) due to complexity that conflicts with subspecialized medicine and clinical guidelines. Multimorbidity is associated with high health care utilization in both primary and specialist care,(8) including emergency department visits.(9)

Multimorbidity is heterogenous, and a mere count of conditions may not imply complexity(1, 5) requiring coordinated multidisciplinary care. In attempts to detect individuals with high needs, guidelines by and large focus on combinations of conditions, such as concurrent mental and somatic conditions(5, 10, 11) or three or more conditions in separate organ systems,(5, 12) and consequences thereof, such as polypharmacy(5, 10, 11) and requirements for assistance in daily living.(5, 10, 11) Individual factors that increase patient complexity include sociodemographic characteristics,(13) social resources,(13) and health and social experiences.(13) Recent recommendations on multimorbidity care have taken into account social networks,(11) socioeconomic positions,(11) and patient experiences, such as treatment burden.(10, 11)

Research results from cross-sectional studies on multimorbidity prevalence have been difficult to compare because of differences in definitions, methods, and the number and types of conditions included.(14, 15) Still, associations with lower socioeconomic position,(3, 14, 16) female sex,(3, 14, 16) and increasing age(3, 14, 16) persist across studies. Further, defining multimorbidity as simultaneously having three or more conditions increases the specificity of the multimorbidity measure into older age groups,(12, 15) and comparability between studies increases when multimorbidity is operationalized as multiple organ systems affected.(12)

Inequalities in health according to socioeconomic position are persistent,(17) even in comparatively egalitarian Nordic societies.(18) The association of socioeconomic differences with the occurrence of multimorbidity has been explored using multiple measures, such as education,(14, 19) income,(19) occupation,(3) and deprivation indexes.(14, 16) In fact, any measure of socioeconomic position will detect health differences in descriptive studies, if differences exist.(20) Using an occupational classification may reflect specific work-related exposures in addition to general associations to income, material resources, and social status.(20)

In sum, multimorbidity represents a challenge both for the individual and clinician, as well as for the coordination of health care. Previous multimorbidity prevalence research suggests that demographic and socioeconomic gradients operate. In Norway, multimorbidity prevalence and patterns have been partly explored.(21) Studies on complex multimorbidity is lacking, and no studies have investigated sociodemographic differences. Such data, can strengthen health care planning and clinical management of multimorbidity, as well as guide public health interventions.

Our aim is to add to former knowledge by assessing the prevalence of complex multimorbidity, defined as three or more conditions in separate organ systems, by age, sex and occupational groups, in a general population health survey.

METHODS

Reporting statement

The STROBE cross sectional reporting guidelines(22) were used for reporting of this observational study.

Study population

The HUNT Study is a population-based health study for all adults 20 years and older living in Nord-Trøndelag County, Norway. Four surveys have been completed since the 1980s, and cohort profiles and data collection procedures have been described in detail elsewhere.(23, 24) This study is a secondary analysis of data from the HUNT3 Survey (2006-2008), where 93860 citizens were invited to participate. In short, the survey consisted of a main questionnaire received with the invitation by mail and handed in when attending a screening station, where participants were interviewed and clinical measurements and biological samples were taken. A second sex- and age-specific questionnaire was handed out at the screening station and returned by mail.

A total of 50807 individuals (54% of 93860 invited) completed the main questionnaire, required to be considered an attendant of the HUNT3 Survey.(23) Sampling is described in figure 1. In this study, 41193 of 50807 participants (81%) had data on all major parts of the survey (both questionnaires, interview, measurements, and samples) and were designated as respondents. Thus, 9610 were excluded due to incomplete participation, while 4 people missed complete participation data. Under the assumption that young adults may not have obtained their highest level of occupational class at the time of participation, 1569 participants younger than 25 years were excluded, as well as 1 person with missing age data. Occupation data was missing for 1571 respondents, and 25 people were excluded due to unspecified occupation data. Finally, 38027 of 41193 (92%) respondents were eligible for data analysis, 11204 were non-eligible and 1576 had missing data.

Participation in the HUNT3 Survey vary with socioeconomic position, age and sex.(25) The distribution of occupational groups among the sample were; 24% (high), 27% (middle) and 49% (low) and in non-eligible; 17% (high), 20% (middle), 52% (low) and 11% (missing). The average (standard deviation) age in the sample was 55 (14) years, in the non-eligible group 44 (18) years and among missing 66 (18) years. Women constituted 55% (n=20813 of 38027) of the sample, 51% (n=5662 of 11203) of the non-eligible and 81% of the missing (n=1281 of 1576).

Figure 1. Flowchart for sample selection; inclusion and exclusion criteria, and missing data.

Outcome variable

Complex multimorbidity was defined as “the co-occurrence of three or more chronic conditions affecting three or more different body [organ] systems within one person without defining an index chronic condition”, as suggested by previous research.(5, 12)

All conditions possible to generate from the HUNT3 Survey data were included to meet recommendations on deriving the best estimate of prevalence of multimorbidity.(12) In total, 51 chronic conditions, defined singly as far as original data permitted, were constructed, and

details are described in appendix A. This list of 51 conditions is more comprehensive and homogenous than previous operationalizations of multimorbidity in the HUNT3 Survey.(21)

Further, the conditions were grouped according to the *ICD-10* in 13 organ-specific chapters and one chapter on symptoms, signs, and abnormal clinical and laboratory findings (table 1), using general terms of the conditions in the Norwegian Directorate of eHealth online search engine(26) on February 1 2017.

Chapters were counted once if affected by at least one chronic condition and a summary score of the chapter variables was generated. In this study, complex multimorbidity was defined as having conditions in at least 3 of 14 chapters.

Sociodemographic Characteristics

Occupation data from the HUNT3 Survey were free-text answers to the interview question, "What is/was the title of your main occupation?" Answers were manually categorized corresponding to Standard Classifications of Occupations by Statistics Norway,(27) which is based on the International Standard Classification of Occupations-88 (ISCO-88).(28) Socioeconomic position was allocated according to the simplified, 3-class version European Socio-economic Classification (ESeC) scheme.(29) The simplified scheme is based solely on occupational data, classified according to ISCO-88.(28) Details are provided in appendix B. The intention of the full ESeC scheme is to measure qualitative distinctions between employment relationships and does not reflect a clear hierarchy.(29) However, income is considered more stable in the salariat class.(29) In the 3-class version, the salariat class consists of large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, and higher-grade technician and supervisory occupations. The intermediate class contains small employers, self-employed individuals, and lower-grade supervisory and technician occupations. The working class represents lower-grade service positions, sales and clerical occupations, and lower-grade technical and routine occupations. For practical reasons in this study, the terms high, middle, and low occupational group replaced the terms salariat, intermediate, and working class, respectively.

In addition, continuous age and categorical sex data, provided by the HUNT databank, were used in the analyses.

Table 1. Conditions grouped by *ICD-10* chapter

***ICD-10* chapter**	Conditions
II	**Neoplasms**
	Cancer
III	**Blood/blood-forming organs/ immune mechanism**
	Sarcoidosis
IV	**Endocrine/nutritional/metabolic**
	Obesity
	Hypercholesterolemia
	Diabetes
	Hypothyroidism
	Hyperthyroidism
V	**Mental/behavioral**
	Alcohol problem
	Depression
	Anxiety
	Insomnia
VI	**Nervous system**
	Epilepsy
	Migraine
	Chronic headache, other
VII	**Eye/adnexa**
	Cataract
	Macula degeneration
	Glaucoma
VIII	**Ear/mastoid**
	Hearing impairment
IX	**Circulatory system**
	Hypertension
	Angina pectoris
	Myocardial infarction
	Heart failure
	Other heart disease[1]
	Stroke or brain haemorrhage[1]
X	**Respiratory system**
	Chronic bronchitis, emphysema, or COPD[1,2]
	Asthma
XI	**Digestive system**
	Dental health status
	Gastro-oesophageal reflux disease
	Irritable bowel syndrome
XII	**Skin/subcutaneous tissue**
	Hand eczema
	Psoriasis
XIII	**Musculoskeletal/connective tissue**
	Rheumatoid arthritis
	Osteoarthritis
	Ankylosing spondylitis
	Fibromyalgia
	Osteoporosis
	Local musculoskeletal pain/stiffness in:
	- Neck
	- Upper back
	- Lower back
	- Shoulder
	- Elbow
	- Hand
	- Hip
	- Knee
	- Foot/ankle
XIV	**Genitourinary system**
	Kidney disease
	Urine incontinence
	Prostate symptoms
	Menopausal hot flashes
XVIII	**Symptoms/signs/abnormal clinical/ laboratory findings**
	Nocturia
	Chronic widespread pain

[1] = Exception to single entity
[2]COPD = Chronic Obstructive Pulmonary Disease

Statistical analysis

Cross-tables were used to present sociodemographic characteristics of the sample by occupational group (table 2) and by complex multimorbidity, stratified by sex (table 3).

Associations between occupational group and complex multimorbidity were analyzed using logistic regression. The final models were stratified by sex, included occupational group, continuous age, and an interaction term between occupational group and age. Choice of models were guided by likelihood ratio tests.

Since complex multimorbidity was highly prevalent, odds ratios would deviate from relative risks(30) and be challenging to interpret. Thus, we used the estimates from the logistic regression models to derive prevalence differences, the difference in mean predicted probability,(31) and prevalence ratios, the ratio between the mean predicted probabilities,(31) between occupational groups, while holding other covariates constant. The high occupational group was chosen as the reference group. Prevalence differences and prevalence ratios were calculated in 5-year intervals from 25 to 100 years, with 95% confidence intervals (CIs) (appendix C) Results for the ages 30, 55, 75, and 90 years are presented in table 4 to represent adult, middle aged, aged and oldest old in the sample.

To visualize the differential association between age and complex multimorbidity in each occupational group, we specified separate models using restricted cubic splines and graphed the findings from each model into a common plot for each sex.

Sensitivity analysis was performed to investigate if the number and types of conditions showed a similar pattern with respect to the overall prevalence as well as differences between occupational groups (appendix D). The alternative complex multimorbidity measure was derived from data in the main questionnaire only (22 conditions, grouped in 12 *ICD-10* chapters)

Complete case analysis was performed, and Stata version 15.1 was used to analyze the data (StataCorp, College Station, TX, USA).

Patient and public involvement

There was a broad participant, patient, and stakeholder involvement during the planning of the HUNT3 Survey. Data collection was performed in 2006-2008. Complex multimorbidity is a universal subject, not represented by any particular patient group, and thus no patient or public representative was involved in the design of this secondary analysis study.

RESULTS

38027 individuals, aged 25 to 100 years, 55% women (n=20813), who had completed all major parts of the HUNT3 Survey and had a classifiable occupation comprised the eligible sample, as fig. 1 depicts. Table 2 presents further sociodemographic characteristics.

Table 2. Sex and age distribution by occupational group. The HUNT Study (2006-08).

	Occupational group							
	High		Middle		Low		Total	
	Freq.	(%)	Freq.	(%)	Freq.	(%)	Freq.	(%)
Total	8 970	(100)	10 243	(100)	18 814	(100)	38 027	(100)
Sex								
Women	4 505	(50)	5 386	(53)	10 922	(58)	20 813	(55)
Men	4 465	(50)	4 857	(47)	7 892	(42)	17 214	(45)
Age, yr.								
25-44	2 837	(32)	2 600	(25)	4 487	(24)	9 924	(26)
45-64	4 468	(50)	4 787	(47)	8 951	(48)	18 206	(48)
65-74	1 118	(12)	1 846	(18)	3 297	(18)	6 261	(16)
75-100	547	(6)	1 010	(10)	2 079	(11)	3 636	(10)

Abbreviations: freq., frequency, yr., years.

Nearly half the sample (49%; n=18814 of 38027; of which 58% were women, n=10922), was allocated in the low occupational group. In absolute numbers, the low occupational group was the largest socioeconomic category in both sexes and all age groups. The proportion of individuals aged 25 to 44 years decreased from 32% in the high occupational group (n=2837) to 24% in the low occupational group (n=4487), while the proportion of individuals aged 75 to 100 years increased from 6% (n=547) to 11% (n=2079). Participants aged 45 to 64 years were the largest age group in total and in all occupational groups (high, n=4468; middle, n=4787; low, n=8951).

Table 3. Sociodemographic distribution of complex multimorbidity. The HUNT Study (2006-08).

	Complex multimorbidity											
	Women						Men					
	No, *n*	(%)	Yes, *n*	(%)	Total, *n*	(%)	No, *n*	(%)	Yes, *n*	(%)	Total, *n*	(%)
Total	8 505	(41)	12 308	(59)	20 813	(100)	9 137	(53)	8 077	(47)	17 214	(100)
Occupational group												
High	2 460	(55)	2 045	(45)	4 505	(100)	2 712	(61)	1 753	(39)	4 465	(100)
Middle	2 384	(44)	3 002	(56)	5 386	(100)	2 525	(52)	2 332	(48)	4 857	(100)
Low	3 661	(34)	7 261	(66)	10 922	(100)	3 900	(49)	3 992	(51)	7 892	(100)
Age, years												
25-44	3 859	(65)	2 122	(35)	5 981	(100)	2 958	(75)	985	(25)	3 943	(100)
45-64	3 668	(37)	6 172	(63)	9 840	(100)	4 621	(55)	3 745	(45)	8 366	(100)
65-74	721	(23)	2 447	(77)	3 168	(100)	1 155	(37)	1 938	(63)	3 093	(100)
75-100	257	(14)	1 567	(86)	1 824	(100)	403	(22)	1 409	(78)	1 812	(100)
Mean (SD)	48	(13)	59	(14)	54	(14)	52	(13)	62	(13)	56	(14)

Overall, a majority (54%; n=20385 of 38027) of the sample met the criteria for having complex multimorbidity, including 59% of women (n=12308) and 47% of men (n=8077; table 3). The percentages increased from high to low occupational group in women from 45% (n=2045) to 66% (n=7261) and in men from 39% (n=1753) to 51% (n=3992). The proportions further increased by age, from 35% (n=2122) of women aged 25 to 44 years to

86% (n=1567) of women aged 75 to 100 years. In men, the increase was from 25% (n=985) to 78% (n=1409) in the same age groups. In absolute numbers, most people classified as having complex multimorbidity were aged 45 to 64 years (women, n=6172; men, n=3745).

Table 4. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational groups, stratified by sex.

Age, years	Occupational group	Women				Men			
		PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
30	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.47	(1.28, 1.68)	0.08	(0.05, 0.11)	1.28	(1.05, 1.55)	0.03	(0.01, 0.06)
	Low	2.06	(1.84, 2.32)	0.19	(0.16, 0.21)	1.92	(1.63, 2.26)	0.10	(0.08, 0.13)
55	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.08	(1.03, 1.12)	0.04	(0.02, 0.06)	1.16	(1.10, 1.23)	0.06	(0.04, 0.08)
	Low	1.22	(1.18, 1.26)	0.12	(0.10, 0.14)	1.35	(1.28, 1.41)	0.13	(0.11, 0.15)
75	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.98	(0.95, 1.02)	-0.01	(-0.04, 0.02)	1.07	(1.02, 1.12)	0.05	(0.02, 0.08)
	Low	1.02	(0.99, 1.05)	0.02	(-0.01, 0.04)	1.10	(1.06, 1.15)	0.07	(0.04, 0.10)
90	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.98	(0.96, 1.00)	-0.02	(-0.04, 0.00)	1.03	(0.99, 1.07)	0.03	(-0.01, 0.06)
	Low	0.99	(0.97, 1.01)	-0.01	(-0.03, 0.01)	1.03	(0.99, 1.07)	0.02	(-0.01, 0.05)

Table 4 shows prevalence ratios and prevalence differences between the occupational groups after adjusting for age and occupation-age interaction and thus presented at ages 30, 55, 75, and 90 years. Prevalence differences for complex multimorbidity between high and low occupational groups varied; at 30 years, 19 (16 to 21) percentage points (pp) in women and 10 (8 to 13) pp in men; at 55 years, 12 (10 to 14) pp in women and 13 (11 to 15) pp in men; at 75 years, 2 (-1 to 4) pp in women and 7 (4 to 10) pp in men; and at 90 years, -1 (-3 to 1) pp in women and 2 (-1 to 5) in men. Compared with the high occupational group, the prevalence ratios for the low occupational group for complex multimorbidity were at 30 years, 2.06 (1.84 to 2.32) in women and 1.92 (1.63 to 2.26) in men; at 55 years, 1.22 (1.18 to 1.26) in women and 1.35 (1.28 to 1.41) in men; at 75 years, 1.02 (0.99 to 1.05) in women and 1.10 (1.06 to 1.15) in men; and at 90 years, 0.99 (0.97 to 1.01) in women and 1.03 (0.99 to 1.07) in men.

In the sensitivity analyses where the complex multimorbidity measure was derived from fewer conditions (22 vs 51) and *ICD-10* chapters (12 vs 14), the total prevalence was 15% (n=5836 of 38027, appendix D). Proportions were greater in women, higher age and the low occupational group. Compared to the results from the main analysis prevalence differences between high and low occupational groups were smaller in women at all ages and in men at age 30 years and 55 years, while prevalence ratios were greater in men at all ages and in women age 30 and 55 years.

Figure 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

Figure 2 depicts estimated prevalence of complex multimorbidity by occupational group and sex individuals aged 25 to 100 years. In all occupational groups in both sexes, the predicted prevalence increased with age throughout the age span. Further, estimated prevalence differed between the occupational groups in women until age 75 years and in men until age 90 years. Women had a consistently higher prevalence for complex multimorbidity than men.

DISCUSSION

Main results

More than half (54%) of this total county adult population sample were identified with complex multimorbidity, measured as occurrence of chronic conditions in minimum three separate organ systems. Prevalence of complex multimorbidity was common from early adulthood, increased with age, and was higher in women and in the low occupational group. Occupational group prevalence differences and ratios in complex multimorbidity were diminishing in women, while still present in men, at age 75 years.

Comparison with existing literature

Few, if any, studies (to our knowledge) have investigated the prevalence and determinants of complex multimorbidity in a general population. The findings are in keeping with known determinants of lower social position, female sex, and higher age for multimorbidity in both general population(19) and primary care studies.(3, 14, 16) An Australian study using a comparable operationalization of complex multimorbidity identified nearly 25% of patients in general practice with complex multimorbidity and estimated a national prevalence of 17%.(32) However, higher prevalence findings from our predominantly self-reported data are compatible with studies comparing prevalence estimates from self-reports and health record data.(33, 34) In absolute numbers, the incidence of individuals identified with the stricter measure of complex multimorbidity is still highest among the group younger than 64 years, as has been shown for multimorbidity.(16, 19, 35) The sensitivity analysis confirms how number and types of conditions influence prevalence(12, 15) and effect estimates of age, sex, and socioeconomic position.(36)

Mechanisms to explain findings

The association between lower socioeconomic position and poor health is well established. In general, unequal distribution of income, power, and wealth are understood to be socially determined fundamental causes that impact conditions of everyday life and result in social health inequities.(17) In Nordic countries assumed to be egalitarian and offering universal health care, social health inequities still exists.(18) Theories put forward are the survival of individuals with greater frailty, who are more likely to obtain a lower social position.(37) The gap in health is also explained by overall morbidity and mortality decreasing faster among the higher than the lower socioeconomic groups.(37)

In this study, occupational group serves as the proxy variable for socioeconomic position. Occupation may affect health outcomes through universal and specific mechanisms. In general, the higher occupational groups will have more secure and higher income,(29, 38) as well as advantageous social networks.(38) In particular, jobs vary in psychosocial factors, such as stress, control, and autonomy and biological factors, such as physical demands or harmful and hazardous work environments.(38) Overall, the higher occupational group have greater autonomy and control,(29) while lower occupational groups are more exposed to

malign work factors.(17) Generations may have different associations between a profession and health outcomes,(38) as occupations, tasks, and exposures shift over time.

The bidirectional relationship between health and occupation,(20) may partly explain the larger prevalence differences and ratios between low and high occupational groups in the younger age categories. Higher rates of multimorbidity in young individuals in lower socioeconomic positions may also be explained by detection bias(35) in which the initiation of therapy and health care follow-up increase the likelihood of diagnosing more conditions. Diminishing occupational ratios and differences among the oldest may be explained by the higher overall prevalence of complex multimorbidity(39) and also survival bias, whereby the individuals with greatest fragility have already died. While probability of complex multimorbidity increase with age, the age distribution results in a higher number of cases occurring in those younger than 64 years.

Strengths and limitations

Strengths of this study is the estimation of prevalence of complex multimorbidity from a general population survey, the most common study design in multimorbidity studies.(40) A vast number of self-reported conditions are included, almost exclusively diagnoses and symptoms.(40) Self-report is considered a valid approach when studying large samples.(15) Furthermore, using all available data will produce the most proper prevalence estimates,(12) which in this study is demonstrated by the sensitivity analysis and which seems necessary to detect occupational differences in younger age groups. The sensitivity analyses confirm that the spectrum of conditions included may affect associations with socioeconomic position, age, and sex.(36)

Our operationalization of complex multimorbidity makes the prevalence estimates comparable to other studies categorizing conditions by any organ-based system.(12) The occurrence of conditions in separate organ, and number of organ systems, could have been explored as a continuous measure with assumed increasing severity, however this was beyond the scope of this study.

The allocation of occupations in the European Socio-economic Classification also makes international comparison of social gradients possible.(29) We presented absolute and relative differences in compliance with recommendations on measurements of socioeconomic inequalities in health.(41) Results are further stratified by age and sex, which are stated as minimum requirements for proper reporting of multimorbidity.(14)

A number of limitations should be noted. Our study is based on data collected for a general health survey, and this limits data on conditions included in the complex multimorbidity measure. In particular, we did not have explicit information on chronicity for a majority of the conditions. Thus, the prevalence of complex multimorbidity may be overestimated.

Socioeconomic position was explored using only occupation, and while social health inequalities will be detected,(20) socioeconomic measures are not interchangeable.(20, 42) Different measures of socioeconomic position will act through varying mechanisms and may associate distinctively with health outcomes.(20, 42) Participants in HUNT3 reported their main occupation, while current or longest-lasting occupation is more often studied.(38) Younger subjects may be misclassified in lower socioeconomic position, which may underestimate the occupational differences in health in this age group, whereas reverse causation, whereby prior health status determines job opportunities, is unavoidable and will

increase detected differences. This study excludes those never having worked, which will underestimate social gradients in complex comorbidity.(43) Further, missing due to unclassifiable occupation, more common in elderly women than other participants, were excluded. Occupational data may misrepresent present social context(38) and thereby underestimate social inequalities. It would have been favorable if the study had included education, income or household indicators for socioeconomic position.

Participation in the HUNT3 Survey varied by age, sex, socioeconomic position, and pattern of morbidity.(25) This may weaken the effect estimates of the determinants to complex multimorbidity. A healthy elders bias is likely, since participation required attendance at a screening station.(23) Overall, prevalence of individual conditions have shown only slight differences between participants and nonparticipants.(25) The HUNT study is considered fairly representative for Norway,(24) and the health development in the material follows western high-income country trends closely.(44-46)

Implications for clinical practice and policy makers

Our study confirms that complex multimorbidity, a suggested measure to identify multimorbid individuals with high need for coordinated multidisciplinary care,(12) is highly prevalent in the general population, where social differences are evident from young to old adulthood. This is in line with international studies, and at policy level, an emphasis on public health intervention to prevent complex multimorbidity and social differences seems necessary. As proposed elsewhere, this will likely require a proportionate universalism life-cycle approach.(47) To improve and secure health care for this large patient group, clinical guidelines and the organization of health care is suggested to adapt to a person-centered, generalist approach.(5, 10, 48)

Future research

Complex multimorbidity is common in this general population sample, with a clear social gradient throughout adulthood. Careful interpretation is necessary, since there are possible biases in measures of multimorbidity and occupation. However, the HUNT3 Survey data covers a broad spectrum of conditions and gives a unique opportunity to create several measures of multimorbidity in the same sample, with directly comparable prevalence estimates and gradients. On this background, we recommend exploring alternative measures suggested to detect individuals with high needs and multimorbidity and investigate differences in patterns, and consequences of such measures by social health determinants. Since multimorbidity is the norm and represents a large challenge to health care across levels, research on overall health care utilization and organization should be a priority, as well as studying competing measures as prognostic factors for mortality. Studies on social differences in use of health care may identify vulnerable subgroups, where any specific organization of treatment later on could be evaluated.

CONCLUSION

Complex multimorbidity, defined as occurrence of chronic conditions in three separate organ systems, is common, and occupational differences exists throughout adulthood in both sexes. The magnitude of complex multimorbidity in all age groups implies the need for public health management to universally improve, targeted proportionate to need and disadvantage in subpopulations, social health determinants throughout the lifespan. Complex multimorbidity, indicating the accumulation of conditions of different etiology requiring

coordinated multidisciplinary care, should inspire health caregivers, health care organizations, educational institutions, and researchers to take on a generalist and person-centered focus. Studying alternative multimorbidity measures, including health care utilization and mortality according to social background, as well as multimorbidity management, should be prioritized in future research.

FIGURES

Fig. 1. Flowchart for sample selection; inclusion and exclusion criteria and missing data.
Fig. 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men.

ACKNOWLEDGEMENTS

L Getz, J Sigurdsson and C Harrison for through discussions on measures of multimorbidity. E Solheim for guidance in the use of the European Socio-economic Classification scheme. MS Newman for writing assistance.
The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between HUNT Research Centre (Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU), Nord-Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health.

COMPETING INTERESTS

None declared.

FUNDING STATEMENT

Funding source: This study was funded by the Faculty of Medicine and Health Science at the Norwegian University of Science and Technology (NTNU) through the PhD program in Behavior and Health (KHV). NTNU has partly funded the HUNT3 Survey and have funded open access for this article. The Liaison Committee for Education, Research and Innovation in Central Norway (17/38297) supported a research stay at the Australian National University, Canberra. The funding sources have had no role in conceptualization this study, its design and methods, analysis and interpretation of data, writing of the article or the decision to submit the article for publication.

AUTHOR CONTRIBUTIONS

KHV, ERS, SK and JHB conceptualized the study and KHV, ERS, SK, JHB, OB and KD contributed to its design. KHV has analysed the data under supervision of ERS and KHV, ERS, SK, JHB, OB and KD have contributed to interpreting the data. KHV wrote the original draft, which has been revised critically by ERS, SK, JHB, OB and KD. KHV, ERS, SK, JHB, OB and KD have read and approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

PATIENT CONSENT

Written informed consent was obtained from all participants in the HUNT3 Survey and all participation was voluntary.

ETHICS APPROVAL

The Regional Committee for Medical and Health Research Ethics in Norway approved the current study (project no. 2014/2265).

DATA SHARING STATEMENT

To protect participants' privacy, HUNT Research Centre aims to limit storage of data outside HUNT databank and cannot deposit data in open repositories. HUNT databank has precise information on all data exported to different projects and are able to reproduce these on request. There are no restrictions regarding data export given approval of applications to HUNT Research Centre. For more information see: http://www.ntnu.edu/hunt/data

SUPPLEMENTARY FILES

Appendix A: Construction of chronic, single entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Appendix B: Operationalizing socioeconomic position using occupation.

Appendix C: Prevalence ratios and differences with 95% CI in complex multimorbidity between occupational groups in 5-year intervals (25 to 100 years), stratified by sex.

Appendix D: Sensitivity analyses, sociodemographic characteristics and prevalence ratios and differences with 95% CI.

REFERENCES

1. Nicholson K, Makovski T, Griffith L, et al. Multimorbidity and comorbidity revisited: refining the concepts for international health research. J Clin Epidemiol. 2019;105:142-6.
2. van Oostrom SH, Gijsen R, Stirbu I, et al. Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. PLoS One. 2016;11(8):e0160264.
3. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. Eur J Gen Pract. 2008;14 Suppl 1(sup1):28-32.
4. Coventry PA, Fisher L, Kenning C, et al. Capacity, responsibility, and motivation: a critical qualitative evaluation of patient and practitioner views about barriers to self-management in people with multimorbidity. BMC Health Serv Res. 2014;14(1):536.
5. Wallace E, Salisbury C, Guthrie B, et al. Managing patients with multimorbidity in primary care. BMJ. 2015;350:h176.
6. Sondergaard E, Willadsen TG, Guassora AD, et al. Problems and challenges in relation to the treatment of patients with multimorbidity: General practitioners' views and attitudes. Scand J Prim Health Care. 2015;33(2):121-6.
7. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. BMJ. 2012;345:e6341.
8. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. Fam Pract. 2011;28(5):516-23.
9. Agborsangaya CB, Lau D, Lahtinen M, et al. Health-related quality of life and healthcare utilization in multimorbidity: results of a cross-sectional survey. Qual Life Res. 2013;22(4):791-9.
10. National Institute for Health and Care Excellence. Multimorbidity: clinical assessment and management. NICE guideline [NG56]. https://www.nice.org.uk/guidance/ng56: National Institute for Health and Care Excellence,; 2016 December 2016.
11. Palmer K, Marengoni A, Forjaz MJ, et al. Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS). Health Policy. 2018;122(1):4-11.
12. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. BMJ Open. 2014;4(7):e004694.
13. Schaink AK, Kuluski K, Lyons RF, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. Journal of comorbidity. 2012;2:1-9.
14. Violan C, Foguet-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(7):e102149.
15. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. Ann Fam Med. 2012;10(2):142-51.
16. 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. 2012;380(9836):37-43.
17. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health. Marmot M, editor. Geneva2008. 256 p.
18. Mackenbach JP, Stirbu I, Roskam AJ, et al. Socioeconomic inequalities in health in 22 European countries. N Engl J Med. 2008;358(23):2468-81.
19. Agborsangaya CB, Lau D, Lahtinen M, et al. Multimorbidity prevalence and patterns across socioeconomic determinants: a cross-sectional survey. BMC Public Health. 2012;12:201.
20. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. Br Med Bull. 2007;81-82(1):21-37.
21. Tomasdottir MO, Getz L, Sigurdsson JA, et al. Co-and multimorbidity patterns in an unselected Norwegian population: Cross-sectional analysis based on the HUNT Study and theoretical

reflections concerning basic medical models. European Journal for Person Centered Healthcare. 2014;2(3):335-45.
22. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014;12(12):1495-9.
23. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: the HUNT Study, Norway. Int J Epidemiol. 2013;42(4):968-77.
24. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. Norsk epidemiologi. 2003;13(1):19-32.
25. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. BMC Med Res Methodol. 2012;12:143.
26. Direktoratet for e-helse. FinnKode - Helsedirektoratet medisinske kodeverk 2017 [Available from: https://finnkode.ehelse.no/#icd10/0/0/0/-1.
27. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway; 1998.
28. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm.
29. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. Eur Soc. 2007;9(3):459-90.
30. Sedgwick P. Relative risks versus odds ratios. Bmj-British Medical Journal. 2014;348(feb07 2):g1407-g.
31. Norton EC, Miller MM, Kleinman LC. Computing Adjusted Risk Ratios and Risk Differences in Stata. The Stata Journal: Promoting communications on statistics and Stata. 2018;13(3):492-509.
32. Harrison C, Henderson J, Miller G, et al. The prevalence of complex multimorbidity in Australia. Aust N Z J Public Health. 2016;40(3):239-44.
33. Cricelli C, Mazzaglia G, Samani F, et al. Prevalence estimates for chronic diseases in Italy: exploring the differences between self-report and primary care databases. J Public Health Med. 2003;25(3):254-7.
34. Fortin M, Haggerty J, Sanche S, et al. Self-reported versus health administrative data: implications for assessing chronic illness burden in populations. A cross-sectional study. CMAJ Open. 2017;5(3):E729-E33.
35. van den Akker M, Buntinx F, Metsemakers JF, et al. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. J Clin Epidemiol. 1998;51(5):367-75.
36. Schafer I, Hansen H, Schon G, et al. The influence of age, gender and socio-economic status on multimorbidity patterns in primary care. First results from the multicare cohort study. BMC Health Serv Res. 2012;12:89.
37. Huijts T, Eikemo TA. Causality, social selectivity or artefacts? Why socioeconomic inequalities in health are not smallest in the Nordic countries. Eur J Public Health. 2009;19(5):452-3.
38. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). J Epidemiol Community Health. 2006;60(1):7-12.
39. Scanlan JP. Guest Editorial. Chance. 2013;19(2):47-51.
40. 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(2):112-21.
41. Mackenbach JP, Kunst AE. Measuring the magnitude of socio-economic inequalities in health: an overview of available measures illustrated with two examples from Europe. Soc Sci Med. 1997;44(6):757-71.

42. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: one size does not fit all. JAMA. 2005;294(22):2879-88.
43. Martikainen P, Valkonen T. Bias related to the exclusion of the economically inactive in studies on social class differences in mortality. Int J Epidemiol. 1999;28(5):899-904.
44. Collaboration NCDRF. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. Nature. 2019;569(7755):260-4.
45. Collaboration NCDRF. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. Lancet. 2017;389(10064):37-55.
46. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017;390(10113):2627-42.
47. Marmot M, Goldblatt P, Allen J, et al. Fair Society, Healthy Lives.: The Marmot Review; 2010. 242 p.
48. World Health Organization. Multimorbidity: Technical Series on Safer Primary Care. In: Organization WH, editor. Licence: CC BY-NC-SA 3.0 IGO. ed. Geneva.: World Health Organization; 2016. p. p. 4-5.

Fig. 1. Flowchart sample selection: inclusion and exclusion criteria and missing data.

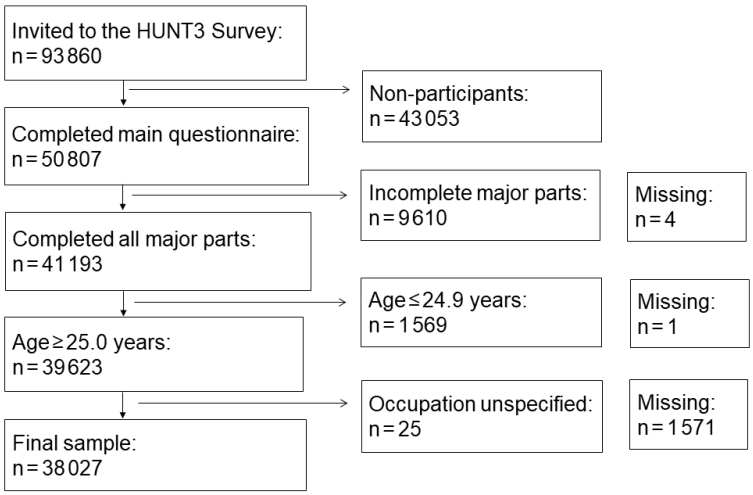

Figure 1. Flowchart for sample selection; inclusion and exclusion criteria, and missing data

338x190mm (96 x 96 DPI)

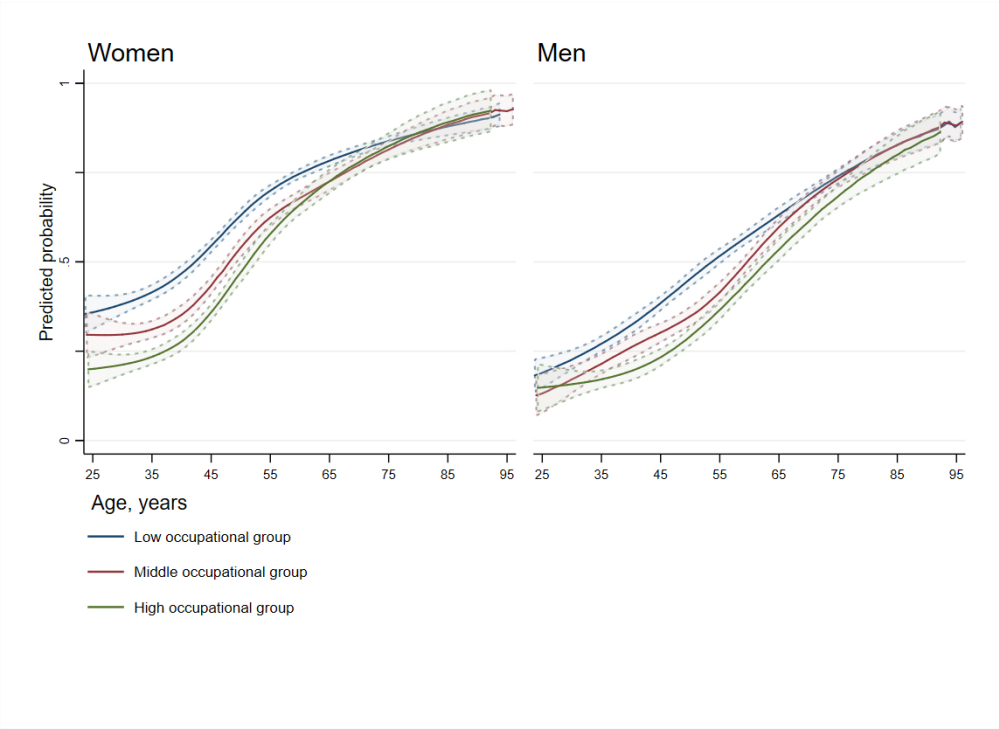

Figure 2. Estimated prevalence of complex multimorbidity with 95% CIs by age and occupational group for women and men

403x293mm (72 x 72 DPI)

Appendix A

Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

ORIGINAL QUESTIONNAIRE, ENGLISH VERSION

Main questionnaire

https://www.ntnu.edu/c/document_library/get_file?uuid=129b68c3-520c-457f-8b98-02c49219b2ee&groupId=140075

Sex- and age-specific questionnaire

https://www.ntnu.edu/c/document_library/get_file?uuid=35ae2816-4155-4b64-a259-770946fa46d4&groupId=140075

GENERAL COMMENTS

Chronicity

Chronicity was defined by either 1: duration (3 months or longer), 2: causing functional limitation (physical, mental, social) or 3: requiring health care management (pharmacological or not, primary or specialist care),[1] or 4: chronicity was assumed based on medical knowledge and clinical experience.

Missing

In variables with index questions and cluster text, missing was in general corrected for affirmed index question and regarded as “no” if replied to any alternative to any of the other questions in the block. Information on missing is also collected from the HUNT Databank.

References

References hold information on construction or accuracy of self-report of, or comparison of prevalence of the conditions to primary care and/or non-participant data. In general, self-report is considered to give reliable estimates of multimorbidity in studies of large samples.[2]

MAIN QUESTIONNAIRE

Hearing impairment[3]

Index question: “Do you suffer from longstanding (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” Yes, no.
Options on follow-up question combined condition type (motor, vision, hearing, somatic, and psychiatric) and severity (slight, moderate, and severe).
Included with hearing impairment were those who reported chronic disease and moderate to severe hearing impairment.

“20 Diseases”: Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis

Cluster text: “Have you had or do you have any of the following;
Myocardial infarction;[4 5] angina pectoris;[5 6] heart failure;[4] other heart disease; stroke[4 5] or brain haemorrhage; kidney disease;[5] asthma;[5] chronic bronchitis, emphysema or chronic obstructive pulmonary disease; diabetes;[4 5] psoriasis;[7] eczema on hands; [8 9] cancer;[5 10] epilepsy;[11] rheumatoid arthritis;[5 12] ankylosing spondylitis;[5 12] sarcoidosis; osteoporosis;[5 13] fibromyalgia[5] and osteoarthritis[5]?”
Separate tick boxes for each diagnosis: Yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

SEX- AND AGE-DIFFERENTIATED QUESTIONNAIRE

Headache[5]

Seven questions in one block. Question 1: “Have you had headaches in the last year?” Yes/no.

Migraine without aura[14]

Of those who affirmed headache last year, migraine without aura was constructed from three of seven questions:

1. “What is the average strength of your headaches?” 1=Mild, 2=Moderate, 3=Strong.
   Recoded to dichotomous variable, where 1=Moderate/Strong.
2. “How long does the headache usually last?” 1=Less than 4 hours, 2=4 hours - 1 day, 3=1 - 3 days, 4= More than 3 days.
   Recoded to dichotomous variable, where 1= Less than 4 hours – 3 days.
3. Cluster text: “Are the headaches usually characterized or accompanied by
   - Throbbing/thumping pain?” Yes, no.
   - Pain on one side of the head?” Yes, no.
   - Worsening with physical activity?” Yes, no.
   - Nausea and/or vomiting?” Yes, no.
   - Hypersensitivity to light and/or noise?” Yes, no.

Included with migraine: were those who affirmed to headache lasting 0 to 72 hours and at least two of four characteristics (pulsating quality, unilateral location, moderate/severe pain intensity, or aggravation by physical activity) and during headache having at least one of two accompanying symptoms (nausea and/or vomiting or increased sensitivity to light and/or noise).[14]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic headache[14]

Of those who affirmed headache last year, chronic headache was constructed from two of seven questions:

1. "If yes (headache in the last year): What type of headache? Migraine, other."
   The HUNT Databank created two variables with range 1: 1) migraine and 2) other headache.
2. "Average number of days a month with headaches:"
   1=Less than 1 day, 2=1-6 days, 3=7-14 days, 4=More than 14 days.
   Recoded to dichotomous variable, where 1= More than 14 days.

Included as case with chronic headache were those reporting "other" type of headache and an average frequency of more than 14 days per month.
Chronicity is assumed based on medical knowledge and clinical experience.

Pain[5]

Index question: "In the last year, have you had pain or stiffness in muscles or joints that has lasted at least 3 consecutive months?" Yes, no.
The follow-up question "If yes: Where have you had this pain or stiffness?" was combined with a figure with arrows and tick boxes at nine locations (neck, upper back, lower back, shoulder, elbow, hand, hip, knee and ankle/foot).

Chronic widespread pain[15]

Dichotomous variables were made for each major body area: 1) Trunk (neck, upper and lower back),
2) Upper limb (shoulder, elbow, hand), and 3) Lower limb (hip, knee, foot/ancle), where 1=At least one painful location. A sum (row total) score variable was made for the major body areas and dichotomized, where 1=3, that is one pain in each major body area.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic widespread pain was defined as pain at more than three sites in all major body areas (trunk, upper and lower limbs) for more than three months in the last year.

Chronic, local pain

Of those who affirmed to pain or stiffness that has lasted more than three consecutive months,
chronic, local pain was defined as pain in the neck or upper back or lower back or shoulder or elbow or hand or hip or knee or ancle/foot, excluding presence of chronic widespread pain, generating nine dichotomous variables.

Thyroidal disease[5]

Cluster text: “Has it ever been verified that you have/have had hypothyroidism or hyperthyroidism?” Separate tick boxes for each condition (yes, no), generating two dichotomous variables, 1=Yes.
For each diagnosis, included were those who affirmed to have or have had the diagnosis. Chronicity is assumed based on medical knowledge and clinical experience.

Irritable bowel syndrome[16 17]

Index question: “Have you had stomach pain or discomfort in the last 12 months?” Answers: Yes, much; yes, a little; no. Irritable bowel syndrome was further constructed from four of six follow-up questions: “If yes:
“In the last 3 months, have you had this as often as 1 day a week for at least 3 weeks?” Yes, no.
“Is the pain/discomfort relieved by having a bowel movement?” Yes, no.
“Is the pain/discomfort related to more frequent or less frequent bowel movements than normal?” Yes,no.
“Is the pain/discomfort related to the stool being softer or harder than usual?” Yes, no.

Included with irritable bowel syndrome were those who affirmed little or much stomach pain or discomfort in the last year, who for as often as 1 day a week for at least 3 weeks in the last 3 months have had at least two of the following: pain/discomfort relieved by having a bowel movement, related to altered frequency of bowel movements, or related to altered stool appearance, resembling a modified version of the Rome criteria.[16 17]

Gastro-oesophageal reflux disease[5 18]

Cluster text: “To what degree have you had the following problems in the last 12 months?” Options combined type (nausea, heartburn/acid regurgitation, diarrhea, constipation, alternating constipation and diarrhea, and bloating) and frequency (never, a little, or much). Generated one dichotomous variable, heartburn, where 1=Much.
Gastro-oesophageal reflux disease is defined as much heartburn/acid regurgitation in the last 12 months.[18]

Anxiety[5 19]

Instrument variable: Hospital Anxiety and Depression Scale.[19] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed a total score for anxiety (HADS-A), if all 7 anxiety items were answered.
Anxiety was defined as HADS-A score >=8/21, indicating mild or possible anxiety.[20-22]
Chronicity is assumed based on medical knowledge and clinical experience.

Depression[5 19]

Instrument variable: Hospital Anxiety and Depression Scale.[19] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed total score depression (HADS-D), if all 7 depression items were answered.

Depression was defined as HADS-D score >=8/21, indicating mild or possible depression.[20-22]

Chronicity is assumed based on medical knowledge and clinical experience.

Chronic insomnia[5 23]

There were nine questions on sleeping pattern in one cluster, including three concerning insomnia. Initial text: “How often in the last 3 months have you
“Had difficulty falling asleep at night?” Never/seldom, sometimes, several times a week.
“Woken up repeatedly during the night?” Never/seldom, sometimes, several times a week.
“Woken too early and couldn’t get back to sleep?” Never/seldom, sometimes, several times a week.
Chronic insomnia was defined as in the last 3 months, several times a week, having difficulty falling asleep at night and waking up repeatedly during the night, and waking up too early. A modified version of the diagnostic criteria for insomnia in the International Classification of Sleep Disorders.[23]

Alcohol use disorder[24]

Instrument variable: Cut down/Annoyed/Guilty/Eye-opener, also known as the CAGE questionnaire.[24] The CAGE questionnaire is a 4-item scale with scores of 0-1. A summary variable was created and dichotomized in which a score of 1 indicates >=2 positive answers.
Alcohol use disorder was defined as CAGE score greater than 2.[25]
Chronicity is assumed based on medical knowledge and clinical experience.

Dental health problem

“How would you say your dental health is?” Very, bad, ok, good, very good.
Dental health problems were defined as self-reported bad or very bad dental health.[26]
Chronicity is assumed based on medical knowledge and clinical experience.

Menopausal hot flashes

Asked to women older than 30 years only.
Two questions were used to define menopausal illness:
“Do you have/have you had hot flashes due to menopause?” During the day, during the night, day and night, haven’t had any.
“If you have had hot flashes, how would you describe them?” Very intense, moderately intense, hardly noticeable.
Included with menopausal hot flashes were those who reported hot flashes occurring daily and/or nightly and of at least moderate severity.
Chronicity is assumed based on medical knowledge[27] and clinical experience.

Nocturia[28]

Age group 20-29 years were excluded.
One question on nocturia, identical to that of the International Prostate Symptom Scale (IPSS), was asked to men and women older than 30 years.
“How many times do you get up during the night to urinate?” None, 1 time, 2 times, 3 times, 4 times, 5 times or more.
Nocturia was defined as two or more voids per night.[28]

Chronicity is assumed based on medical knowledge and clinical experience.

Urine incontinence[5 29]

Men 20-29 years were excluded.
Instrument variable: The Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) questionnaire.[29]
Index question: Do you have involuntary loss of urine? Yes, no.
Urine incontinence was constructed from two of six follow up questions. "If yes":
"How often do you have involuntary loss of urine?" Less than once a month, once or more per month, once or more per week, every day and/or night
"How much urine do you leak each time?" Drops or little, small amount, large amounts.

Self-reported frequency and volume of leakage were multiplied to obtain the validated 4-level Sandvik Severity Index, categorizing incontinence as slight, moderate, severe, and very severe.[29]
Urine incontinence were included if severe to very severe.
Chronicity is assumed based on medical knowledge and clinical experience.

Prostate symptoms[30 31]

Asked of men older than 30 years only.
Instrument variable: The International Prostate Symptom Scale[30] was slightly modified in HUNT3,[31] becoming a 7-item scale with scores of 0-5 per question.
Included were prostate symptoms of at least moderate severity, i.e. summary score >= 8 points.[30]
Chronicity is assumed based on medical knowledge and clinical experience.

Eye diseases[32]

The age group 20-29 years were excluded.
Cluster text: "Do you have any of the following eye conditions?" Cataract, glaucoma, and macula degeneration. Separate tick boxes, yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

MEASUREMENTS

Obesity[33 34]

HUNT Databank constructed the BMI variable, defined as (weight in kg)/(height in m2).
Obesity was defined as either BMI>=35 or a BMI 25-34.9 and an increased waist circumference (>= 88 cm for females; >= 102 cm for males).[33 34]
Chronicity is assumed based on medical knowledge and clinical experience.

Hypertension[5 26]

Blood pressure in HUNT3 is measured three times at one consultation. The mean of measurement 2 and 3 is calculated by HUNT Databank.

Hypertension was defined as measured mean systolic BP>= 180 mmHg or diastolic BP >= 110 mmHg or reporting use of antihypertensive medications, excluding self-reported cardiovascular disease, diabetes, or kidney disease, and excluding extreme measures. Chronicity is assumed based on medical knowledge and clinical experience.

Hypercholesterolemia[35]

Hypercholesterolemia was defined as total-cholesterol >= 8 mmol/L.[35]
Chronicity is assumed based on medical knowledge and clinical experience.

REFERENCES

1. Goodman RA, Posner SF, Huang ES, et al. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. *Prev Chronic Dis* 2013;10:E66. doi: 10.5888/pcd10.120239 [published Online First: 2013/04/27]
2. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10(2):142-51. doi: 10.1370/afm.1337 [published Online First: 2012/03/14]
3. Valete-Rosalino CM, Rozenfeld S. Auditory screening in the elderly: comparison between self-report and audiometry. *Braz J Otorhinolaryngol* 2005;71(2):193-200. doi: /S0034-72992005000200013 [published Online First: 2006/02/01]
4. Okura Y, Urban LH, Mahoney DW, et al. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol* 2004;57(10):1096-103.
5. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol* 2012;12:143. doi: 10.1186/1471-2288-12-143 [published Online First: 2012/09/18]
6. Merzenich H, Blettner M, Niehoff D, et al. Cardiac late events in German breast cancer patients: a validation study on the agreement between patient self-reports and information from physicians. *BMC Cardiovasc Disord* 2018;18(1):218. doi: 10.1186/s12872-018-0961-7 [published Online First: 2018/12/01]
7. Modalsli EH, Snekvik I, Asvold BO, et al. Validity of Self-Reported Psoriasis in a General Population: The HUNT Study, Norway. *J Invest Dermatol* 2016;136(1):323-5. doi: 10.1038/jid.2015.386 [published Online First: 2016/01/15]
8. Svensson Å, Lindberg M, Meding B, et al. Self-reported hand eczema: symptom-based reports do not increase the validity of diagnosis. *Br J Dermatol* 2002;147(2):281-84.
9. Meding B, Barregård L. Validity of self-reports of hand eczema. *Contact Dermatitis* 2001;45(2):99-103.
10. Navarro C, Chirlaque MD, Tormo MJ, et al. Validity of self reported diagnoses of cancer in a major Spanish prospective cohort study. *J Epidemiol Community Health* 2006;60(7):593-9. doi: 10.1136/jech.2005.039131 [published Online First: 2006/06/23]
11. Keezer MR, Bouma HK, Wolfson C. The diagnostic accuracy of screening questionnaires for the identification of adults with epilepsy: A systematic review. *Epilepsia* 2014;55(11):1772-80. doi: 10.1111/epi.12811
12. Videm V, Thomas R, Brown MA, et al. Self-reported Diagnosis of Rheumatoid Arthritis or Ankylosing Spondylitis Has Low Accuracy: Data from the Nord-Trondelag Health Study. *J Rheumatol* 2017;44(8):1134-41. doi: 10.3899/jrheum.161396 [published Online First: 2017/04/17]
13. Cunningham TD, DeShields SC. Factors associated with the accuracy of self-reported osteoporosis in the community. *Rheumatol Int* 2016;36(12):1633-40. doi: 10.1007/s00296-016-3573-5 [published Online First: 2016/10/08]

14. Hagen K, Zwart JA, Aamodt AH, et al. The validity of questionnaire-based diagnoses: the third Nord-Trondelag Health Study 2006-2008. *J Headache Pain* 2010;11(1):67-73. doi: 10.1007/s10194-009-0174-7 [published Online First: 2009/12/01]
15. Mundal I, Grawe RW, Bjorngaard JH, et al. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. *BMC Musculoskelet Disord* 2014;15:213. doi: 10.1186/1471-2474-15-213 [published Online First: 2014/06/22]
16. Hammer J, Talley NJ. Diagnostic criteria for the irritable bowel syndrome. *Am J Med* 1999;107(5A):5S-11S. doi: 10.1016/s0002-9343(99)00276-4 [published Online First: 1999/12/10]
17. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480-91. doi: 10.1053/j.gastro.2005.11.061 [published Online First: 2006/05/09]
18. Ness-Jensen E, Lindam A, Lagergren J, et al. Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study. *Gut* 2012;61(10):1390-7. doi: 10.1136/gutjnl-2011-300715 [published Online First: 2011/12/23]
19. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(6):361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x [published Online First: 1983/06/01]
20. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *Br J Psychiatry* 2001;179:540-4. doi: 10.1192/bjp.179.6.540 [published Online First: 2001/12/04]
21. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
22. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res* 1997;42(1):17-41. doi: 10.1016/s0022-3999(96)00216-4 [published Online First: 1997/01/01]
23. Medicine AAoS. The international classification of sleep disorders: diagnostic and coding manual: American Acad. of Sleep Medicine 2005.
24. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984;252(14):1905-7. doi: 10.1001/jama.252.14.1905 [published Online First: 1984/10/12]
25. Skogen JC, Overland S, Knudsen AK, et al. Concurrent validity of the CAGE questionnaire. The Nord-Trondelag Health Study. *Addict Behav* 2011;36(4):302-7. doi: 10.1016/j.addbeh.2010.11.010 [published Online First: 2010/12/21]
26. Tomasdottir MO, Getz L, Sigurdsson JA, et al. Co-and multimorbidity patterns in an unselected Norwegian population: Cross-sectional analysis based on the HUNT Study and theoretical reflections concerning basic medical models. *European Journal for Person Centered Healthcare* 2014;2(3):335-45.
27. Avis NE, Crawford SL, Greendale G, et al. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA Intern Med* 2015;175(4):531-9. doi: 10.1001/jamainternmed.2014.8063 [published Online First: 2015/02/17]
28. Tikkinen KA, Johnson TM, 2nd, Tammela TL, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. *Eur Urol* 2010;57(3):488-96. doi: 10.1016/j.eururo.2009.03.080 [published Online First: 2009/04/14]
29. Sandvik H, Seim A, Vanvik A, et al. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. *Neurourol Urodyn* 2000;19(2):137-45. doi: 10.1002/(sici)1520-6777(2000)19:2<137::aid-nau4>3.0.co;2-g [published Online First: 2000/02/19]

30. Barry MJ, Fowler FJ, Jr., O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148(5):1549-57; discussion 64. doi: 10.1016/s0022-5347(17)36966-5 [published Online First: 1992/11/11]
31. HUNT Databank. International Prostate Symptom Scale in HUNT3 Questionnaire 2 [Webpage]. Levanger: HUNT Databank; 2019 [cited 2019 05.20.]. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#/instrumentpart/45_11 2019.
32. MacLennan PA, McGwin G, Jr., Searcey K, et al. Medical record validation of self-reported eye diseases and eye care utilization among older adults. *Curr Eye Res* 2013;38(1):1-8. doi: 10.3109/02713683.2012.733054 [published Online First: 2012/10/20]
33. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79(3):379-84. doi: 10.1093/ajcn/79.3.379 [published Online First: 2004/02/27]
34. Perreault L. Obesity in adults: Prevalence, screening, and evaluation. Waltham, MA: UpToDate 2018.
35. Helsedirektoratet. Nasjonal faglig retningslinje for individuell primærforebygging av hjerte-og karsykdommer, kortversjon, IS-1675. In: Helsedirektoratet, ed., 2009.

Appendix B

OPERATIONALIZING SOCIOECONOMIC POSITION USING OCCUPATION.

In the HUNT3 Survey interview, all participants were asked: "What is/was the title of your main occupation?" Free-text answers were manually classified according to the *Standard Classifications of Occupations* by Statistics Norway,[1] which is based on the European Union's version of the *International Standard Classification of Occupations-88.*[2]

The standard categorize occupations according to skill level and specialization, degree of independence, and manual labor but not social position.[1] Occupations are coded with up to four digits, with increasing detail. One digit indicates major groups; two digits, submajor groups; three digits, minor groups; and four digits, unit groups. The minor occupational group was the highest level of detail available in the HUNT3 Survey.

Occupational socioeconomic position was operationalized using the European Socio-economic Classification scheme.[3] The full version of the scheme requires employment status and size of organization in addition to occupation to assign a class position. We used the simplified class scheme, based on minor occupational group only[3], as the HUNT3 Survey did not have data corresponding to employment status and size of organization. It is shown that the agreement between three-digit full and simplified version of this scheme is 79.7% for the total workforce.[3]

The syntax is available from https://www.iser.essex.ac.uk/archives/esec/matrices-and-syntax. It was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA).

Table 1 gives details of transformation of data, discrepancies between the Norwegian and European Union standard and the allocated position in the full classification scheme. 2179 individuals had alterations to their occupational data to fit the syntax, 5.7% (2179/38027) of the total sample.

In the HUNT3 Survey data, the minor occupational group was a string variable. To perform the syntax, it had to be altered to a numeric variable. The string "011" changed to numeric value "11," which was manually corrected in the syntax. In the 3-digit variable, some participants were classified with 1 digit and 2 digits only. These were transformed to the corresponding 3-digit minor group, at the lowest level of detail, by manually adding suffix digits 0 or 00. This is in line with operationalizing of European Socio-economic Classification (see footnote table 1).[3]

Norwegian minor groups, which were not found in the European Union standard, were altered to the level of detail in which corresponding groups could be identified. These were *Standard Classifications of Occupations* by Statistics Norway codes: 112 (corresponding to 2 digits), 25 (corresponding to 1 digit), 251-6 (corresponding to 1 digit), 349 (corresponding to 2 digits), 631 (corresponding to 1 digit), 641 (corresponding to 1 digit), 735 (corresponding to 2 digits), and 745 (corresponding to 2 digits). See table 1.

In total, 9 classes were created. To increase power and simplify interpretation, the full scheme was collapsed into a 3-class version, with “high” combining class 1 and 2, “middle” combining 3 to 6, and “low” combining 7 to 9. [3] The high occupational class represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, higher-grade technician occupations, and supervisory occupations. The middle occupational class consist of small employers, self-employed individuals, lower supervisory occupations, and lower technician occupations. The low occupational class contain lower services, sales and clerical occupations, lower technical occupations, and routine occupations.

Table 1. The distribution of transformed occupational data and discrepancies between the Norwegian and International Standard Classifications of Occupations, and allocation in the European Socio-economic Classification scheme.

Standard Classifications of Occupations		European Socio-economic		
Norwegian	**International**	**Classification scheme**	***n***	**%**
1	100	1	262	(0.69)
011 (=num 11)	011=11	3	134	(0.35)
112*	→ 11=110	1	31	(0.08)
12	120	1	73	(0.19)
13	130	4	20	(0.05)
2	200	1	10	(0.03)
21	210	1	10	(0.03)
22	220	1	1	(0.00)
23	230	2	27	(0.07)
24	240	1	9	(0.02)
25	→ 2=200	1	4	(0.01)
251*	→ 2=200	1	296	(0.78)
252*	→ 2=200	1	48	(0.13)
253*	→ 2=200	1	20	(0.05)
254*	→ 2=200	1	138	(0.36)
255*	→ 2=200	1	64	(0.17)
256*	→ 2=200	1	46	(0.12)
3	300	3	39	(0.10)
31	310	2	37	(0.10)
33	330	3	241	(0.63)
34	340	3	45	(0.12)
349*	→34=340	3	160	(0.42)
4	400	3	1	(0.00)
41	410	3	1	(0.00)
42	420	3	1	(0.00)
5	500	7	1	(0.00)
51	510	7	8	(0.02)
61	610	5	4	(0.01)
631*	→6=600	5	93	(0.24)
641*	→6=600	5	99	(0.26)
7	700	8	20	(0.05)
71	710	8	1	(0.00)
72	720	8	6	(0.02)
73	730	6	1	(0.00)
735*	→73=730	6	38	(0.10)
74	740	8	1	(0.00)
745*	→74=740	8	46	(0.12)
8	800	9	62	(0.16)
81	810	9	38	(0.10)
82	820	9	35	(0.09)
83	830	9	6	(0.02)
9	900	9	1	(0.00)
93	930	9	1	(0.00)
Sum			2179	(5.73)

Bold* = Divergence of *Standard Classifications of Occupations* by Statistics Norway from the European Union's version of *The International Standard Classification of Occupations-88*.

References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
2. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
3. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518

Appendix C

Table C1 Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational groups in 5-year intervals (25 to 100 years), stratified by sex.

Age,	Occup.*	Women						Men					
years	group	PR	95% CI		PD	95% CI		PR	95% CI		PD	95% CI	
25	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.58	1.34	1.88	0.08	0.05	0.10	1.30	1.03	1.63	0.03	0.00	0.05
	Low	2.34	2.02	2.72	0.18	0.15	0.20	2.06	1.69	2.50	0.09	0.07	0.11
30	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.47	1.28	1.68	0.08	0.05	0.11	1.28	1.05	1.55	0.03	0.01	0.06
	Low	2.06	1.84	2.32	0.19	0.16	0.21	1.92	1.63	2.26	0.10	0.08	0.13
35	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.36	1.23	1.51	0.08	0.06	0.11	1.26	1.07	1.47	0.04	0.01	0.06
	Low	1.82	1.67	2.00	0.19	0.16	0.22	1.79	1.56	2.04	0.12	0.09	0.14
40	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.27	1.18	1.37	0.08	0.05	0.11	1.24	1.09	1.40	0.04	0.02	0.07
	Low	1.62	1.52	1.73	0.19	0.16	0.21	1.66	1.50	1.84	0.13	0.10	0.15
45	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.19	1.13	1.26	0.07	0.05	0.09	1.21	1.10	1.33	0.05	0.03	0.08
	Low	1.45	1.39	1.53	0.17	0.15	0.19	1.55	1.43	1.67	0.13	0.11	0.15
50	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.13	1.08	1.18	0.06	0.04	0.08	1.19	1.11	1.27	0.06	0.03	0.08
	Low	1.32	1.27	1.37	0.15	0.13	0.17	1.44	1.36	1.53	0.13	0.11	0.15
55	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.08	1.03	1.12	0.04	0.02	0.06	1.16	1.10	1.23	0.06	0.04	0.08
	Low	1.22	1.18	1.26	0.12	0.10	0.14	1.35	1.28	1.41	0.13	0.11	0.15
60	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.04	1.00	1.08	0.02	0.00	0.05	1.14	1.08	1.19	0.06	0.04	0.08
	Low	1.14	1.10	1.18	0.09	0.07	0.11	1.27	1.21	1.32	0.12	0.10	0.14
65	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	1.01	0.97	1.05	0.01	-0.02	0.04	1.11	1.06	1.17	0.06	0.03	0.08
	Low	1.08	1.05	1.12	0.06	0.04	0.08	1.20	1.15	1.25	0.10	0.08	0.13
70	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.99	0.96	1.03	0.00	-0.03	0.02	1.09	1.04	1.14	0.05	0.03	0.08
	Low	1.05	1.01	1.08	0.04	0.01	0.06	1.15	1.10	1.20	0.09	0.06	0.11
75	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.02	-0.01	-0.04	0.02	1.07	1.02	1.12	0.05	0.02	0.08
	Low	1.02	0.99	1.05	0.02	-0.01	0.04	1.10	1.06	1.15	0.07	0.04	0.10

80	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.01	-0.02	-0.04	0.01	1.06	1.01	1.11	0.04	0.01	0.08
	Low	1.00	0.98	1.03	0.00	-0.02	0.02	1.07	1.02	1.12	0.05	0.02	0.08
85	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.95	1.00	-0.02	-0.04	0.00	1.04	1.00	1.09	0.03	0.00	0.07
	Low	0.99	0.97	1.02	-0.01	-0.03	0.01	1.05	1.00	1.09	0.04	0.00	0.07
90	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.96	1.00	-0.02	-0.04	0.00	1.03	0.99	1.07	0.03	-0.01	0.06
	Low	0.99	0.97	1.01	-0.01	-0.03	0.01	1.03	0.99	1.07	0.02	-0.01	0.05
95	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.96	1.00	-0.02	-0.04	0.00	1.02	0.99	1.06	0.02	-0.01	0.05
	Low	0.99	0.97	1.00	-0.01	-0.03	0.00	1.02	0.98	1.05	0.01	-0.02	0.04
100	High	1.0	ref		0.0	ref		1.0	ref		0.0	ref	
	Medium	0.98	0.97	1.00	-0.02	-0.03	0.00	1.02	0.99	1.05	0.02	-0.01	0.04
	Low	0.98	0.97	1.00	-0.01	-0.03	0.00	1.01	0.98	1.04	0.01	-0.02	0.03

*Occup. = occupational

Appendix D – Sensitivity analysis

In the sensitivity analysis the outcome complex multimorbidity was created from available conditions in the main questionnaire only. In total 22 conditions, grouped in 12 *ICD-10* chapters were included vs 51 conditions, grouped in *14 ICD-10* chapters in the original measure.

The sensitivity analysis was performed to investigate if fewer number and types of conditions included in the complex multimorbidity measure, produced a similar pattern with respect to the overall prevalence as well as differences between occupational groups.

Total prevalences and prevalences by occupational group and age, stratified by sex (table D1), were obtained by cross tables.

Table D1. Sociodemographic distribution of complex multimorbidity

	Women						Men					
	No, *n*	**(%)**	**Yes, *n***	**(%)**	**Total, *n***	**(%)**	**No, *n***	**(%)**	**Yes, *n***	**(%)**	**Total, *n***	**(%)**
Total	17376	(83)	3437	(17)	20813	(100)	14815	(86)	2399	(14)	17214	(100)
Occupational group												
High	4032	(90)	473	(11)	4505	(100)	4026	(90)	439	(10)	4465	(100)
Middle	4612	(86)	774	(14)	5386	(100)	4147	(85)	710	(15)	4857	(100)
Low	8732	(80)	2190	(20)	10922	(100)	6642	(84)	1250	(16)	7892	(100)
Age, years												
25-44	5610	(94)	371	(6)	5981	(100)	3776	(96)	167	(4)	3943	(100)
45-64	8233	(84)	1607	(16)	9840	(100)	7381	(88)	985	(12)	8366	(100)
65-74	2331	(74)	837	(26)	3168	(100)	2417	(78)	676	(22)	3093	(100)
75-100	1202	(66)	622	(34)	1824	(100)	1241	(68)	571	(32)	1812	(100)
Mean, (SD)	53	(14)	62	(13)	54	(14)	55	(14)	65	(12)	56	(14)

Prevalence ratios and differences between occupational groups at ages 30, 55, 75 and 90 years were derived from logistic regression estimates (table D2).

Table D2. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) in complex multimorbidity between occupational classes, stratified by sex.

Age, years	Occupational group	Women				Men			
		PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
30	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.91	(1.41, 2.57)	0.02	(0.01, 0.03)	1.28	(0.88, 1.86)	0.01	(0.00, 0.01)
	Low	3.47	(2.68, 4.49)	0.05	(0.04, 0.06)	1.96	(1.42, 2.71)	0.02	(0.01, 0.03)
55	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	1.18	(1.05, 1.33)	0.02	(0.01, 0.03)	1.31	(1.13, 1.52)	0.02	(0.01, 0.04)
	Low	1.59	(1.44, 1.76)	0.07	(0.05, 0.08)	1.68	(1.48, 1.91)	0.05	(0.04, 0.06)
75	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.88	(0.77, 1.01)	-0.04	(-0.08, 0.00)	1.28	(1.12, 1.47)	0.06	(0.03, 0.09)
	Low	0.96	(0.85, 1.08)	-0.01	(-0.05, 0.02)	1.44	(1.27, 1.64)	0.09	(0.06, 0.12)
90	High	1.00	(ref.)	0.00	(ref.)	1.00	(ref.)	0.00	(ref.)
	Middle	0.80	(0.69, 0.93)	-0.12	(-0.20, -0.04)	1.23	(1.03, 1.46)	0.09	(0.01, 0.16)
	Low	0.78	(0.69, 0.88)	-0.13	(-0.20, -0.06)	1.27	(1.08, 1.50)	0.10	(0.04, 0.17)

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 (Title page)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6, tab. 1
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	Appendix A
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	8
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	5, 8
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2, p.9
		(b) Indicate number of participants with missing data for each variable of interest	5
Outcome data	15*	Report numbers of outcome events or summary measures	Table 3, pp. 9-10
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	Table 4, p 10. 8
		(*b*) Report category boundaries when continuous variables were categorized	5
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk ~~for a meaningful time period~~	8, table 4
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10, appendix E
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	14

*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.