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Title page

Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

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Objectives: Prevalence estimates for specific chronic conditions and multimorbidity (MM) in Eastern Europe are scarce. This national study estimates the prevalence of MM by age group and gender in Estonia.

Design: Population-based cross-sectional study utilizing administrative data.

Setting: Data were collected on 55 chronic conditions from the Estonian Health Insurance Fund during 2015-2017. MM was defined as the coexistence of two or more conditions.

Participants: The Estonian Health Insurance Fund includes data for approximately 95% of the Estonian population receiving public health insurance.

Primary and secondary outcome measures: Prevalence and 95% confidence intervals (CI) for MM stratified by age group and gender.

Results: Nearly half (49.1%) of the individuals (95% CI 49.0–49.3) had at least one chronic condition, and 30.1% (95% CI 30.0–30.2) had MM (2 or more chronic conditions). The number of conditions and the prevalence of MM increased with age, ranging from a MM prevalence of 3.5% (3.5–3.6) in the youngest (0–24 years) to as high as 80.4% (79.4–81.3) in the oldest (≥85) age group. Half of all individuals had MM by 60 years, and 75% of the population had MM by 75 years of age. Women had a higher prevalence of MM (34.9%, 95% CI 34.7–35.0) than men (24.4%, 95% CI 24.3–24.5). Hypertension was by far the most frequent chronic condition (24.5%), followed by chronic pain (12.4%) and arthritis (7.7%).

Conclusions: Hypertension is an important chronic condition amenable to treatment with lifestyle and therapeutic interventions. Given the established correlation between uncontrolled

hypertension and exacerbation of other cardiovascular conditions as well as acute illnesses, this leading MM may be suitable for targeted public health interventions.

Strengths and limitations of this study

- One of the strengths of our study is the methodological comparability with previous research.
- The second strength is the nearly 95% nationwide coverage of our dataset, the validity of which has been tested and proven.
- A limitation of our study is the definition of a chronic condition and multimorbidity used in our study which is contestable in all studies of MM.

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Competing Interests Statement

The authors declare no conflict of interests.

Background

The management of patients with multimorbidity (MM) has become a challenge for healthcare systems as most of those with long-term disorders are multimorbid. [1] The prevalence of MM is increasing along with population aging, [2] but aging is not the only factor predisposing the population increase in MM [3] and healthcare utilization has experienced a concomitant increase in response to managing these complex patients. [4–6] In addition to aging, MM is associated with other sociodemographic factors, such as female gender, lower education, lower household income, and living alone [7–9] as well as health conditions, such as obesity, hypertension, having one chronic condition at baseline, social deprivation, and ethnicity. Behavioral factors like smoking and physical inactivity are also influential. [10] Having multiple chronic conditions is associated with poor outcomes: patients have a decreased quality of life, psychological distress, longer hospital stays, more postoperative complications, a higher cost of care, and higher mortality. [11]

The management of patients with multimorbidity (MM) is a formidable challenge for healthcare systems as most individuals presenting with long-term chronic conditions are MM. Research in this area is perhaps most urgently needed in low- and middle-income countries (LMIC) where the burden of multimorbidity is high, the specific distributions and determinants of disease may differ, and access to care may be impeded by a fragmented healthcare system which is continuing to modernize and restructure [12]. Although research is beginning to elucidate the distribution of comorbid conditions in these countries, the comparability of findings is limited by methodolgical differences. This study presents an important contribution to this developing literature with a comprehensive set of prevalence estimates for MM in Eastern Europe.

MM is a growing global health problem affecting all nations regardless of wealth [13]. A better understanding of the national or regional epidemiology of MM is necessary to allocate health care resources and develop treatment strategies that allow clinicians to deliver patient-centered care that appreciates the potential for competing priorities. [1,13] Furthermore, in the context of the coronavirus pandemic, the clinician is faced with the challenge of reconciling competing priorities: maintain stable health among those with MM via telemedicine and other access interventions while preventing the exacerbation of acute SARS-CoV-2 if the patient becomes infected. Certainly, the time has come for all nations to better support individuals in preventing or modifying MM in the interest of improved overall health as well as optimizing patient outcomes following infection. The prevalence of MM has been extensively studied in Western European countries. For example, in a recent MM prevalence study utilizing a medical practice database in Scotland, 23.2% of patients were multimorbid. [1] A recent systematic review and meta-analysis of observational studies [14] found an overall pooled 33.1% prevalence of MM. There was a considerable difference in the pooled estimates between high and low-income countries, with a prevalence of 37.9% and 29.7%, respectively. Still, data are scarce regarding the prevalence of MM in Eastern Europe, where life expectancy is shorter than in Western Europe, particularly among men. The recent Survey of Health, Ageing, and Retirement in Europe study found that among all European countries, Eastern and Central Europe (SHARE) had the highest MM prevalence, revealing a remarkable health inequality across European regions. [7] To illustrate the gap, 70-79-year-old Central and Eastern Europeans suffer from about the same level of MM as ≥80-year old Northern Europeans. [7] However, the SHARE study is limited to self-reported data among individuals aged 50 years or more. Given the limited population-based research in Eastern Europe, administrative health data is necessary to develop more accurate regional MM prevalence estimates.

Estonia belongs to the group of Eastern European high-middle income countries with relatively low life expectancy and a large gender health gap. The life expectancy among Estonian men is 73.8 years (compared to that of 82.1 in Estonian women) and is comparable to male life expectancy in China (74.5 years), Argentina (73.6 years), and Mexico (72.6 years). Estonian male life expectancy is markedly shorter than that of regional neighboring countries, such as Finland (78.6 years), Sweden (80.8 years), or France (79.8 years). [15] Disability-free life expectancy in Estonia is also low, being 52.8 years for men and 55.6 years for women in 2018. [16] The burden of multimorbid chronic disease, leading to disability and premature death, be an important contributor to this reduced life expectancy in Estonia.

In Estonia, national public health insurance covers approximately 95% of the population. Family physicians are responsible for providing a core package of health services to the individuals registering with the practice for care. [17] Following Estonian independence in 1992, important steps were implemented to modernize the health system and improve coordination and access to primary care. In particular, access to family physicians was expanded prior to streamlining the hospital network, centralizing specialty care, and establishing a pharmaceutical formulary and treatment guidelines. [18] One of the stated goals of restructuring was to provide better chronic disease management, coordinated by the general practitioner, for whom a bonus system was implemented in 2005 to take on these duties. Although management guidelines and quality standards have been implemented for specific chronic conditions, this process has been slow to consider multimorbidity. [18] Family physicians in Estonia lack clear evidence-based standards for the management of patients with multiple chronic diseases, and the applicability of a single evidence-based guideline to MM is limited and can be problematic. [19]

A definitive, population-based assessment of MM prevalence by age and gender is needed to inform the continued restructuring of the health care system to accommodate the growing proportion of these patients.

Methods

For this population-based cross-sectional study, we obtained data from the Estonian Health Insurance Fund (EHIF) which is essentially the sole health insurance provider in Estonia covering approximately 95% of the population. [20] We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. The data abstraction from the EHIF database included year and month of birth, sex assigned at birth, dates for health claims, type of care (in- and outpatient care, rehabilitation, nursing care, etc.), provided services, all diagnosis codes on claims, and the date and diagnosis code on prescriptions. Study subjects were assigned a unique identifier decoupled from personal identification information to enable longitudinal tracking of care while maintaining patient privacy.

To identify all patients with chronic physical and mental conditions, the ICD-10 diagnosis codes for main and other (accompanying) diagnoses were used. For the chronic physical and mental conditions analysis, we selected 55 conditions (Supplementary appendix, Table 1). The list of conditions was based on previous MM research to enable comparability [1,21,22] and adjusted by the authors (MJ, RK, AU, MO, HP) for use in Estonia. According to Barnett, et al., we included morbidities that were likely to be chronic, defined as having a significant impact on patients over at least the most recent year, defined in terms of the need for chronic treatment, reduced function, reduced quality of life, and risk of future morbidity and mortality. [1]

We constructed the case definition for a chronic condition as follows: the presence of at least two diagnosis codes at least 6 weeks apart for the same condition (i.e., matching ICD-10 category) during the study period January 1, 2015, through December 31, 2017 (Supplementary

Appendix, Table 1). This definition enabled us to include chronic conditions while excluding patients with previously diagnosed but improved conditions (e.g., conditions where remission is possible, such as epilepsy, asthma, pain, or depression). The 6-week interval between the diagnoses reduced double-counting and over-ascertainment of cases. The inclusion of prescriptions in the data query allowed us to identify patients whose claims profile included diagnosis codes for only one condition, whereas their prescription history identified treatment for multiple conditions.

The ascertainment period was extended to 3 years because some patients visit their physician infrequently. For instance, 17% of publicly insured individuals had no evidence of a visit to a family physician and 37% had no evidence of a visit to a specialist in 2017. [20] If we had elected a shorter study period, we might have inadvertently excluded the MM profile of nearly 20% of the population. Any correlation between lower health care utilization and sociodemographic characteristics that impede access (such as lack of paid time off from work for illness, lack of transportation in rural areas, etc.) would bias our claims-driven prevalence estimates to undercount MM among individuals facing these access challenges. The prevalence of chronic conditions among all publicly insured individuals was estimated at 31 December 2017 among all persons who were publicly insured at that time.

The study procedures were conducted according to local data protection regulations. The study was approved by the Tartu University Research Ethics Committee.

Patient and public involvement

This was an administrative claims study, and as such there were no patients enrolled in this study.

Statistical analysis

The outcomes were the prevalence of chronic disorders, MM, and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured. All results are presented with 95% confidence intervals. Adjustment by age and sex were done using uni- and multivariate Poisson regression. Prevalence ratios and 95% confidence intervals are presented. The analysis was performed using STATA version 14.

Results

We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). [20,23] Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33) (Table 1).

The prevalence of chronic conditions increased with age, from 18.2% (95% CI 18.0-18.3) in the youngest age group (0-24 years) to as high as 65.6% (95% CI 65.3–65.8) in the group of 45-64 years, and 90.4% (95% CI 89.4–91.4) among the oldest (85+ years) (Table 1). In the youngest age group, 0-24 years, the mean number of conditions was 0.23 (0.22–0.23), and it increased with age, reaching 3.22 (3.21–3.22) in age 65-84 and 3.92 (3.9–3.94) among those ≥85 years. The prevalence and number of chronic conditions in 5-year age groups are presented in Figure 1.

The prevalence of MM also increased with age, from 3.5% (95% CI 3.5–3.6) in the age of 0-24 to as high as 80.4% (95% CI 79.4–81.3) among those ≥85 years. MM prevalence was higher among women than men, with about every third woman and every fourth man having MM. At a younger age, the prevalence of MM among women was comparable to that in men: the prevalence ratio ($PR_{women/men}$) was 1.00 (95% CI 0.99-1.02) in the age group of 0-24 years. It

increased gradually from 1.10 (95% CI 1.09-1.10 among those of 25-29 years to 1.27 (95% CI 1.24-1.29) in 65-69 years, and declined again to be more similar between women and men among those aged 85+ (1.09, 95% CI 1.05-1.13).

Table 1. Study population, the prevalence of chronic conditions, mean number of chronic conditions, and MM by age group and sex.

		Population (%)	Prevalence of chronic conditions (95% CI)	Mean number of conditions (95% CI)	Prevalence of MM (95% CI)
Total		1 240 927 (100.0)	49.1 (49.0–49.3)	1.33 (1.32–1.33)	30.1 (30.0–30.2)
Age group (years)	0–24	331 450 (26.7)	18.2 (18.0–18.3)	0.23 (0.22–0.23)	3.5 (3.5–3.6)
	25–44	326 460 (26.3)	34.8 (34.6–35.0)	0.56 (0.55–0.56)	12.6 (12.5–12.7)
	45–64	323 256 (26.0)	65.6 (65.3–65.8)	1.64 (1.63–1.64)	41.0 (40.7–41.2)
	65–84	225 705 (18.2)	85.6 (85.2–85.9)	3.22 (3.21–3.22)	71.1 (70.8–71.5)
	≥85	34 056 (2.7)	90.4 (89.4–91.4)	3.92 (3.9–3.94)	80.4 (79.4–81.3)
Sex	Men	569 087 (45.9)	43.6 (43.4–43.7)	1.06 (1.06–1.07)	24.4 (24.3–24.5)
	Women	671 840 (54.1)	53.8 (53.7–54.0)	1.55 (1.54–1.55)	34.9 (34.7–35.0)
Number of conditions	0	631 299 (50.9)	...	...	...
	1	236 547 (19.1)	...	...	...
	2	128 263 (10.3)	...	...	...
	3	83 751 (6.7)	...	...	...
	4	57 501 (4.6)	...	...	...
	5	39 159 (3.2)	...	...	...
	6	25 567 (2.1)	...	...	...
	7	16 259 (1.3)	...	...	...
	≥8	22 581 (1.8)	...	...	...

/Figure 1 here/

Figure 1. Prevalence of chronic conditions and multimorbidity (in numbers) by 5-year age groups.

The prevalence of the 10 most common chronic conditions in men and women by age group is shown in Figure 2, and the prevalence of all chronic conditions in the study (in the total population and among MM patients) in the Supplementary Appendix, Table 1. Hypertension was by far the most frequent chronic condition in the three oldest age groups for both men and women. Hypertension affects one in four individuals (24.5 %) in the total population and about two-thirds (67.4%) among MM patients.

Chronic pain ranked second with a prevalence of 12.4% in the total population and 32.3% among MM patients. Chronic pain was defined according to Barnett, et al. [1] as chronic pain associated with selected physical conditions such as osteoarthritis and low back pain (Supplementary appendix, Table 1). The prevalence of painful conditions increases in older age as does the prevalence of cardiovascular diseases and conditions (e.g., atrial fibrillation, ischaemic heart disease, and heart failure).

Rheumatoid arthritis and other inflammatory arthropathies ranked third in the total population and MM patients, with the respective prevalences of 7.6% and 23.6%. This condition was closely followed by dyspepsia, with 7.4% of the total population and 22.12% of MM patients. The conditions with prevalence over 10% among MM patients included diabetes, sleep disorders, atrial fibrillation, asthma, thyroid disorders, blindness and low vision, ischaemic heart diseases, anxiety, and heart failure. In older men (65+ years), prostate disorders were frequent (22.8%) while in older women (65+ years) arthritis was quite prevalent (26.4%). Diseases such as asthma, diabetes, and dyspepsia were common across all age groups. In

younger age groups, asthma, chronic pain, psoriasis or eczema, and mental health conditions were most frequent.

/Figure 2 here/

Figure 2. The prevalence of the 10 most common chronic conditions in men and women by age group.

Discussion

The disease burden from chronic conditions is high in Estonia. Half of the individuals had at least one chronic disorder, and one-third had MM. The burden is increasing with age, being high already among middle-aged population groups (aged 45-64 years), where 82/3 of individuals have a prevalent condition Among those with MM, hypertension is the most prominent chronic condition, followed by chronic pain and arthritis.

Our results were overall very similar to the results of global and regional studies. A recent systematic review and meta-analysis of observational studies [14] resulted in an overall 33.1% pooled prevalence of MM. Still, their estimate of MM for the high-income countries in that review was 37.9%, whereas our estimate of 30.1% is a bit lower, apparently due to the methodological differences discussed above. As described earlier in the background, disability-free life expectancy is low for Estonia, perhaps owing to the relatively high burden of MM. Comparing our results to the Scottish primary care research, MM was higher in our study (30.1% compared to 23.2% in Scotland). [1]

As for the types of prevalent chronic conditions, our findings converge with several other studies that identified hypertension, diabetes, asthma, and arthritis as the most prevalent

conditions. In a recent Canadian study, the top five chronic conditions of the 17 examined among those with MM were mood disorders, hypertensive disorders, asthma, arthritis, and diabetes. [24] Lenzi, et al., found that hypertension, diabetes, and depression were highly prevalent among Italians. [25] Our national data also concur that morbidity increases with age, an association that has been demonstrated in other studies as well [1,3,24–26]. In a Canadian study of self-reported chronic conditions, the prevalence of 3+ conditions increased with age from 30% in the 45-49-year-old age group to 52% in individuals aged 60-64 years [26]. In Lithuania, the risk of acquiring an additional chronic condition was found to increase exponentially from the age of 29 years and stabilize between the age of 51 and 57 years [27,28].

Acknowledging the gender gap in health that is characteristic of Eastern Europe, we aimed to assess the sex-specific differences in MM. We found that in women age 25+, the prevalence of MM is higher than men, with the largest difference among those aged 65-69 years. This elevated prevalence of MM among women has been confirmed in some studies [3,26], but not in the others [24].

Some limitations of our study may affect generalizability. First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. [29,30] A universal definition and list of conditions used for MM research do not exist. [30] We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. [1,14] Third, it is possible that some people

with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. [23] However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.

One of the strengths of our study is the effort expended to enable comparability with the results of other studies. We used the list of conditions from previous research [1,21,22,28] with only minor adjustments to reflect the diagnostic practices. Another strength of our analysis lies in the use of a data source with 95% nationwide coverage and complete follow-up, free of recall and social desirability biases. Furthermore, the validity of EHIF data, although established for financial and not health research purposes, has been tested recently [31] and the study concluded that these data can be used for monitoring changes in chronic condition prevalence with a precision sufficient for informing health care policy. Our study thus provides high validity and generalizability of results allowing inferences to other Eastern European populations.

Conclusions

The prevalence of multimorbidity in Estonia is relatively high compared to other European countries, and higher among women than men. The prevalence of MM increases with age, with hypertension by far the most frequent chronic condition, followed by chronic pain, and arthritis. As the public health infrastructure continues to modernize, efforts must be placed on primary

prevention of the conditions which lead to hypertension, such as obesity. The development of patient-centered, evidence-based treatment recommendations will help align patient and physician with respect to health goals and the means to achieve these outcomes.

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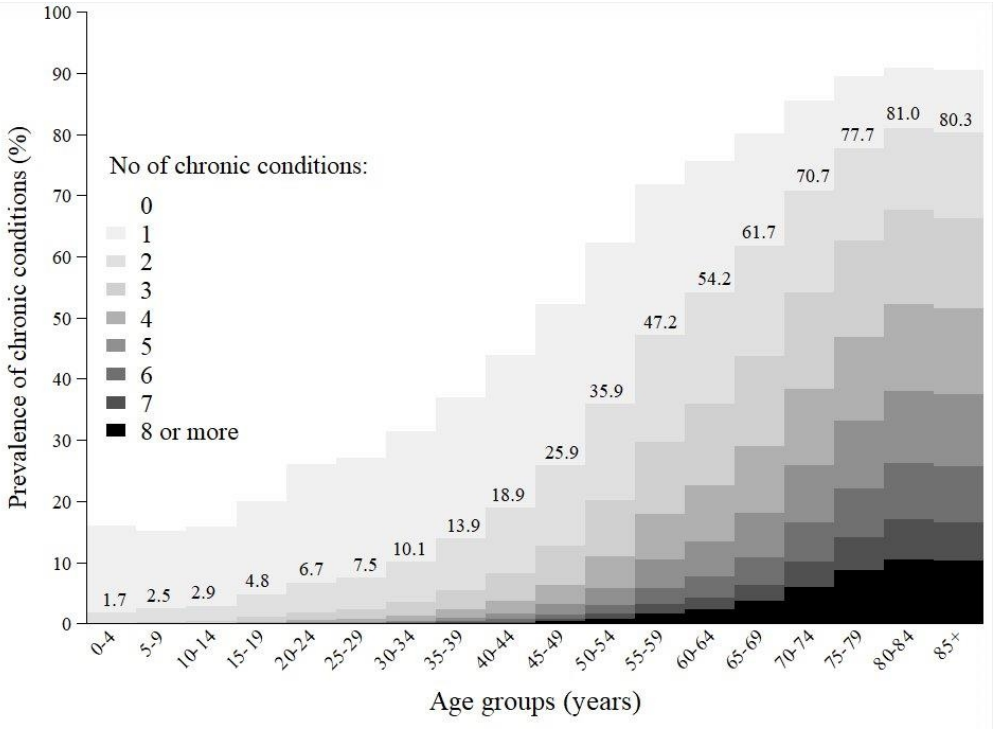

Figure 1. Prevalence of chronic conditions and multimorbidity (in numbers) by 5-year age groups.

249x181mm (96 x 96 DPI)

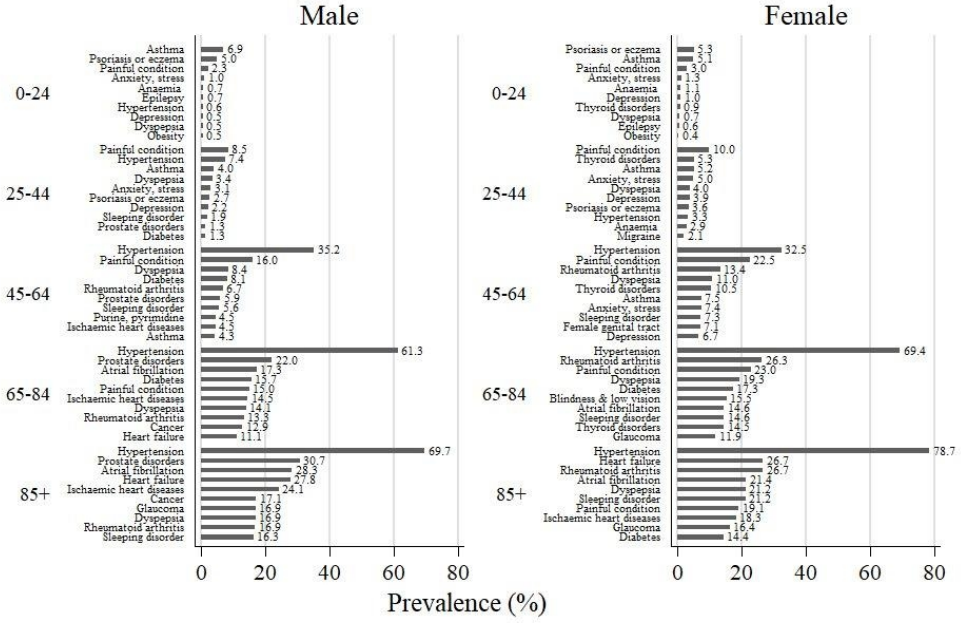

Figure 2. The prevalence of the 10 most common chronic conditions in men and women by age group.

251x167mm (96 x 96 DPI)

Supplementary appendix.

Table 1. List and prevalence of chronic conditions (in the total population and among MM patients) in the study.

Disorder	ICD-10 codes	Prevalence (%)	
		Total	among MM patients
Hypertension	[I10–I15]	24.49	67.40
Painful condition	[G44, R51] [M25.5] [M42–M54] [M77] [M79.1–79.9] [R10.1–10.4] [R07.0–07.4] [R30] [R52.0] [R52.1] [R52.2] [R52.9] [S22.0] [S22.1] [S12] [S32] [S72]	12.37	32.30
Rheumatoid arthritis, other inflammatory arthropathies and systemic connective tissue disorders	[M30–M36] [M05–M09, M79.0] [M91] [M15–M19]	7.65	23.56
Dyspepsia	[K21, K25–K30]	7.41	22.12
Asthma	[J45–J46] [J30]	5.91	12.94
Diabetes	[E10–14]	5.62	17.69
Sleeping disorders	[F51, G47]	5.11	15.80
Thyroid disorders	[E01–05, E06.1–.9, E07]	4.72	12.93

Atrial fibrillation	[I44–I45, I47–I49]	4.7	14.99
Psoriasis or eczema	[L20] [L23] [L28] [L29] [L40] [L50] [L56]	4.17	8.25
Anxiety and other neurotic, stress-related, and somatoform disorders	[F40–F43, F45, F48]	4.09	11.20
Blindness and low vision	[H17–18, H25–28, H31, H33, H34.1–.9, H35–H36, H43, H47, H54]	3.62	11.39
Ischaemic heart diseases	[I20–I25]	3.44	11.27
Depression	[F32–F33]	3.32	9.21
Heart failure	[I50]	3.24	10.65
Glaucoma	[H40–H42]	3.17	9.86
Cancer **	C00–97, D00–09, D37–48	3.05	8.84
Prostate disorders	[N40] [N41]	2.52	7.33
Disorders of purine and pyrimidine metabolism	[E79, M10]	2.07	6.56
Anemia	[D50–59, D60–D61, D63–64]	1.88	4.75
Obesity	[E66]	1.64	5.11

Noninflammatory disorders of the female genital tract	[N81] [N93] [N95]	1.57	4.45
Neuropathies	[G50–G64]	1.56	4.78
Disorders of vestibular function	[H81, H82, R42]	1.52	4.75
Stroke and transient ischaemic attack	[I60–66, I69, G45, I67.2]	1.45	4.71
Chronic obstructive pulmonary disease/bronchitis	[J40–J44]	1.4	4.42
Peripheral vascular disease	[I73.0] [I70]	0.93	2.98
Osteoporosis	[M80, M81, M82]	0.89	2.83
Schizophrenia or bipolar disorder	[F20–F29] [F31]	0.85	1.75
Epilepsy	[G40–G41]	0.84	1.84
Hearing loss	[H90–H91]	0.74	2.17
Migraine	[G43]	0.72	1.57
Cholelithiasis / Cholecystitis	[K80, K81.1]	0.5	1.47
Dementia	[F00, F01, F02, F03, F05.1, G30, G31, R54]	0.48	1.48
Chronic kidney disease	[N18–N19]	0.47	1.57

Mental and behavioral disorders due to use of alcohol	[F10]	0.43	1.16
Chronic liver disease	[K70–74, K76]	0.42	1.31
Valve disorders	[I34–I37]	0.37	1.20
Viral Hepatitis	[B18]	0.36	1.02
Irritable bowel syndrome	[K58]	0.33	0.97
Parkinson's disease	[G20, G21, G22]	0.31	0.97
HIV	[Z21, B20–B24]	0.30	0.70
disorders of the urinary system	[N39.3, N39.4, R32]	0.27	0.84
Calculus of kidney and ureter	[N20]	0.26	0.76
Inflammatory bowel	[K50–K52]	0.24	0.52
Chronic sinusitis	[J32]	0.21	0.57
Diverticular disease of the intestine	[K57]	0.2	0.63
Other psychoactive substance misuses	[F11–19]	0.16	0.45
Treated constipation	[K59.0]	0.16	0.42
Multiple sclerosis	[G35]	0.12	0.26
Coagulation defects	[D65-D69]	0.08	0.22
Learning disability	[F81]	0.06	0.08
Anorexia or bulimia	[F50]	0.05	0.13

Bronchiectasis	[J47]	0.05	0.16
Celiac disease	[K90.0]	0.03	0.07

* [ ] repetition of diagnostic codes within the boundaries of brackets

** Each cancer diagnosis code counted separately

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1	Title: population-based cross-sectional study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3	Abstract provides a short summary
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6	MM is a growing global health problem, the data are scarce regarding the prevalence of MM in Eastern Europe.
Objectives	3	State specific objectives, including any prespecified hypotheses	7	A definitive, population-based assessment of MM prevalence by age and gender is needed to inform the continued restructuring of the health care system to accommodate the growing proportion of these patients.
Methods				
Study design	4	Present key elements of study design early in the paper	7-8	Key elements of the cross-sectional study were described in the Methods section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8	We obtained data (year and month of birth, sex, dates for health claims, type of care, provided services, all diagnosis codes on claims, and the date and diagnosis code on prescriptions) from the Estonian Health Insurance Fund (EHIF) which is the sole health insurance provider in Estonia covering approximately 95% of the population. We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. To identify all patients with chronic physical and mental conditions, the ICD-10

				diagnosis codes for main and other (accompanying) diagnoses were used. For the prevalence analysis, we selected 55 conditions, whereas the list was based on previous MM research to enable comparability. We constructed the case definition for a chronic condition as the presence of at least two diagnosis codes at least 6 weeks apart for the same condition during the study period January 1, 2015, through December 31, 2017.
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	7-8, Supplementary appendix	We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. We constructed the case definition for a chronic condition as follows: the presence of at least two diagnosis codes at least 6 weeks apart for the same condition (i.e., matching ICD-10 category) during the study period January 1, 2015, through December 31, 2017. This definition enabled us to include chronic conditions while excluding patients with previously diagnosed but improved conditions (e.g., conditions where remission is possible, such as epilepsy, asthma, pain, or depression). The 6-week interval between the diagnoses reduced double-counting and over-ascertainment of cases. The inclusion of prescriptions in the data query allowed us to identify patients whose claims profile included diagnosis codes for only one condition, whereas their prescription history identified treatment for multiple conditions. The ascertainment period was extended to 3 years

				because some patients visit their physician infrequently.
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9	The outcomes were the prevalence of chronic disorders, multimorbidity (MM), and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8	The prevalence of conditions and MM were assessed using the population-based health data (health claims, prescriptions) from EHIF
Bias	9	Describe any efforts to address potential sources of bias	14-15	Selection and measurement bias were possible. First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. A universal definition and list of conditions used for MM research do not exist.

				We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. Third, it is possible that some people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.
Study size	10	Explain how the study size was arrived at	7	This was a population-based study. We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017)

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	13 (Table 1)	We assessed the prevalence of chronic conditions, mean number of chronic conditions, and MM by age group and sex
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9	The outcomes were the prevalence of chronic disorders, MM, and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured. All results are presented with 95% confidence intervals. Adjustment by age and sex were done using uni- and multivariate Poisson regression. Prevalence ratios and 95% confidence intervals are presented.
		(b) Describe any methods used to examine subgroups and interactions	13 (Table 1)	Prevalence ratios (by age group and sex) and 95% confidence intervals are presented.
		(c) Explain how missing data were addressed		It was not possible to identify any missing health claims or prescriptions from the EHIF data, but we assume that the impact of missing data on results is small as the health care institutions are interested in submitting the claims for reimbursement
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		
		(e) Describe any sensitivity analyses		No sensitivity analyses were performed
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		This was a cross-sectional study where all claims and prescriptions of all insured individuals were collected at a single time point.

		(b) Give reasons for non-participation at each stage		This was a cross-sectional study where all claims and prescriptions of all insured individuals were collected at a single time point.
		(c) Consider use of a flow diagram		No flow diagram was used as all data were collected and analysed at a single time point.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9	This was a population-based study. We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM.
		(b) Indicate number of participants with missing data for each variable of interest		It was not possible to identify any missing health claims or prescriptions from the EHIF data, but we assume that the impact of missing data on results is small as the health care institutions are interested in submitting the claims for reimbursement
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)		This was a cross-sectional study.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time		This was a cross-sectional study.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		This was a cross-sectional study.
		Cross-sectional study—Report numbers of outcome events or summary measures	9	Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33)
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	9-10, 13 (Table 1, Figure 1)	We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). Half of the individuals (49.1%, 95% CI 49.0–49.3) had one

		or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33). The prevalence of chronic conditions increased with age, from 18.2% (95% CI 18.0-18.3) in the youngest age group (0-24 years) to as high as 65.6% (95% CI 65.3–65.8) in the group of 45-64 years, and 90.4% (95% CI 89.4–91.4) among the oldest (85+ years). In the youngest age group, 0-24 years, the mean number of conditions was 0.23 (0.22–0.23), and it increased with age, reaching 3.22 (3.21–3.22) in age 65-84 and 3.92 (3.9–3.94) among those ≥85 years. The prevalence of MM also increased with age, from 3.5% (95% CI 3.5–3.6) in the age of 0-24 to as high as 80.4% (95% CI 79.4–81.3) among those ≥85 years. MM prevalence was higher among women than men, with about every third woman and every fourth man having MM. At a younger age, the prevalence of MM among women was comparable to that in men: the prevalence ratio (PR women/men) was 1.00 (95% CI 0.99-1.02) in the age group of 0-24 years. It increased gradually from 1.10 (95% CI 1.09-1.10 among those of 25-29 years to 1.27 (95% CI 1.24-1.29) in 65-69 years, and declined again to be more similar between women and men among those aged 85+ (1.09, 95% CI 1.05-1.13).
	(b) Report category boundaries when continuous variables were categorized	
	(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	This was a prevalence study.

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13, Figure 2, Supplementary appendix	Hypertension was the most frequent chronic condition in the three oldest age groups for both men and women. Hypertension affects one in four individuals (24.5 %) in the total population and about two-thirds (67.4%) among MM patients. Chronic pain ranked second with a prevalence of 12.4% in the total population and 32.3% among MM patients. Chronic pain was defined according to Barnett, et al. as chronic pain associated with selected physical conditions such as osteoarthritis and low back pain. The prevalence of painful conditions increases in older age as does the prevalence of cardiovascular diseases and conditions. Rheumatoid arthritis and other inflammatory arthropathies ranked third in the total population and MM patients, with the respective prevalences of 7.6% and 23.6%. This condition was closely followed by dyspepsia, with 7.4% of the total population and 22.12% of MM patients. The conditions with prevalence over 10% among MM patients included diabetes, sleep disorders, atrial fibrillation, asthma, thyroid disorders, blindness and low vision, ischaemic heart diseases, anxiety, and heart failure. In older men (65+ years), prostate disorders were frequent (22.8%) while in older women (65+ years) arthritis was quite prevalent (26.4%). Diseases such as asthma, diabetes, and dyspepsia were common across all age groups. In younger age groups, asthma, chronic pain, psoriasis or eczema, and mental health conditions were most frequent.

Discussion				
Key results	18	Summarise key results with reference to study objectives	13	The disease burden from chronic conditions is high in Estonia. Half of the individuals had at least one chronic disorder, and one-third had MM. The burden is increasing with age, being high already among middle-aged population groups (aged 45-64 years), where 82/3 of individuals have a prevalent condition Among those with MM, hypertension is the most prominent chronic condition, followed by chronic pain and arthritis.
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	14-15	First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. A universal definition and list of conditions used for MM research do not exist. [30] We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. Third, it is possible that some

				people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15	The prevalence of multimorbidity in Estonia is relatively high compared to other European countries, and higher among women than men. The prevalence of MM increases with age, with hypertension by far the most frequent chronic condition, followed by chronic pain, and arthritis. As the public health infrastructure continues to modernize, efforts must be placed on primary prevention of the conditions which lead to hypertension, such as obesity. The development of patient-centered, evidence-based treatment recommendations will help align patient and physician with respect to health goals and the means to achieve these outcomes.

Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15	One of the strengths of our study is the effort expended to enable comparability with the results of other studies. We used the list of conditions from previous research with only minor adjustments to reflect the diagnostic practices. Another strength of our analysis lies in the use of a data source with 95% nationwide coverage and complete follow-up, free of recall and social desirability biases. Furthermore, the validity of EHIF data, although established for financial and not health research purposes, has been tested recently and the study concluded that these data can be used for monitoring changes in chronic condition prevalence with a precision sufficient for informing health care policy. Our study thus provides high validity and generalizability of results allowing inferences to other Eastern European populations.
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	3	This work was supported by the Estonian Ministry of Education and Research Grant IUT34-17. Funders had no role in the study.

*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

Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

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Title page

Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

Mikk Jürisson, Heti Pisarev, Anneli Uusküla, Katrin Lang, Marje Oona, Ruth Kalda

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Word count: 2975

Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

Objectives: Prevalence estimates for specific chronic conditions and multimorbidity (MM) in Eastern Europe are scarce. This national study estimates the prevalence of MM by age group and sex in Estonia.

Design: Population-based cross-sectional study utilizing administrative data.

Setting: Data were collected on 55 chronic conditions from the Estonian Health Insurance Fund from 2015-2017. MM was defined as the coexistence of two or more conditions.

Participants: The Estonian Health Insurance Fund includes data for approximately 95% of the Estonian population receiving public health insurance.

Primary and secondary outcome measures: Prevalence and 95% confidence intervals (CI) for MM stratified by age group and sex.

Results: Nearly half (49.1%) of the individuals (95% CI 49.0–49.3) had at least one chronic condition, and 30.1% (95% CI 30.0–30.2) had MM (2 or more chronic conditions). The number of conditions and the prevalence of MM increased with age, ranging from a MM prevalence of 3.5% (3.5–3.6) in the youngest (0–24 years) to as high as 80.4% (79.4–81.3) in the oldest (≥85 years) age group. Half of all individuals had MM by 60 years, and 75% of the population had MM by 75 years of age. Women had a higher prevalence of MM (34.9%, 95% CI 34.7–35.0) than men (24.4%, 95% CI 24.3–24.5). Hypertension was the most frequent chronic condition (24.5%), followed by chronic pain (12.4%) and arthritis (7.7%).

Conclusions: Hypertension is an important chronic condition amenable to treatment with lifestyle and therapeutic interventions. Given the established correlation between uncontrolled hypertension and exacerbation of other cardiovascular conditions as well as acute illnesses, this

most common condition within the context of MM may be suitable for targeted public health interventions.

Strengths and limitations of this study

- One of the strengths of our study is the methodological comparability with previous research.
- The second strength is the nearly 95% nationwide coverage of our dataset, the validity of which has been tested and proven.
- A limitation of our study is the definition of a chronic condition and multimorbidity used in our study which is contestable in all studies of MM.

Data availability

The authors confirm that all data associated with the study are fully available without restriction from the Estonian Health Insurance Fund at https://www.haigekassa.ee/en. The data can be requested by completing the application at the following address: https://ankeet.haigekassa.ee/surveys/?s=4KXEPFDEKF or sending a written request to info@haigekassa.ee

Ethics approval

The study was conducted in accordance with local data protection regulations. The study was approved by the Tartu University Research Ethics Committee (280/T-7, 19.2018). The ethics committee waived the requirement for informed consent for the analysis presented in the manuscript.

Contributors

MJ, RK, HP, AU, and MO conceptualized and designed the study. MJ and HP collected, managed, and analyzed the data. All co-authors contributed to the interpretation of the findings

and drafting of the manuscript. MJ wrote the original draft, and MJ and KL wrote the final version. HP provided visualizations. All co-authors approved the final version for submission.

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Competing Interests Statement

The authors declare no conflict of interest.

Background

The management of patients with MM has become a challenge for healthcare systems as most individuals with long-term conditions are living with multiple long-term conditions. [1] The prevalence of MM is increasing along with population aging, [2] but aging is not the only factor predisposing the population increase in MM [3] and healthcare utilization has experienced a concomitant increase in response to managing these complex patients. [4–6] In addition to aging, MM is associated with other sociodemographic factors, such as female sex, lower education, lower household income, and living alone [7–10] as well as health conditions, such as obesity [11], hypertension, having one chronic condition at baseline, social deprivation, and ethnicity. Behavioral factors like smoking and physical inactivity are also influential. [12] Having multiple chronic conditions is associated with poor outcomes: patients have a decreased quality of life, psychological distress, longer hospital stays, more postoperative complications, a higher cost of care, and higher mortality. [13]

The management of patients with MM is a formidable challenge for healthcare systems. Research in this area is perhaps most urgently needed in low- and middle-income countries (LMIC) where the burden of multimorbidity is high, the specific distributions and determinants

of the disease may differ, and access to care may be impeded by a fragmented healthcare system which is continuing to modernize and restructure [14]. Although research is beginning to elucidate the distribution of co-occurring conditions in these countries, the comparability of findings is limited by methodological differences. This work demonstrates the utility of administrative data for constructing prevalence estimates, an approach that is particularly helpful for middle and high-to-middle-income-countries where resource limitations make administrative data not only immediately useful but also scalable, allowing for rate comparisons with other countries. In addition, the transition from a hospital-centric system in Estonia following independence from the Soviet Union was motivated by a desire to strengthen primary health care and thereby improve population health [15]. Having a set of prevalence estimates for MM is essential for measuring the ongoing success of this transition, adjusted by the prevalence of various conditions amenable to outpatient treatment. Finally, and perhaps most importantly, the SARS-CoV-2 pandemic drew attention to the important contribution of MM to the need for sound public health measures and rapid identification of effective medical interventions based on risk stratification. Frailty has been linked to infection [16], severity [16,17], geographic differences in severity and mortality by MM [18], prompting a renewed focus on improving global health and access to care, probabilistic modelling [19], the triage of care and shielding of the most vulnerable [20]. This study presents an important contribution to this developing literature with a comprehensive set of prevalence estimates for MM in Eastern Europe.

MM is a growing global health problem affecting all nations regardless of wealth [21]. A better understanding of the national or regional epidemiology of MM is necessary to allocate health care resources and develop treatment strategies that allow clinicians to deliver patient-centered care that appreciates the potential for competing priorities. [1,21] Furthermore, in the context of the coronavirus pandemic, the clinician is faced with the challenge of reconciling competing priorities: maintain stable health among those with MM via telemedicine and other access interventions while preventing the exacerbation of acute SARS-CoV-2 if the patient becomes infected. Certainly, the time has come for all nations to better support individuals in preventing

or modifying MM in the interest of improved overall health as well as optimizing patient outcomes following infection. The prevalence of MM has been extensively studied in Western European countries. For example, in a recent MM prevalence study utilizing a medical practice database in Scotland, 23.2% of patients were living with multimorbidity. [1] A recent systematic review and meta-analysis of observational studies [22] found an overall pooled 33.1% prevalence of MM. There was a considerable difference in the pooled estimates of MM between high and low-income countries, with a prevalence of 37.9% and 29.7%, respectively. Still, data are scarce regarding the prevalence of MM in Eastern Europe, where life expectancy is shorter than in Western Europe, particularly among men. The recent Survey of Health, Ageing, and Retirement in Europe (SHARE) study found that among all European countries, Eastern and Central Europe had the highest MM prevalence, revealing a remarkable health inequality across European regions. [7] To illustrate the gap, 70-79-year-old Central and Eastern Europeans suffer from about the same level of MM as ≥80-year old Northern Europeans. [7] However, the SHARE study is limited to self-reported data among individuals aged 50 years or more. Given the limited population-based research in Eastern Europe, the use of administrative health data is necessary to develop more accurate regional MM prevalence estimates.

Estonia belongs to the group of Eastern European high-middle income countries with relatively low life expectancy and a large sex health gap. The life expectancy among Estonian men is 73.8 years (compared to that of 82.1 in Estonian women) and is comparable to male life expectancy in China (74.5 years), Argentina (73.6 years), and Mexico (72.6 years). Estonian male life expectancy is markedly shorter than that of regional neighboring countries, such as Finland (78.6 years), Sweden (80.8 years), or France (79.8 years). [23] Disability-free life expectancy in Estonia is also low, being 52.8 years for men and 55.6 years for women in 2018. [24] The

burden of co-occurring chronic disease, leading to disability and premature death, is an important contributor to this reduced life expectancy in Estonia.

In Estonia, national public health insurance covers approximately 95% of the population. Family physicians are responsible for providing a core package of health services to the individuals registering with the practice for care. [25] Following Estonian independence in 1992, important steps were implemented to modernize the health system and improve coordination and access to primary care. In particular, access to family physicians was expanded before streamlining the hospital network, centralizing specialty care, and establishing a pharmaceutical formulary and treatment guidelines. [26] One of the stated goals of restructuring was to provide better chronic disease management, coordinated by the general practitioner, for whom a bonus system was implemented in 2005 to take on these duties. Although management guidelines and quality standards have been implemented for specific chronic conditions, this process has been slow to consider multimorbidity. [26] Family physicians in Estonia lack clear evidence-based standards for the management of patients with multiple chronic diseases, and the applicability of a single evidence-based guideline to MM is limited and can be problematic. [27]

A definitive, population-based assessment of MM prevalence by age and between males and females is needed to inform the continued restructuring of the health care system to accommodate the growing proportion of these patients.

Methods

For this population-based cross-sectional study, we obtained data from the Estonian Health Insurance Fund (EHIF) which is essentially the sole health insurance provider in Estonia covering approximately 95% of the population. [28] We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. The data abstraction from the

EHIF database included year and month of birth, sex assigned at birth, dates for health claims, type of care (in- and outpatient care, rehabilitation, nursing care, etc.), services provided, all diagnosis codes on claims, and the date and diagnosis code on prescriptions. Study subjects were assigned a unique identifier decoupled from personal identification information to enable longitudinal tracking of care while maintaining patient privacy.

To identify all patients with chronic physical and mental conditions, the ICD-10 diagnosis codes for main and other (accompanying) diagnoses were used. For the chronic physical and mental conditions analysis, we selected 55 conditions (Supplementary appendix, Table 1). The list of conditions was based on previous MM research to enable comparability [1,29,30] and adjusted by the authors (MJ, RK, AU, MO, HP) for use in Estonia. According to Barnett, et al., we included morbidities that were likely to be chronic, defined as having a significant impact on patients over at least the most recent year, defined in terms of the need for chronic treatment, reduced function, reduced quality of life, and risk of future morbidity and mortality. [1]

We constructed the case definition for a chronic condition as follows: the presence of at least two diagnosis codes at least 6 weeks apart for the same condition (i.e., matching ICD-10 category) during the study period January 1, 2015, through December 31, 2017 (Supplementary Appendix, Table 1). This definition enabled us to include chronic conditions while excluding patients with previously diagnosed but improved conditions (e.g., conditions where remission is possible, such as epilepsy, asthma, pain, or depression). The 6-week interval between the diagnoses reduced double-counting and over-ascertainment of cases. The inclusion of prescriptions in the data query allowed us to identify patients whose claims profile included diagnosis codes for only one condition, whereas their prescription history identified treatment for multiple conditions.

The ascertainment period was extended to 3 years because some patients visit their physician infrequently. For instance, 17% of publicly insured individuals had no evidence of a visit to a

family physician and 37% had no evidence of a visit to a specialist in 2017. [28] If we had elected a shorter study period, we might have inadvertently excluded the MM profile of nearly 20% of the population. Any correlation between lower health care utilization and sociodemographic characteristics that impede access (such as lack of paid time off from work for illness, lack of transportation in rural areas, etc.) would bias our claims-driven prevalence estimates to undercount MM among individuals facing these access challenges. The prevalence of chronic conditions among all publicly insured individuals was estimated on 31 December 2017 among all persons who were publicly insured at that time.

The study procedures were conducted according to local data protection regulations. The study was approved by the Tartu University Research Ethics Committee.

Patient and public involvement

This was an administrative claims study, and as such there were no patients enrolled in this study.

Statistical analysis

The outcomes were the prevalence of chronic conditions, MM, and the mean number of conditions by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured. All results are presented with 95% confidence intervals. Adjustment by age and sex were done using uni- and multivariate Poisson regression. Prevalence ratios and 95% confidence intervals are presented. The analysis was performed using STATA version 14.

Results

We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). [28,31] Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33) (Table 1).

The prevalence of any chronic condition increased with age, from 18.2% (95% CI 18.0-18.3) in the youngest age group (0-24 years) to as high as 65.6% (95% CI 65.3–65.8) in the group of 45-64 years, and 90.4% (95% CI 89.4–91.4) among the oldest (85+ years) (Table 1). In the youngest age group, 0-24 years, the mean number of conditions was 0.23 (0.22–0.23), and it increased with age, reaching 3.22 (3.21–3.22) in age 65-84 and 3.92 (3.9–3.94) among those ≥85 years. The prevalence and number of chronic conditions in 5-year age groups are presented in Figure 1.

The prevalence of MM also increased with age, from 3.5% (95% CI 3.5–3.6) among those younger than 25 years to as high as 80.4% (95% CI 79.4–81.3) among those ≥85 years. MM prevalence was higher among women than men, with about every third woman and every fourth man having MM. At a younger age, the prevalence of MM among women was comparable to that in men: the prevalence ratio ($PR_{women/men)}$ was 1.00 (95% CI 0.99-1.02) in the age group of 0-24 years. It increased gradually from 1.10 (95% CI 1.09-1.10 among those of 25-29 years to 1.27 (95% CI 1.24-1.29) in 65-69 years, and declined again to be more similar between women and men among those aged 85 years and older (1.09, 95% CI 1.05-1.13).

Table 1. Study population, the prevalence of chronic conditions, mean number of chronic conditions, and MM by age group and sex.

		Population (%)	Prevalence of chronic conditions (95% CI)	Mean number of conditions (95% CI)	Prevalence of MM (95% CI)
Total		1 240 927 (100.0)	49.1 (49.0–49.3)	1.33 (1.32–1.33)	30.1 (30.0–30.2)
Age group (years)	0–24	331 450 (26.7)	18.2 (18.0–18.3)	0.23 (0.22–0.23)	3.5 (3.5–3.6)
	25–44	326 460 (26.3)	34.8 (34.6–35.0)	0.56 (0.55–0.56)	12.6 (12.5–12.7)
	45–64	323 256 (26.0)	65.6 (65.3–65.8)	1.64 (1.63–1.64)	41.0 (40.7–41.2)
	65–84	225 705 (18.2)	85.6 (85.2–85.9)	3.22 (3.21–3.22)	71.1 (70.8–71.5)
	≥85	34 056 (2.7)	90.4 (89.4–91.4)	3.92 (3.9–3.94)	80.4 (79.4–81.3)
Sex	Men	569 087 (45.9)	43.6 (43.4–43.7)	1.06 (1.06–1.07)	24.4 (24.3–24.5)
	Women	671 840 (54.1)	53.8 (53.7–54.0)	1.55 (1.54–1.55)	34.9 (34.7–35.0)
Number of conditions	0	631 299 (50.9)	...	...	...
	1	236 547 (19.1)	...	...	...
	2	128 263 (10.3)	...	...	...
	3	83 751 (6.7)	...	...	...
	4	57 501 (4.6)	...	...	...
	5	39 159 (3.2)	...	...	...
	6	25 567 (2.1)	...	...	...
	7	16 259 (1.3)	...	...	...
	≥8	22 581 (1.8)	...	...	...

/Figure 1 here/

Figure 1. Prevalence of chronic conditions and multimorbidity (in numbers) by 5-year age groups.

The prevalence of the 10 most common chronic conditions in men and women by age group is shown in Figure 2, and the prevalence of all chronic conditions in the study (in the total population and among MM patients) in the Supplementary Appendix, Table 1. Hypertension was the most frequent chronic condition in the three oldest age groups for both men and women. Hypertension affects one in four individuals (24.5 %) in the total population and about two-thirds (67.4%) among MM patients.

Chronic pain ranked second with a prevalence of 12.4% in the total population and 32.3% among MM patients. Chronic pain was defined according to Barnett, et al. [1] as chronic pain associated with selected physical conditions such as osteoarthritis and low back pain (Supplementary appendix, Table 1). The prevalence of painful conditions increases in older age as does the prevalence of cardiovascular diseases and conditions (e.g., atrial fibrillation, ischaemic heart disease, and heart failure).

Rheumatoid arthritis and other inflammatory arthropathies ranked third in the total population and MM patients, with the respective prevalences of 7.6% and 23.6%. This condition was closely followed by dyspepsia, with 7.4% of the total population and 22.12% of MM patients. The conditions with prevalence over 10% among MM patients included diabetes, sleep disorders, atrial fibrillation, asthma, thyroid disorders, blindness and low vision, ischaemic heart diseases, anxiety, and heart failure. In older men (65+ years), prostate disorders were frequent (22.8%) while in older women (65+ years) arthritis was quite prevalent (26.4%). Diseases such as asthma, diabetes, and dyspepsia were common across all age groups. In

younger age groups, asthma, chronic pain, psoriasis or eczema, and mental health conditions were most frequent.

/Figure 2 here/

Figure 2. The prevalence of the 10 most common chronic conditions in men and women by age group.

Discussion

The disease burden from chronic conditions is high in Estonia. Half of the individuals had at least one chronic disorder, and one-third had MM. The burden is increasing with age, being high already among middle-aged population groups (aged 45-64 years), where 66% of individuals have a prevalent condition. Among those with MM, hypertension was the most prominent chronic condition, followed by chronic pain and arthritis.

Our results were overall very similar to the results of global and regional studies. A recent systematic review and meta-analysis of observational studies [22] calculated an overall 33.1% pooled prevalence of MM. Still, their estimate of MM for the high-income countries in that review was 37.9%, whereas our estimate of 30.1% is a bit lower, apparently due to the methodological differences discussed above. As described earlier in the background, disability-free life expectancy is low for Estonia, perhaps owing to the relatively high burden of MM. Comparing our results to the Scottish primary care research, MM was higher in our study (30.1% compared to 23.2% in Scotland). [1]

As for the types of prevalent chronic conditions, our findings converge with several other studies that identified hypertension, diabetes, asthma, and arthritis as the most prevalent

conditions. In a recent Canadian study, the top five chronic conditions of the 17 examined among those with MM were mood disorders, hypertensive disorders, asthma, arthritis, and diabetes. [32] Lenzi, et al., found that hypertension, diabetes, and depression were highly prevalent among Italians. [33] Our national data also concur that morbidity increases with age, an association that has been demonstrated in other studies as well [1,3,32–34]. In a Canadian study of self-reported chronic conditions, the prevalence of 3+ conditions increased with age from 30% in the 45-49-year-old age group to 52% in individuals aged 60-64 years [34]. In Lithuania, the risk of acquiring an additional chronic condition was found to increase exponentially from the age of 29 years and stabilize between the age of 51 and 57 years [35,36].

Acknowledging the sex gap in health that is characteristic of Eastern Europe, we aimed to assess the sex-specific differences in MM. We found that in women age 25+, the prevalence of MM is higher than men, with the largest difference among those aged 65-69 years. This elevated prevalence of MM among women has been confirmed in some studies [3,34], but not in the others [32].

Some limitations of our study may affect generalizability. First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. [37,38] A universal definition and list of conditions used for MM research do not exist. [38] We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. [1,22] Third, it is possible that some people

with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. [31] However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.

One of the strengths of our study is the effort expended to enable comparability with the results of other studies. We used the list of conditions from previous research [1,29,30,36] with only minor adjustments to reflect the diagnostic practices. Another strength of our analysis lies in the use of a data source with 95% nationwide coverage and complete follow-up, free of recall and social desirability biases. Furthermore, the validity of EHIF data, although established for financial and not health research purposes, has been tested recently [39] and the study concluded that these data can be used for monitoring changes in chronic condition prevalence with a precision sufficient for informing health care policy. Our study thus provides high validity and generalizability of results allowing inferences to other Eastern European populations.

Conclusions

The prevalence of multimorbidity in Estonia is relatively high compared to other European countries, and higher among women than men. The prevalence of MM increases with age, with hypertension the most frequent chronic condition, followed by chronic pain, and arthritis. As the public health infrastructure continues to modernize, efforts must be placed on primary

prevention of the conditions which lead to hypertension, such as obesity. The development of patient-centered, evidence-based treatment recommendations will help align patient and physician with respect to health goals and the means to achieve these outcomes.

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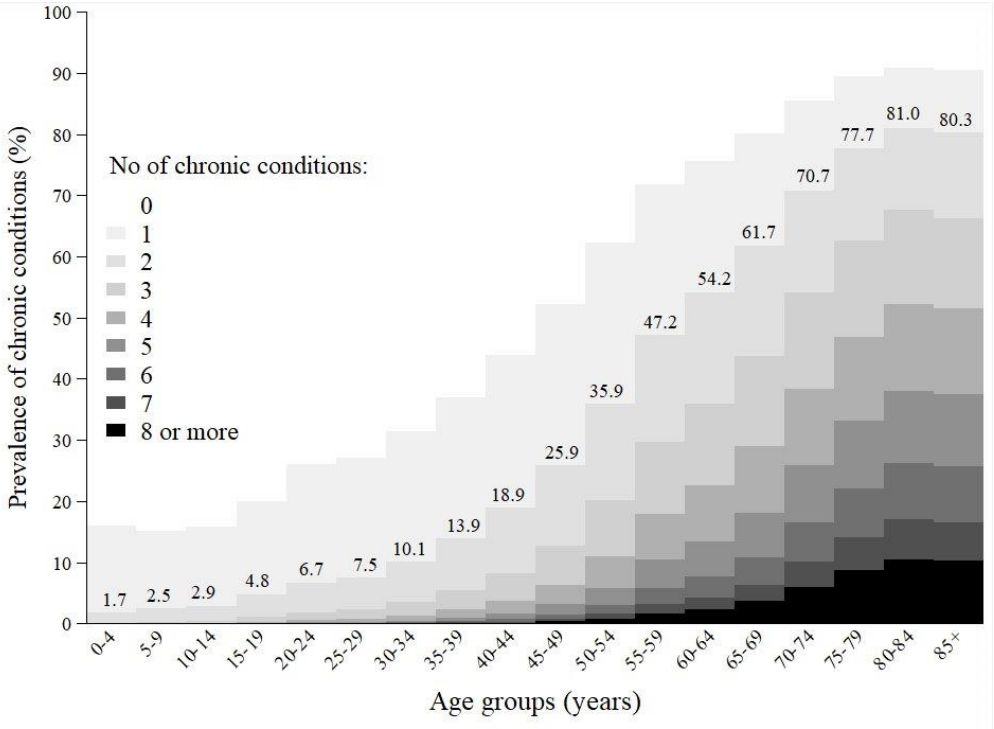

Figure 1. Prevalence of chronic conditions and multimorbidity (in numbers) by 5-year age groups.

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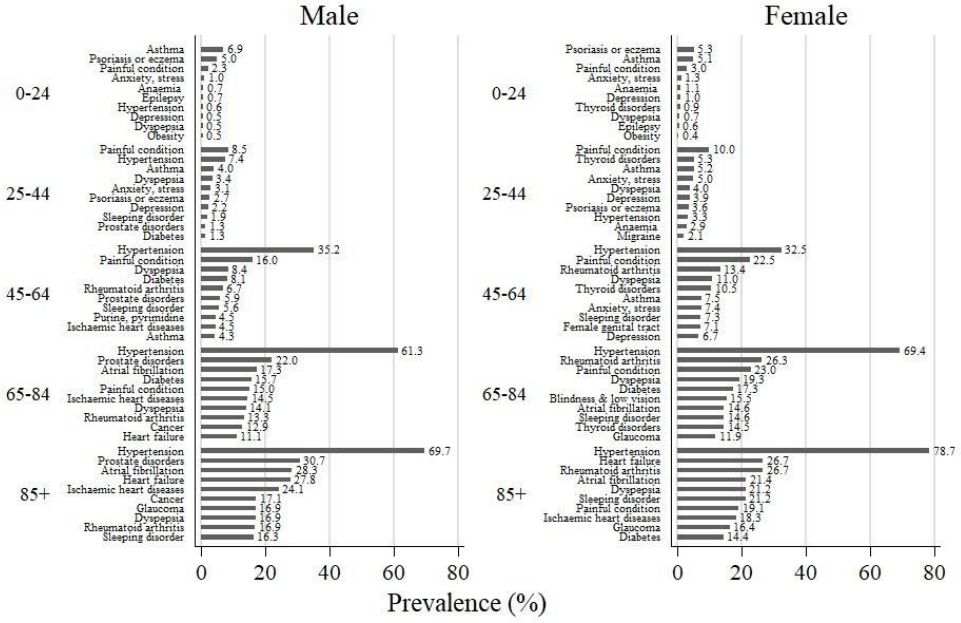

Figure 2. The prevalence of the 10 most common chronic conditions in men and women by age group.

251x167mm (96 x 96 DPI)

Supplementary appendix.

Table 1. List and prevalence of chronic conditions (in the total population and among MM patients) in the study.

Disorder	ICD-10 codes	Prevalence (%)	
		Total	among MM patients
Hypertension	[I10–I15]	24.49	67.40
Painful condition	[G44, R51] [M25.5] [M42–M54] [M77] [M79.1–79.9] [R10.1–10.4] [R07.0–07.4] [R30] [R52.0] [R52.1] [R52.2] [R52.9] [S22.0] [S22.1] [S12] [S32] [S72]	12.37	32.30
Rheumatoid arthritis, other inflammatory arthropathies and systemic connective tissue disorders	[M30–M36] [M05–M09, M79.0] [M91] [M15–M19]	7.65	23.56
Dyspepsia	[K21, K25–K30]	7.41	22.12
Asthma	[J45–J46] [J30]	5.91	12.94
Diabetes	[E10–14]	5.62	17.69
Sleeping disorders	[F51, G47]	5.11	15.80
Thyroid disorders	[E01–05, E06.1–.9, E07]	4.72	12.93

Atrial fibrillation	[I44–I45, I47–I49]	4.7	14.99
Psoriasis or eczema	[L20] [L23] [L28] [L29] [L40] [L50] [L56]	4.17	8.25
Anxiety and other neurotic, stress-related, and somatoform disorders	[F40–F43, F45, F48]	4.09	11.20
Blindness and low vision	[H17–18, H25–28, H31, H33, H34.1–.9, H35–H36, H43, H47, H54]	3.62	11.39
Ischaemic heart diseases	[I20–I25]	3.44	11.27
Depression	[F32–F33]	3.32	9.21
Heart failure	[I50]	3.24	10.65
Glaucoma	[H40–H42]	3.17	9.86
Cancer **	C00–97, D00–09, D37–48	3.05	8.84
Prostate disorders	[N40] [N41]	2.52	7.33
Disorders of purine and pyrimidine metabolism	[E79, M10]	2.07	6.56
Anemia	[D50–59, D60–D61, D63–64]	1.88	4.75
Obesity	[E66]	1.64	5.11

Noninflammatory disorders of the female genital tract	[N81] [N93] [N95]	1.57	4.45
Neuropathies	[G50–G64]	1.56	4.78
Disorders of vestibular function	[H81, H82, R42]	1.52	4.75
Stroke and transient ischaemic attack	[I60–66, I69, G45, I67.2]	1.45	4.71
Chronic obstructive pulmonary disease/bronchitis	[J40–J44]	1.4	4.42
Peripheral vascular disease	[I73.0] [I70]	0.93	2.98
Osteoporosis	[M80, M81, M82]	0.89	2.83
Schizophrenia or bipolar disorder	[F20–F29] [F31]	0.85	1.75
Epilepsy	[G40–G41]	0.84	1.84
Hearing loss	[H90–H91]	0.74	2.17
Migraine	[G43]	0.72	1.57
Cholelithiasis / Cholecystitis	[K80, K81.1]	0.5	1.47
Dementia	[F00, F01, F02, F03, F05.1, G30, G31, R54]	0.48	1.48
Chronic kidney disease	[N18–N19]	0.47	1.57

Mental and behavioral disorders due to use of alcohol	[F10]	0.43	1.16
Chronic liver disease	[K70–74, K76]	0.42	1.31
Valve disorders	[I34–I37]	0.37	1.20
Viral Hepatitis	[B18]	0.36	1.02
Irritable bowel syndrome	[K58]	0.33	0.97
Parkinson's disease	[G20, G21, G22]	0.31	0.97
HIV	[Z21, B20–B24]	0.30	0.70
disorders of the urinary system	[N39.3, N39.4, R32]	0.27	0.84
Calculus of kidney and ureter	[N20]	0.26	0.76
Inflammatory bowel	[K50–K52]	0.24	0.52
Chronic sinusitis	[J32]	0.21	0.57
Diverticular disease of the intestine	[K57]	0.2	0.63
Other psychoactive substance misuses	[F11–19]	0.16	0.45
Treated constipation	[K59.0]	0.16	0.42
Multiple sclerosis	[G35]	0.12	0.26
Coagulation defects	[D65-D69]	0.08	0.22
Learning disability	[F81]	0.06	0.08
Anorexia or bulimia	[F50]	0.05	0.13

Bronchiectasis	[J47]	0.05	0.16
Celiac disease	[K90.0]	0.03	0.07

* [ ] repetition of diagnostic codes within the boundaries of brackets

** Each cancer diagnosis code counted separately

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1	Title: population-based cross-sectional study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3	Abstract provides a short summary
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6	MM is a growing global health problem, the data are scarce regarding the prevalence of MM in Eastern Europe.
Objectives	3	State specific objectives, including any prespecified hypotheses	7	A definitive, population-based assessment of MM prevalence by age and gender is needed to inform the continued restructuring of the health care system to accommodate the growing proportion of these patients.
Methods				
Study design	4	Present key elements of study design early in the paper	7-8	Key elements of the cross-sectional study were described in the Methods section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8	We obtained data (year and month of birth, sex, dates for health claims, type of care, provided services, all diagnosis codes on claims, and the date and diagnosis code on prescriptions) from the Estonian Health Insurance Fund (EHIF) which is the sole health insurance provider in Estonia covering approximately 95% of the population. We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. To identify all patients with chronic physical and mental conditions, the ICD-10

				diagnosis codes for main and other (accompanying) diagnoses were used. For the prevalence analysis, we selected 55 conditions, whereas the list was based on previous MM research to enable comparability. We constructed the case definition for a chronic condition as the presence of at least two diagnosis codes at least 6 weeks apart for the same condition during the study period January 1, 2015, through December 31, 2017.
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	7-8, Supplementary appendix	We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. We constructed the case definition for a chronic condition as follows: the presence of at least two diagnosis codes at least 6 weeks apart for the same condition (i.e., matching ICD-10 category) during the study period January 1, 2015, through December 31, 2017. This definition enabled us to include chronic conditions while excluding patients with previously diagnosed but improved conditions (e.g., conditions where remission is possible, such as epilepsy, asthma, pain, or depression). The 6-week interval between the diagnoses reduced double-counting and over-ascertainment of cases. The inclusion of prescriptions in the data query allowed us to identify patients whose claims profile included diagnosis codes for only one condition, whereas their prescription history identified treatment for multiple conditions. The ascertainment period was extended to 3 years

				because some patients visit their physician infrequently.
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9	The outcomes were the prevalence of chronic disorders, multimorbidity (MM), and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8	The prevalence of conditions and MM were assessed using the population-based health data (health claims, prescriptions) from EHIF
Bias	9	Describe any efforts to address potential sources of bias	14-15	Selection and measurement bias were possible. First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. A universal definition and list of conditions used for MM research do not exist.

				We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. Third, it is possible that some people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.
Study size	10	Explain how the study size was arrived at	7	This was a population-based study. We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017)

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	13 (Table 1)	We assessed the prevalence of chronic conditions, mean number of chronic conditions, and MM by age group and sex
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9	The outcomes were the prevalence of chronic disorders, MM, and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured. All results are presented with 95% confidence intervals. Adjustment by age and sex were done using uni- and multivariate Poisson regression. Prevalence ratios and 95% confidence intervals are presented.
		(b) Describe any methods used to examine subgroups and interactions	13 (Table 1)	Prevalence ratios (by age group and sex) and 95% confidence intervals are presented.
		(c) Explain how missing data were addressed		It was not possible to identify any missing health claims or prescriptions from the EHIF data, but we assume that the impact of missing data on results is small as the health care institutions are interested in submitting the claims for reimbursement
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		
		(e) Describe any sensitivity analyses		No sensitivity analyses were performed
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		This was a cross-sectional study where all claims and prescriptions of all insured individuals were collected at a single time point.

		(b) Give reasons for non-participation at each stage		This was a cross-sectional study where all claims and prescriptions of all insured individuals were collected at a single time point.
		(c) Consider use of a flow diagram		No flow diagram was used as all data were collected and analysed at a single time point.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9	This was a population-based study. We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM.
		(b) Indicate number of participants with missing data for each variable of interest		It was not possible to identify any missing health claims or prescriptions from the EHIF data, but we assume that the impact of missing data on results is small as the health care institutions are interested in submitting the claims for reimbursement
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)		This was a cross-sectional study.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time		This was a cross-sectional study.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		This was a cross-sectional study.
		Cross-sectional study—Report numbers of outcome events or summary measures	9	Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33)
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	9-10, 13 (Table 1, Figure 1)	We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). Half of the individuals (49.1%, 95% CI 49.0–49.3) had one

		or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33). The prevalence of chronic conditions increased with age, from 18.2% (95% CI 18.0-18.3) in the youngest age group (0-24 years) to as high as 65.6% (95% CI 65.3–65.8) in the group of 45-64 years, and 90.4% (95% CI 89.4–91.4) among the oldest (85+ years). In the youngest age group, 0-24 years, the mean number of conditions was 0.23 (0.22–0.23), and it increased with age, reaching 3.22 (3.21–3.22) in age 65-84 and 3.92 (3.9–3.94) among those ≥85 years. The prevalence of MM also increased with age, from 3.5% (95% CI 3.5–3.6) in the age of 0-24 to as high as 80.4% (95% CI 79.4–81.3) among those ≥85 years. MM prevalence was higher among women than men, with about every third woman and every fourth man having MM. At a younger age, the prevalence of MM among women was comparable to that in men: the prevalence ratio (PR women/men) was 1.00 (95% CI 0.99-1.02) in the age group of 0-24 years. It increased gradually from 1.10 (95% CI 1.09-1.10 among those of 25-29 years to 1.27 (95% CI 1.24-1.29) in 65-69 years, and declined again to be more similar between women and men among those aged 85+ (1.09, 95% CI 1.05-1.13).
	(b) Report category boundaries when continuous variables were categorized	
	(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	This was a prevalence study.

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13, Figure 2, Supplementary appendix	Hypertension was the most frequent chronic condition in the three oldest age groups for both men and women. Hypertension affects one in four individuals (24.5 %) in the total population and about two-thirds (67.4%) among MM patients. Chronic pain ranked second with a prevalence of 12.4% in the total population and 32.3% among MM patients. Chronic pain was defined according to Barnett, et al. as chronic pain associated with selected physical conditions such as osteoarthritis and low back pain. The prevalence of painful conditions increases in older age as does the prevalence of cardiovascular diseases and conditions. Rheumatoid arthritis and other inflammatory arthropathies ranked third in the total population and MM patients, with the respective prevalences of 7.6% and 23.6%. This condition was closely followed by dyspepsia, with 7.4% of the total population and 22.12% of MM patients. The conditions with prevalence over 10% among MM patients included diabetes, sleep disorders, atrial fibrillation, asthma, thyroid disorders, blindness and low vision, ischaemic heart diseases, anxiety, and heart failure. In older men (65+ years), prostate disorders were frequent (22.8%) while in older women (65+ years) arthritis was quite prevalent (26.4%). Diseases such as asthma, diabetes, and dyspepsia were common across all age groups. In younger age groups, asthma, chronic pain, psoriasis or eczema, and mental health conditions were most frequent.

Discussion				
Key results	18	Summarise key results with reference to study objectives	13	The disease burden from chronic conditions is high in Estonia. Half of the individuals had at least one chronic disorder, and one-third had MM. The burden is increasing with age, being high already among middle-aged population groups (aged 45-64 years), where 82/3 of individuals have a prevalent condition Among those with MM, hypertension is the most prominent chronic condition, followed by chronic pain and arthritis.
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	14-15	First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. A universal definition and list of conditions used for MM research do not exist. [30] We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. Third, it is possible that some

				people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15	The prevalence of multimorbidity in Estonia is relatively high compared to other European countries, and higher among women than men. The prevalence of MM increases with age, with hypertension by far the most frequent chronic condition, followed by chronic pain, and arthritis. As the public health infrastructure continues to modernize, efforts must be placed on primary prevention of the conditions which lead to hypertension, such as obesity. The development of patient-centered, evidence-based treatment recommendations will help align patient and physician with respect to health goals and the means to achieve these outcomes.

Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15	One of the strengths of our study is the effort expended to enable comparability with the results of other studies. We used the list of conditions from previous research with only minor adjustments to reflect the diagnostic practices. Another strength of our analysis lies in the use of a data source with 95% nationwide coverage and complete follow-up, free of recall and social desirability biases. Furthermore, the validity of EHIF data, although established for financial and not health research purposes, has been tested recently and the study concluded that these data can be used for monitoring changes in chronic condition prevalence with a precision sufficient for informing health care policy. Our study thus provides high validity and generalizability of results allowing inferences to other Eastern European populations.
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	3	This work was supported by the Estonian Ministry of Education and Research Grant IUT34-17. Funders had no role in the study.

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

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

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Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

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Title page

Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

Mikk Jürisson, Heti Pisarev, Anneli Uusküla, Katrin Lang, Marje Oona, Ruth Kalda

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Prevalence of chronic conditions and multimorbidity in Estonia: a population-based cross-sectional study

Objectives: Prevalence estimates for specific chronic conditions and multimorbidity (MM) in Eastern Europe are scarce. This national study estimates the prevalence of MM by age group and sex in Estonia.

Design: Population-based cross-sectional study utilizing administrative data.

Setting: Data were collected on 55 chronic conditions from the Estonian Health Insurance Fund from 2015-2017. MM was defined as the coexistence of two or more conditions.

Participants: The Estonian Health Insurance Fund includes data for approximately 95% of the Estonian population receiving public health insurance.

Primary and secondary outcome measures: Prevalence and 95% confidence intervals (CI) for MM stratified by age group and sex.

Results: Nearly half (49.1%) of the individuals (95% CI 49.0–49.3) had at least one chronic condition, and 30.1% (95% CI 30.0–30.2) had MM (2 or more chronic conditions). The number of conditions and the prevalence of MM increased with age, ranging from a MM prevalence of 3.5% (3.5–3.6) in the youngest (0–24 years) to as high as 80.4% (79.4–81.3) in the oldest (≥85 years) age group. Half of all individuals had MM by 60 years, and 75% of the population had MM by 75 years of age. Women had a higher prevalence of MM (34.9%, 95% CI 34.7–35.0) than men (24.4%, 95% CI 24.3–24.5). Hypertension was the most frequent chronic condition (24.5%), followed by chronic pain (12.4%) and arthritis (7.7%).

Conclusions: Hypertension is an important chronic condition amenable to treatment with lifestyle and therapeutic interventions. Given the established correlation between uncontrolled hypertension and exacerbation of other cardiovascular conditions as well as acute illnesses, this

most common condition within the context of MM may be suitable for targeted public health interventions.

Strengths and limitations of this study

- One of the strengths of our study is the methodological comparability with previous research.
- The second strength is the nearly 95% nationwide coverage of our dataset, the validity of which has been tested and proven.
- A limitation of our study is the definition of a chronic condition and multimorbidity used in our study which is contestable in all studies of MM.

Data availability

The authors confirm that all data associated with the study are fully available without restriction from the Estonian Health Insurance Fund at https://www.haigekassa.ee/en. The data can be requested by completing the application at the following address: https://ankeet.haigekassa.ee/surveys/?s=4KXEPFDEKF or sending a written request to info@haigekassa.ee

Ethics approval

The study was conducted in accordance with local data protection regulations. The study was approved by the Tartu University Research Ethics Committee (280/T-7, 19.2018). The ethics committee waived the requirement for informed consent for the analysis presented in the manuscript.

Contributors

MJ, RK, HP, AU, and MO conceptualized and designed the study. MJ and HP collected, managed, and analyzed the data. All co-authors contributed to the interpretation of the findings

and drafting of the manuscript. MJ wrote the original draft, and MJ and KL wrote the final version. HP provided visualizations. All co-authors approved the final version for submission.

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Competing Interests Statement

The authors declare no conflict of interest.

Background

The management of patients with MM has become a challenge for healthcare systems as most individuals with long-term conditions are living with multiple long-term conditions. [1] The prevalence of MM is increasing along with population aging, [2] but aging is not the only factor predisposing the population increase in MM [3] and healthcare utilization has experienced a concomitant increase in response to managing these complex patients. [4–6] In addition to aging, MM is associated with other sociodemographic factors, such as female sex, lower education, lower household income, living alone, social deprivation and ethnicity [7–10], as well as health conditions, such as obesity [11], hypertension, having one chronic condition at baseline. Behavioral factors like smoking and physical inactivity are also influential. [12] Having multiple chronic conditions is associated with poor outcomes: patients have a decreased quality of life, psychological distress, longer hospital stays, more postoperative complications, a higher cost of care, and higher mortality. [13]

The management of patients with MM is a formidable challenge for healthcare systems. Research in this area is perhaps most urgently needed in low- and middle-income countries (LMIC) where the burden of multimorbidity is high, the specific distributions and determinants

of the disease may differ, and access to care may be impeded by a fragmented healthcare system which is continuing to modernize and restructure [14]. Although research is beginning to elucidate the distribution of co-occurring conditions in these countries, the comparability of findings is limited by methodological differences. This work demonstrates the utility of administrative data for constructing prevalence estimates, an approach that is particularly helpful for middle and high-to-middle-income-countries where resource limitations make administrative data not only immediately useful but also scalable, allowing for rate comparisons with other countries. In addition, the transition from a hospital-centric system in Estonia following independence from the Soviet Union was motivated by a desire to strengthen primary health care and thereby improve population health [15]. Having a set of prevalence estimates for MM is essential for measuring the ongoing success of this transition, adjusted by the prevalence of various conditions amenable to outpatient treatment. Finally, and perhaps most importantly, the SARS-CoV-2 pandemic drew attention to the important contribution of MM to the need for sound public health measures and rapid identification of effective medical interventions based on risk stratification. Frailty has been linked to infection [16], severity [16,17], geographic differences in severity and mortality by MM [18], prompting a renewed focus on improving global health and access to care, probabilistic modelling [19], the triage of care and shielding of the most vulnerable [20]. This study presents an important contribution to this developing literature with a comprehensive set of prevalence estimates for MM in Eastern Europe.

MM is a growing global health problem affecting all nations regardless of wealth [21]. A better understanding of the national or regional epidemiology of MM is necessary to allocate health care resources and develop treatment strategies that allow clinicians to deliver patient-centered care that appreciates the potential for competing priorities. [1,21] Furthermore, in the context of the coronavirus pandemic, the clinician is faced with the challenge of reconciling competing

priorities: maintain stable health among those with MM via telemedicine and other access interventions while preventing the exacerbation of acute SARS-CoV-2 if the patient becomes infected. Certainly, the time has come for all nations to better support individuals in preventing or modifying MM in the interest of improved overall health as well as optimizing patient outcomes following infection. The prevalence of MM has been extensively studied in Western European countries. For example, in a recent MM prevalence study utilizing a medical practice database in Scotland, 23.2% of patients were living with multimorbidity. [1] A recent systematic review and meta-analysis of observational studies [22] found an overall pooled 33.1% prevalence of MM. There was a considerable difference in the pooled estimates of MM between high and low-income countries, with a prevalence of 37.9% and 29.7%, respectively. Still, data are scarce regarding the prevalence of MM in Eastern Europe, where life expectancy is shorter than in Western Europe, particularly among men. The recent Survey of Health, Ageing, and Retirement in Europe (SHARE) study found that among all European countries, Eastern and Central Europe had the highest MM prevalence, revealing a remarkable health inequality across European regions. [7] To illustrate the gap, 70-79-year-old Central and Eastern Europeans suffer from about the same level of MM as ≥80-year old Northern Europeans. [7] However, the SHARE study is limited to self-reported data among individuals aged 50 years or more. Given the limited population-based research in Eastern Europe, the use of administrative health data is necessary to develop more accurate regional MM prevalence estimates.

Estonia belongs to the group of Eastern European high-middle income countries with relatively low life expectancy and a large sex health gap. The life expectancy among Estonian men is 73.8 years (compared to that of 82.1 in Estonian women) and is comparable to male life expectancy in China (74.5 years), Argentina (73.6 years), and Mexico (72.6 years). Estonian male life expectancy is markedly shorter than that of regional neighboring countries, such as Finland

(78.6 years), Sweden (80.8 years), or France (79.8 years). [23] Disability-free life expectancy in Estonia is also low, being 52.8 years for men and 55.6 years for women in 2018. [24] The burden of co-occurring chronic disease, leading to disability and premature death, is an important contributor to this reduced life expectancy in Estonia.

In Estonia, national public health insurance covers approximately 95% of the population. Family physicians are responsible for providing a core package of health services to the individuals registering with the practice for care. [25] Following Estonian independence in 1992, important steps were implemented to modernize the health system and improve coordination and access to primary care. In particular, access to family physicians was expanded before streamlining the hospital network, centralizing specialty care, and establishing a pharmaceutical formulary and treatment guidelines. [26] One of the stated goals of restructuring was to provide better chronic disease management, coordinated by the general practitioner, for whom a bonus system was implemented in 2005 to take on these duties. Although management guidelines and quality standards have been implemented for specific chronic conditions, this process has been slow to consider multimorbidity. [26] Family physicians in Estonia lack clear evidence-based standards for the management of patients with multiple chronic diseases, and the applicability of a single evidence-based guideline to MM is limited and can be problematic. [27]

A definitive, population-based assessment of MM prevalence by age and between males and females is needed to inform the continued restructuring of the health care system to accommodate the growing proportion of these patients.

Methods

For this population-based cross-sectional study, we obtained data from the Estonian Health Insurance Fund (EHIF) which is essentially the sole health insurance provider in Estonia

covering approximately 95% of the population. [28] We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. The data abstraction from the EHIF database included year and month of birth, sex assigned at birth, dates for health claims, type of care (in- and outpatient care, rehabilitation, nursing care, etc.), services provided, all diagnosis codes on claims, and the date and diagnosis code on prescriptions. Study subjects were assigned a unique identifier decoupled from personal identification information to enable longitudinal tracking of care while maintaining patient privacy.

To identify all patients with chronic physical and mental conditions, the ICD-10 diagnosis codes for main and other (accompanying) diagnoses were used. For the chronic physical and mental conditions analysis, we selected 55 conditions (Supplementary appendix, Table 1). The list of conditions was based on previous MM research to enable comparability [1,29,30] and adjusted by the authors (MJ, RK, AU, MO, HP) for use in Estonia. According to Barnett, et al., we included morbidities that were likely to be chronic, defined as having a significant impact on patients over at least the most recent year, defined in terms of the need for chronic treatment, reduced function, reduced quality of life, and risk of future morbidity and mortality. [1]

We constructed the case definition for a chronic condition as follows: the presence of at least two diagnosis codes at least 6 weeks apart for the same condition (i.e., matching ICD-10 category) during the study period January 1, 2015, through December 31, 2017 (Supplementary Appendix, Table 1). This definition enabled us to include chronic conditions while excluding patients with previously diagnosed but improved conditions (e.g., conditions where remission is possible, such as epilepsy, asthma, pain, or depression). The 6-week interval between the diagnoses reduced over-ascertainment of cases. The inclusion of prescriptions in the data query allowed us to identify patients whose claims profile included diagnosis codes for only one condition, whereas their prescription history identified treatment for multiple conditions.

The ascertainment period was extended to 3 years because some patients visit their physician infrequently. For instance, 17% of publicly insured individuals had no evidence of a visit to a family physician and 37% had no evidence of a visit to a specialist in 2017. [28] If we had elected a shorter study period, we might have inadvertently excluded the MM profile of nearly 20% of the population. Any correlation between lower health care utilization and sociodemographic characteristics that impede access (such as lack of paid time off from work for illness, lack of transportation in rural areas, etc.) would bias our claims-driven prevalence estimates to undercount MM among individuals facing these access challenges. The prevalence of chronic conditions among all publicly insured individuals was estimated on 31 December 2017 among all persons who were publicly insured at that time.

The study procedures were conducted according to local data protection regulations. The study was approved by the Tartu University Research Ethics Committee.

Patient and public involvement

This was an administrative claims study, and as such there were no patients enrolled in this study.

Statistical analysis

The outcomes were the prevalence of chronic conditions, MM, and the mean number of conditions by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured. All results are presented with 95% confidence intervals. Adjustment by age and sex were done using uni- and multivariate Poisson regression. Prevalence ratios and 95% confidence intervals are presented. The analysis was performed using STATA version 14.

Results

We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). [28,31] Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33) (Table 1).

The prevalence of any chronic condition increased with age, from 18.2% (95% CI 18.0-18.3) in the youngest age group (0-24 years) to as high as 65.6% (95% CI 65.3–65.8) in the group of 45-64 years, and 90.4% (95% CI 89.4–91.4) among the oldest (85+ years) (Table 1). In the youngest age group, 0-24 years, the mean number of conditions was 0.23 (0.22–0.23), and it increased with age, reaching 3.22 (3.21–3.22) in age 65-84 and 3.92 (3.90–3.94) among those ≥85 years. The prevalence and number of chronic conditions in 5-year age groups are presented in Figure 1.

The prevalence of MM also increased with age, from 3.5% (95% CI 3.5–3.6) among those younger than 25 years to as high as 80.4% (95% CI 79.4–81.3) among those ≥85 years. MM prevalence was higher among women than men, with about every third woman and every fourth man having MM. At a younger age, the prevalence of MM among women was comparable to that in men: the prevalence ratio ($PR_{women/men)}$ was 1.00 (95% CI 0.99-1.02) in the age group of 0-24 years. It increased gradually from 1.10 (95% CI 1.09-1.10 among those of 25-29 years to 1.27 (95% CI 1.24-1.29) in 65-69 years, and declined again to be more similar between women and men among those aged 85 years and older (1.09, 95% CI 1.05-1.13).

Table 1. Study population, the prevalence of chronic conditions, mean number of chronic conditions, and MM by age group and sex.

		Population (%)	Prevalence of chronic conditions (95% CI)	Mean number of conditions (95% CI)	Prevalence of MM (95% CI)
Total		1 240 927 (100.0)	49.1 (49.0–49.3)	1.33 (1.32–1.33)	30.1 (30.0–30.2)
Age group (years)	0–24	331 450 (26.7)	18.2 (18.0–18.3)	0.23 (0.22–0.23)	3.5 (3.5–3.6)
	25–44	326 460 (26.3)	34.8 (34.6–35.0)	0.56 (0.55–0.56)	12.6 (12.5–12.7)
	45–64	323 256 (26.0)	65.6 (65.3–65.8)	1.64 (1.63–1.64)	41.0 (40.7–41.2)
	65–84	225 705 (18.2)	85.6 (85.2–85.9)	3.22 (3.21–3.22)	71.1 (70.8–71.5)
	≥85	34 056 (2.7)	90.4 (89.4–91.4)	3.92 (3.90–3.94)	80.4 (79.4–81.3)
Sex	Men	569 087 (45.9)	43.6 (43.4–43.7)	1.06 (1.06–1.07)	24.4 (24.3–24.5)
	Women	671 840 (54.1)	53.8 (53.7–54.0)	1.55 (1.54–1.55)	34.9 (34.7–35.0)
Number of conditions	0	631 299 (50.9)	...	...	...
	1	236 547 (19.1)	...	...	...
	2	128 263 (10.3)	...	...	...
	3	83 751 (6.7)	...	...	...
	4	57 501 (4.6)	...	...	...
	5	39 159 (3.2)	...	...	...
	6	25 567 (2.1)	...	...	...
	7	16 259 (1.3)	...	...	...
	≥8	22 581 (1.8)	...	...	...

/Figure 1 here/

Figure 1. Prevalence of chronic conditions and multimorbidity (in numbers) by 5-year age groups.

The prevalence of the 10 most common chronic conditions in men and women by age group is shown in Figure 2, and the prevalence of all chronic conditions in the study (in the total population and among MM patients) in the Supplementary Appendix, Table 1. Hypertension was the most frequent chronic condition in the three oldest age groups for both men and women. Hypertension affects one in four individuals (24.5 %) in the total population and about two-thirds (67.4%) among MM patients.

Chronic pain ranked second with a prevalence of 12.4% in the total population and 32.3% among MM patients. Chronic pain was defined according to Barnett, et al. [1] as chronic pain associated with selected physical conditions such as osteoarthritis and low back pain (Supplementary appendix, Table 1). The prevalence of painful conditions increases in older age as does the prevalence of cardiovascular diseases and conditions (e.g., atrial fibrillation, ischaemic heart disease, and heart failure).

Rheumatoid arthritis and other inflammatory arthropathies ranked third in the total population and MM patients, with the respective prevalences of 7.6% and 23.6%. This condition was closely followed by dyspepsia, with 7.4% of the total population and 22.12% of MM patients. The conditions with prevalence over 10% among MM patients included diabetes, sleep disorders, atrial fibrillation, asthma, thyroid disorders, blindness and low vision, ischaemic heart diseases, anxiety, and heart failure. In older men (65+ years), prostate disorders were frequent (22.8%) while in older women (65+ years) arthritis was quite prevalent (26.4%). Diseases such as asthma, diabetes, and dyspepsia were common across all age groups. In

younger age groups, asthma, chronic pain, psoriasis or eczema, and mental health conditions were most frequent.

/Figure 2 here/

Figure 2. The prevalence of the 10 most common chronic conditions in men and women by age group.

Discussion

The disease burden from chronic conditions is high in Estonia. Half of the individuals had at least one chronic disorder, and one-third had MM. The burden is increasing with age, being high already among middle-aged population groups (aged 45-64 years), where 66% of individuals have a prevalent condition. Among those with MM, hypertension was the most prominent chronic condition, followed by chronic pain and arthritis.

Our results were overall very similar to the results of global and regional studies. A recent systematic review and meta-analysis of observational studies [22] calculated an overall 33.1% pooled prevalence of MM. Still, their estimate of MM for the high-income countries in that review was 37.9%, whereas our estimate of 30.1% is a bit lower, apparently due to the methodological differences discussed above. As described earlier in the background, disability-free life expectancy is low for Estonia, perhaps owing to the relatively high burden of MM. Comparing our results to the Scottish primary care research, MM was higher in our study (30.1% compared to 23.2% in Scotland). [1] Age group comparisons reveal that MM is more prevalent in Estonia in all age groups, especially in 45-64 years (41.0% in Estonia vs 30.4% in

Scotland) and 65-84 years (71.1% vs 64.9%), except for the ≥85 years age group, where it is very similar (80.4% vs 81.5%).

As for the types of prevalent chronic conditions, our findings converge with several other studies that identified hypertension, diabetes, asthma, and arthritis as the most prevalent conditions. In a recent Canadian study, the top five chronic conditions of the 17 examined among those with MM were mood disorders, hypertensive disorders, asthma, arthritis, and diabetes. [32] Lenzi, et al., found that hypertension, diabetes, and depression were highly prevalent among Italians. [33] Our national data also concur that morbidity increases with age, an association that has been demonstrated in other studies as well [1,3,32–34]. In a Canadian study of self-reported chronic conditions, the prevalence of 3+ conditions increased with age from 30% in the 45-49-year-old age group to 52% in individuals aged 60-64 years [34]. In Lithuania, the risk of acquiring an additional chronic condition was found to increase exponentially from the age of 29 years and stabilize between the age of 51 and 57 years [35,36].

Acknowledging the sex gap in health that is characteristic of Eastern Europe, we aimed to assess the sex-specific differences in MM. We found that in women aged 25+ years, the prevalence of MM is higher than men, with the largest difference among those aged 65-69 years. This elevated prevalence of MM among women has been confirmed in some studies [3,34], but not in others [32].

Some limitations of our study may affect generalizability. First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of

conditions accounted for, the age range, data source, and collection of data. [37,38] A universal definition and list of conditions used for MM research do not exist. [38] We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. [1,22] Third, it is possible that some people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. [31] However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.

One of the strengths of our study is the effort expended to enable comparability with the results of other studies. We used the list of conditions from previous research [1,29,30,36] with only minor adjustments to reflect the regional diagnostic practices. Another strength of our analysis lies in the use of a data source with 95% nationwide coverage and complete follow-up, free of recall and social desirability biases. Furthermore, the validity of EHIF data, although established for financial and not health research purposes, has been tested recently [39] and the study concluded that these data can be used for monitoring changes in chronic condition prevalence with a precision sufficient for informing health care policy. Our study thus provides high validity and generalizability of results allowing inferences to other Eastern European populations.

Conclusions

The prevalence of multimorbidity in Estonia is relatively high compared to other European countries, and higher among women than men. The prevalence of MM increases with age, with hypertension the most frequent chronic condition, followed by chronic pain, and arthritis. As the public health infrastructure continues to modernize, efforts must be placed on primary prevention of the conditions which lead to hypertension, such as obesity. The development of patient-centered, evidence-based treatment recommendations will help align patient and physician with respect to health goals and the means to achieve these outcomes.

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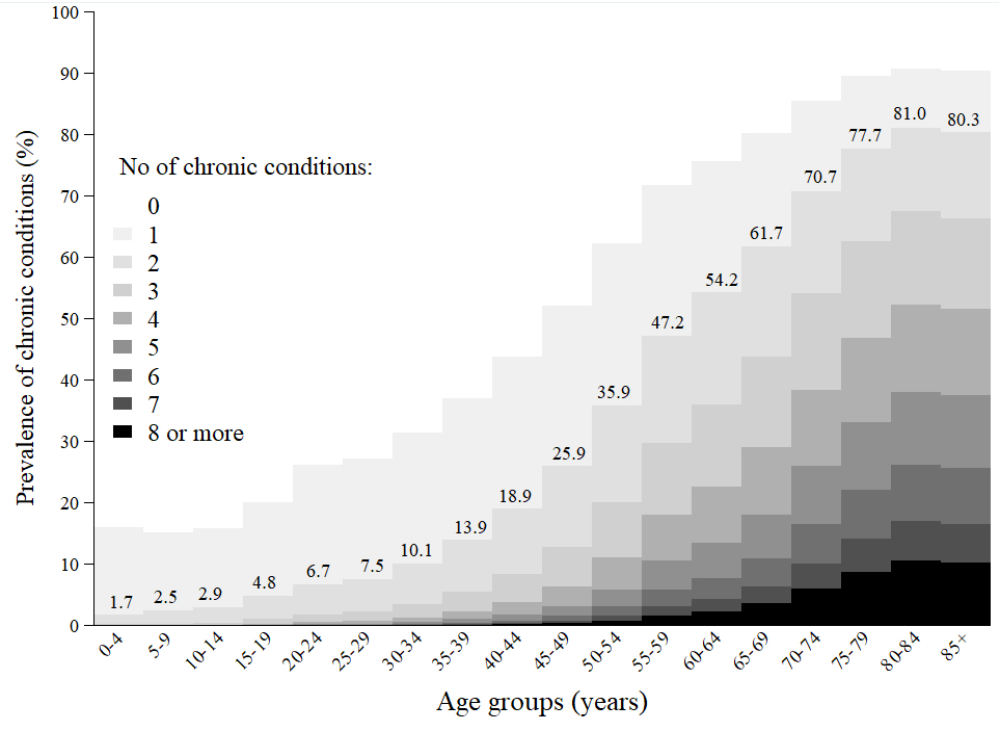

Figure 1

339x247mm (72 x 72 DPI)

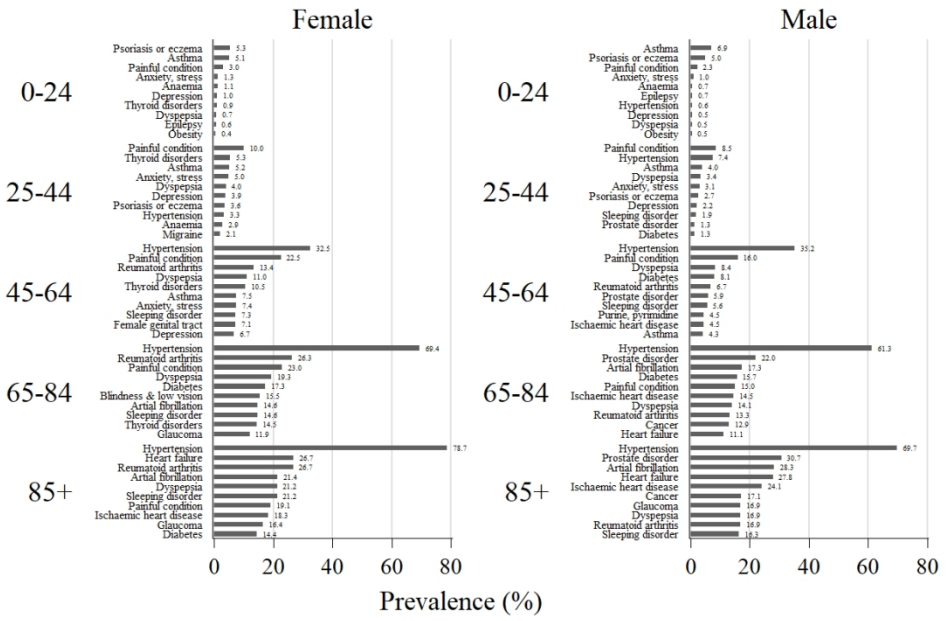

Figure 2

461x307mm (72 x 72 DPI)

Supplementary appendix.

Table 1. List and prevalence of chronic conditions (in the total population and among MM patients) in the study.

Disorder	ICD-10 codes	Prevalence (%)	
		Total	among MM patients
Hypertension	[I10–I15]	24.49	67.40
Painful condition	[G44, R51] [M25.5] [M42–M54] [M77] [M79.1–79.9] [R10.1–10.4] [R07.0–07.4] [R30] [R52.0] [R52.1] [R52.2] [R52.9] [S22.0] [S22.1] [S12] [S32] [S72]	12.37	32.30
Rheumatoid arthritis, other inflammatory arthropathies and systemic connective tissue disorders	[M30–M36] [M05–M09, M79.0] [M91] [M15–M19]	7.65	23.56
Dyspepsia	[K21, K25–K30]	7.41	22.12
Asthma	[J45–J46] [J30]	5.91	12.94
Diabetes	[E10–14]	5.62	17.69
Sleeping disorders	[F51, G47]	5.11	15.80
Thyroid disorders	[E01–05, E06.1–.9, E07]	4.72	12.93

Atrial fibrillation	[I44–I45, I47–I49]	4.7	14.99
Psoriasis or eczema	[L20] [L23] [L28] [L29] [L40] [L50] [L56]	4.17	8.25
Anxiety and other neurotic, stress-related, and somatoform disorders	[F40–F43, F45, F48]	4.09	11.20
Blindness and low vision	[H17–18, H25–28, H31, H33, H34.1–.9, H35–H36, H43, H47, H54]	3.62	11.39
Ischaemic heart diseases	[I20–I25]	3.44	11.27
Depression	[F32–F33]	3.32	9.21
Heart failure	[I50]	3.24	10.65
Glaucoma	[H40–H42]	3.17	9.86
Cancer **	C00–97, D00–09, D37–48	3.05	8.84
Prostate disorders	[N40] [N41]	2.52	7.33
Disorders of purine and pyrimidine metabolism	[E79, M10]	2.07	6.56
Anemia	[D50–59, D60–D61, D63–64]	1.88	4.75
Obesity	[E66]	1.64	5.11

Noninflammatory disorders of the female genital tract	[N81] [N93] [N95]	1.57	4.45
Neuropathies	[G50–G64]	1.56	4.78
Disorders of vestibular function	[H81, H82, R42]	1.52	4.75
Stroke and transient ischaemic attack	[I60–66, I69, G45, I67.2]	1.45	4.71
Chronic obstructive pulmonary disease/bronchitis	[J40–J44]	1.4	4.42
Peripheral vascular disease	[I73.0] [I70]	0.93	2.98
Osteoporosis	[M80, M81, M82]	0.89	2.83
Schizophrenia or bipolar disorder	[F20–F29] [F31]	0.85	1.75
Epilepsy	[G40–G41]	0.84	1.84
Hearing loss	[H90–H91]	0.74	2.17
Migraine	[G43]	0.72	1.57
Cholelithiasis / Cholecystitis	[K80, K81.1]	0.5	1.47
Dementia	[F00, F01, F02, F03, F05.1, G30, G31, R54]	0.48	1.48
Chronic kidney disease	[N18–N19]	0.47	1.57

Mental and behavioral disorders due to use of alcohol	[F10]	0.43	1.16
Chronic liver disease	[K70–74, K76]	0.42	1.31
Valve disorders	[I34–I37]	0.37	1.20
Viral Hepatitis	[B18]	0.36	1.02
Irritable bowel syndrome	[K58]	0.33	0.97
Parkinson's disease	[G20, G21, G22]	0.31	0.97
HIV	[Z21, B20–B24]	0.30	0.70
disorders of the urinary system	[N39.3, N39.4, R32]	0.27	0.84
Calculus of kidney and ureter	[N20]	0.26	0.76
Inflammatory bowel	[K50–K52]	0.24	0.52
Chronic sinusitis	[J32]	0.21	0.57
Diverticular disease of the intestine	[K57]	0.2	0.63
Other psychoactive substance misuses	[F11–19]	0.16	0.45
Treated constipation	[K59.0]	0.16	0.42
Multiple sclerosis	[G35]	0.12	0.26
Coagulation defects	[D65-D69]	0.08	0.22
Learning disability	[F81]	0.06	0.08
Anorexia or bulimia	[F50]	0.05	0.13

Bronchiectasis	[J47]	0.05	0.16
Celiac disease	[K90.0]	0.03	0.07

* [ ] repetition of diagnostic codes within the boundaries of brackets

** Each cancer diagnosis code counted separately

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1	Title: population-based cross-sectional study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3	Abstract provides a short summary
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6	MM is a growing global health problem, the data are scarce regarding the prevalence of MM in Eastern Europe.
Objectives	3	State specific objectives, including any prespecified hypotheses	7	A definitive, population-based assessment of MM prevalence by age and gender is needed to inform the continued restructuring of the health care system to accommodate the growing proportion of these patients.
Methods				
Study design	4	Present key elements of study design early in the paper	7-8	Key elements of the cross-sectional study were described in the Methods section.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8	We obtained data (year and month of birth, sex, dates for health claims, type of care, provided services, all diagnosis codes on claims, and the date and diagnosis code on prescriptions) from the Estonian Health Insurance Fund (EHIF) which is the sole health insurance provider in Estonia covering approximately 95% of the population. We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. To identify all patients with chronic physical and mental conditions, the ICD-10

				diagnosis codes for main and other (accompanying) diagnoses were used. For the prevalence analysis, we selected 55 conditions, whereas the list was based on previous MM research to enable comparability. We constructed the case definition for a chronic condition as the presence of at least two diagnosis codes at least 6 weeks apart for the same condition during the study period January 1, 2015, through December 31, 2017.
Participants	6	(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants	7-8, Supplementary appendix	We included all subjects from the EHIF database from January 1, 2015, through December 31, 2017. We constructed the case definition for a chronic condition as follows: the presence of at least two diagnosis codes at least 6 weeks apart for the same condition (i.e., matching ICD-10 category) during the study period January 1, 2015, through December 31, 2017. This definition enabled us to include chronic conditions while excluding patients with previously diagnosed but improved conditions (e.g., conditions where remission is possible, such as epilepsy, asthma, pain, or depression). The 6-week interval between the diagnoses reduced double-counting and over-ascertainment of cases. The inclusion of prescriptions in the data query allowed us to identify patients whose claims profile included diagnosis codes for only one condition, whereas their prescription history identified treatment for multiple conditions. The ascertainment period was extended to 3 years

				because some patients visit their physician infrequently.
		(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed Case-control study—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9	The outcomes were the prevalence of chronic disorders, multimorbidity (MM), and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8	The prevalence of conditions and MM were assessed using the population-based health data (health claims, prescriptions) from EHIF
Bias	9	Describe any efforts to address potential sources of bias	14-15	Selection and measurement bias were possible. First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. A universal definition and list of conditions used for MM research do not exist.

				We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. Third, it is possible that some people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.
Study size	10	Explain how the study size was arrived at	7	This was a population-based study. We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017)

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	13 (Table 1)	We assessed the prevalence of chronic conditions, mean number of chronic conditions, and MM by age group and sex
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9	The outcomes were the prevalence of chronic disorders, MM, and the mean number of disorders by age and sex, estimated as a proportion of individuals with the current characteristics and among the total number of people insured. All results are presented with 95% confidence intervals. Adjustment by age and sex were done using uni- and multivariate Poisson regression. Prevalence ratios and 95% confidence intervals are presented.
		(b) Describe any methods used to examine subgroups and interactions	13 (Table 1)	Prevalence ratios (by age group and sex) and 95% confidence intervals are presented.
		(c) Explain how missing data were addressed		It was not possible to identify any missing health claims or prescriptions from the EHIF data, but we assume that the impact of missing data on results is small as the health care institutions are interested in submitting the claims for reimbursement
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed Case-control study—If applicable, explain how matching of cases and controls was addressed Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy		
		(e) Describe any sensitivity analyses		No sensitivity analyses were performed
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		This was a cross-sectional study where all claims and prescriptions of all insured individuals were collected at a single time point.

		(b) Give reasons for non-participation at each stage		This was a cross-sectional study where all claims and prescriptions of all insured individuals were collected at a single time point.
		(c) Consider use of a flow diagram		No flow diagram was used as all data were collected and analysed at a single time point.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9	This was a population-based study. We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM.
		(b) Indicate number of participants with missing data for each variable of interest		It was not possible to identify any missing health claims or prescriptions from the EHIF data, but we assume that the impact of missing data on results is small as the health care institutions are interested in submitting the claims for reimbursement
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)		This was a cross-sectional study.
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time		This was a cross-sectional study.
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		This was a cross-sectional study.
		Cross-sectional study—Report numbers of outcome events or summary measures	9	Half of the individuals (49.1%, 95% CI 49.0–49.3) had one or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33)
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	9-10, 13 (Table 1, Figure 1)	We analyzed the data of all publicly insured individuals (n = 1 240 927, 94.1% of the total population as of December 31, 2017). Half of the individuals (49.1%, 95% CI 49.0–49.3) had one

		or more chronic conditions, and 30.1% (95% CI 30.0–30.2) had MM. The mean number of conditions was 1.33 (95% CI 1.21-1.33). The prevalence of chronic conditions increased with age, from 18.2% (95% CI 18.0-18.3) in the youngest age group (0-24 years) to as high as 65.6% (95% CI 65.3–65.8) in the group of 45-64 years, and 90.4% (95% CI 89.4–91.4) among the oldest (85+ years). In the youngest age group, 0-24 years, the mean number of conditions was 0.23 (0.22–0.23), and it increased with age, reaching 3.22 (3.21–3.22) in age 65-84 and 3.92 (3.9–3.94) among those ≥85 years. The prevalence of MM also increased with age, from 3.5% (95% CI 3.5–3.6) in the age of 0-24 to as high as 80.4% (95% CI 79.4–81.3) among those ≥85 years. MM prevalence was higher among women than men, with about every third woman and every fourth man having MM. At a younger age, the prevalence of MM among women was comparable to that in men: the prevalence ratio (PR women/men) was 1.00 (95% CI 0.99-1.02) in the age group of 0-24 years. It increased gradually from 1.10 (95% CI 1.09-1.10 among those of 25-29 years to 1.27 (95% CI 1.24-1.29) in 65-69 years, and declined again to be more similar between women and men among those aged 85+ (1.09, 95% CI 1.05-1.13).
	(b) Report category boundaries when continuous variables were categorized	
	(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	This was a prevalence study.

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13, Figure 2, Supplementary appendix	Hypertension was the most frequent chronic condition in the three oldest age groups for both men and women. Hypertension affects one in four individuals (24.5 %) in the total population and about two-thirds (67.4%) among MM patients. Chronic pain ranked second with a prevalence of 12.4% in the total population and 32.3% among MM patients. Chronic pain was defined according to Barnett, et al. as chronic pain associated with selected physical conditions such as osteoarthritis and low back pain. The prevalence of painful conditions increases in older age as does the prevalence of cardiovascular diseases and conditions. Rheumatoid arthritis and other inflammatory arthropathies ranked third in the total population and MM patients, with the respective prevalences of 7.6% and 23.6%. This condition was closely followed by dyspepsia, with 7.4% of the total population and 22.12% of MM patients. The conditions with prevalence over 10% among MM patients included diabetes, sleep disorders, atrial fibrillation, asthma, thyroid disorders, blindness and low vision, ischaemic heart diseases, anxiety, and heart failure. In older men (65+ years), prostate disorders were frequent (22.8%) while in older women (65+ years) arthritis was quite prevalent (26.4%). Diseases such as asthma, diabetes, and dyspepsia were common across all age groups. In younger age groups, asthma, chronic pain, psoriasis or eczema, and mental health conditions were most frequent.

Discussion				
Key results	18	Summarise key results with reference to study objectives	13	The disease burden from chronic conditions is high in Estonia. Half of the individuals had at least one chronic disorder, and one-third had MM. The burden is increasing with age, being high already among middle-aged population groups (aged 45-64 years), where 82/3 of individuals have a prevalent condition Among those with MM, hypertension is the most prominent chronic condition, followed by chronic pain and arthritis.
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	14-15	First, the definition of a chronic condition used in our study is contestable. However, we sought to ensure conformance with the methodologies used in prior research and establish the chronicity of the disease. Thus, the health care claim or prescription with a specific condition had to be identified at least 2 times during the period of observation. The second limitation is the heterogenous MM prevalence estimates due to methodological differences, including the MM definition, the list and grouping of conditions accounted for, the age range, data source, and collection of data. A universal definition and list of conditions used for MM research do not exist. [30] We attempted to optimize generalizability by adopting the list from previous research. To allow accurate estimations of disease burden, and effective disease management and resource distribution, a standardized operationalization of MM are needed. Third, it is possible that some

				people with chronic conditions did not visit a physician or made only one visit over the study period, thus the under-ascertainment of conditions cannot be ruled out. Fourth, the EHIF database covers approximately 95% of the population but lacks the data for approximately 5% of uninsured individuals. However, given that all individuals aged 64 years and older are covered by health insurance, we acknowledge that a minor ascertainment bias may exist in younger age groups, as the health data for the uninsured individuals were not available. Fifth, not all individuals who were insured at the date of observation (December 31, 2017) were insured during the entire three-year study period, which might result in minor under-ascertainment among those newly enrolled.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15	The prevalence of multimorbidity in Estonia is relatively high compared to other European countries, and higher among women than men. The prevalence of MM increases with age, with hypertension by far the most frequent chronic condition, followed by chronic pain, and arthritis. As the public health infrastructure continues to modernize, efforts must be placed on primary prevention of the conditions which lead to hypertension, such as obesity. The development of patient-centered, evidence-based treatment recommendations will help align patient and physician with respect to health goals and the means to achieve these outcomes.

Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15	One of the strengths of our study is the effort expended to enable comparability with the results of other studies. We used the list of conditions from previous research with only minor adjustments to reflect the diagnostic practices. Another strength of our analysis lies in the use of a data source with 95% nationwide coverage and complete follow-up, free of recall and social desirability biases. Furthermore, the validity of EHIF data, although established for financial and not health research purposes, has been tested recently and the study concluded that these data can be used for monitoring changes in chronic condition prevalence with a precision sufficient for informing health care policy. Our study thus provides high validity and generalizability of results allowing inferences to other Eastern European populations.
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	3	This work was supported by the Estonian Ministry of Education and Research Grant IUT34-17. Funders had no role in the study.

*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.