Population Health Metrics

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Patient-centred estimation of multimorbidity in chronic disease populations: a novel approach integrating global burden of disease metrics and healthcare administrative data

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Abstract

Background Although chronic diseases represent a growing global health priority, significant gaps remain in understanding the burden of multimorbidity. This study developed an original methodology to estimate the burden of thirty major chronic diseases at the individual patient level, in terms of Disability-Adjusted Life years (DALYs), Years Lived with Disability (YLD), and Years of Life Lost due to premature death (YLL).

Methods The Disability weights (DWs) estimated by the Global Burden of Disease (GBD) study were integrated with information from healthcare databases. A panel of medical specialists established the criteria for assigning the level of severity, and thus a specific DW, to each chronic disease. The patient-centred YLD metric was estimated as the cumulative of the combined DWs over the previous ten years. We also measured the Disability Weight Fraction of each coexisting disease (DWF). We illustrated this method using healthcare databases from a large Italian region to assess the impact of chronic diseases and multimorbidity at progressive levels of analysis: health status of the regional chronic disease population, burden of individual chronic diseases and patient clinical complexity.

Results Unlike the standard GBD estimates, the new method provided precise metrics for multimorbidity, as shown by the comparison on the disability calculated for 4 main chronic diseases. Real-world estimates from the new method highlighted that comorbidity accounted for most of the YLD: for instance, about 88% of the YLD of patients with heart failure was explained by concomitant conditions. DALYs were higher among females than males in most age groups. In the younger groups, psychiatric conditions explained approximately 40% and 25% of YLD among males and females, respectively. Finally, the patient-centred YLD metric was a good predictor of death (c-statistic = 0.779).

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Conclusions This novel method provides insights into the measurement of multimorbidity, based on the disability fraction of each concomitant health condition, which is crucial for defining priority areas for healthcare interventions. The patient-centred estimates may serve to identify subgroups of chronic disease patients with specific healthcare needs and trajectories among **a given** population. Importantly, measuring the relative contribution of each disease to the patient's burden of multimorbidity favours the planning of multidisciplinary care pathways that are more responsive to individual needs.

Keywords Multimorbidity, Patient-centred burden of chronic disease, Disability adjusted life years, Years lived with disability, Disability weight fraction attributable

Background

Chronic non-communicable diseases are long-lasting health conditions resulting from a combination of genetic, physiological, environmental, and behavioural factors, and require ongoing medical attention and/or limit activities of daily living [1]. People living with chronic diseases often experience health complications that affect their quality of life and can shorten their life expectancy [2]. Globally, approximately one in three adults suffer from more than one chronic condition, or multimorbidity. This figure is higher in developed countries and is expected to progressively increase with the overall improvement in health conditions, the rise in survival rates and the aging of the population [3]. Chronic diseases and multimorbidity are the leading causes of disability and death around the world, and are often the main drivers of decreased productivity and increased healthcare costs [1], thus representing a global health priority.

The Global Burden of Disease (GBD) Study [4, 5] coordinated by the Institute for Health Metrics and Evaluation (IHME), is the most comprehensive effort to quantify health loss of populations across places and over time for a wide range of diseases, injuries, and major risk factors. This global initiative aims to ensure that the most current and detailed results are used by policymakers to make decisions to improve population health. A set of disability weights (DWs), developed and periodically updated to evaluate loss of functioning due to living with a given health condition, is at the heart of the GBD approach. DWs are used to calculate the Years Lived with Disability (YLD), a health metric reflecting the impact that a specific illness has on quality of life before it resolves or leads to death in a given population [6]. The burden of disease (BoD), expressed in terms of Disability-Adjusted Life Years (DALYs), is the sum of YLD and Years of Life Lost due to premature death (YLL), and allows comparisons of different health conditions and populations. Despite continuous improvements, the method for calculating DALYs has inherent limitations. Among them, the YLD component is derived from different data sources around the world with potential intrinsic biases, therefore leading to inaccuracies in the estimation of the BoD [7–9]. The limitations of GBD calculations when applied to patients with more than one chronic disease have been pointed out by several modelling studies, which have explored alternative methods to adjust for multimorbidity [10–12]. The GBD study uses a microsimulation approach to adjust for multimorbidity, but its assumptions of independence of diseases, failure to account for their progression over time, and lack of individual-level clinical data, may oversimplify the true impact of multiple coexisting conditions. Hence, while it is generally accepted that multimorbidity represents an increasing challenge for global health, there remain significant gaps in understanding the burden of multiple coexisting health conditions, which is key to developing effective strategies and interventions [13]. In particular, we lack a metric of the burden of multimorbidity accounting for the nature, duration, evolution and interaction of the different diseases [14].

This study presents a novel approach that aims to overcome these limitations, by adapting the GBD metrics to reflect real-world disease-related disability, frequently associated with two or more co-occurring chronic conditions in the same individual, especially in the elderly. Our method integrates DWs estimated by the IHME with healthcare administrative databases, which are typically usable for scientific research questions and cover entire patient populations over extended time periods, otherwise unattainable through survey methods alone. Leveraging these comprehensive data sources to reconstruct each patient's medical history, we propose new BoD metrics that capture the burden of individual multimorbidity over time and quantify the disability attributable to each coexisting chronic disease, considering its onset and duration. In this work, we illustrate the process of deriving these patient-centred BoD estimates using healthcare administrative data from a large region in Northern Italy to offer an accurate account of the impact of chronic diseases across an entire sub-national population.

Methods

Study design and population

This is a population-based retrospective study, resulting from the health policy-making oriented research of the Health Department of Emilia-Romagna (ER). ER is a large Italian region with about 4.5 million inhabitants,

Fig. 1 (See legend on next page.)

(See figure on previous page.)

Fig. 1 Main steps of the patient-centred BoD methodology (all the metrics are estimated for an example patient k)
Legend: DWs = Disability Weights; yld = years lived with disability, calculated by summing up the DWs of the disease (in the case of a single chronic disease) or the combined DWs of 2 or more coexisting diseases (in the case of multimorbidity) of each year; dwfi = disability weight fraction of a specific disease, calculated as the ratio of the yld of that disease to the sum of the yld of all coexisting diseases; dwai = disability weight attributable to a specific disease, calculated as the dwfi re-proportioned to the combined DWs of the coexisting chronic diseases; yll = years of life lost due to premature death, calculated for each deceased patient as the difference between the actual and expected age of death; dalys = disability-adjusted life years, calculated as the sum of the yld and yll components

more than 1.5 million of whom present at least one chronic disease every year. About 70% of the regional health resources are dedicated to people with chronic conditions.

In Italy, the healthcare system operates on the principle of universal coverage, ensuring that every individual's access to public or private healthcare services is routinely documented. Since Italian health services are organized, managed, and evaluated at the regional level, regional information systems maintain detailed records of each health service provided to individual residents.

For the present work, we used the ER health information system, which is updated monthly and routinely checked for consistency. The study was conducted following the guidelines outlined in the REporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement [15]. The study population consisted of people residing in ER in 2022 with at least one out of thirty prevalent chronic diseases, identified as seriously disabling or life-threatening, and requiring significant dedicated healthcare resources [16].

The patients were selected based on their ER anonymous identifier. Each disease was detected through at least one of the following criteria: International Classification of Diseases 9th Revision, Clinical Modification (ICD9-CM) diagnoses reported in one of the available regional data sources, in the last three years (period 2020–2022); Anatomic Therapeutic Chemical (ATC) classification system codes of drug prescriptions in the last year; specific disease-exemption codes effective during 2022. A list of the regional data sources used for the identification of the pathologies is reported in Additional File 1, Supplementary Table 1; ICD9-CM diagnosis codes, ATC drug codes and exemption codes for tracing individual health conditions are shown in Additional File 1, Supplementary Table 2.

For the specific purposes of this study, additional information was retrieved from the following documentation: ER mortality tables for the year 2022 provided by the National Institute of Statistics (ISTAT) [17]; datasets of the DWs for the GBD estimates [18]; GBD diagnostic categories [18] used as a reference to align with the ICD9-CM codes of the chronic diseases included in this study.

The medical history of each patient was estimated using information (frequency and type of healthcare received) from ER healthcare databases, collected over the previous ten years (period 2013–2022).

BoD results are shown with the thirty chronic diseases grouped into eleven exploratory categories, identified using the GBD Compare tool [19]: cardiovascular diseases, respiratory diseases, metabolic diseases, Chronic Kidney Disease (CKD), gastrointestinal/liver conditions, stroke, neurological disorders, psychiatric disorders, neoplasms, vision/hearing impairment, and musculoskeletal diseases (see Additional File 1, Supplementary Table 2 for grouping details). These chronic diseases and categories are of course not exhaustive of the entire spectrum of diseases and BoD results would vary if additional or different diseases were included.

Burden of disease metrics

The BoD of individual chronic disease patients was assessed by four GBD combined metrics. The following definitions are the same reported in previous GBD studies [20].

1) GBD Disability Weights (DWs): DWs represent the severity of the chronic condition, assessed on the basis of the patient's physical, mental and social conditions, and are calculated on a scale from 0 to 1, where 0 equals a state of full health and 1 equals death [7, 21]. For example, a DW of 0.55 associated with a certain disease indicates that the disease causes a 55% loss of life in full health in the year in which it occurs.

2) Years Lived with Disability (YLD): the YLD component represents the years of healthy life lost due to disability, i.e. years of life in which the disability equates to a fraction of one year lived in full health. In this study, this measure is calculated differently for patients suffering from one chronic disease and for multimorbid patients.

3) Years of Life Lost due to premature death (YLL): the YLL component is calculated as the difference between the corresponding standard life expectancy for that person's age and sex, and the age of actual death.

4) Disability-Adjusted Life Years (DALYs): DALYs are a composite measure of morbidity (YLD) and mortality (YLL).

All these metrics were indicated with lowercase letters when referred to the patient level, to distinguish them from the population-level aggregate ones.

Patient-centred burden of disease methodology

The following paragraphs describe how the GBD metrics were applied to prevalent chronic disease cases identified through healthcare administrative databases in 2022.

Figure 1 summarises the steps to estimate the dalys and other derived measures for an example chronic disease patient k. The calculation of the yld component is different for patients with one chronic disease and those with multiple diseases.

Criteria for attributing levels of disease severity

DWs are typically associated with three levels of disease severity (mild, moderate, and severe) [22], which can be valued through different approaches. Our approach involved a panel of seventeen medical specialists with backgrounds in clinical management and epidemiological research, who established a priori criteria for assigning the level of severity, and thus a specific DW, to each chronic disease considered in this study. Once the criteria were established, they were automatically applied to each patient's disease history, based on the patient information (i.e., types of healthcare services used) available in the ER administrative databases.

A given chronic disease was to be assigned a mild severity level if only drug therapy and/or disease-specific exemptions were present. To assign a severe level, both a set of general criteria, valid for all thirty chronic diseases, and additional criteria specific for twelve diseases, were to be satisfied. A moderate level was to be attributed by exclusion (Additional File 1, Supplementary Table 3). These criteria were determined by consensus development among all panel members. The specific criteria for the twelve diseases were judged blindly by at least two experts in a first round, while the final consensus was reached in a second round.

The GBD DWs and the related 95% Uncertainty Intervals (95%UI), associated with each level of disease severity determined through these criteria were then used in the next steps of this methodology (Additional File 1, Supplementary Table 4 shows the GBD DWs used in the present study).

Calculation of years lived with disability (yld)

For patients with one single chronic disease, the yld measure was obtained by summing up the DWs for each year of the disease: $yldi=\Sigma jDWij$, where *i* indicates the *i-th* pathology, *j* is the *j-th* year (with *j* ranging between 1 and the duration of the disease), and *DWij* is the disability weight assigned to the *i-th* disease in the *j-th* year, varying according to the evolution of the chronic condition over time.

For patients with multiple chronic conditions, the sum of the disability weights associated with each of the co-occurring conditions may lead to an overestimation of the yld, and may even be greater than 1, where 1 is the upper limit of disability corresponding to death. To overcome this problem, the disability weights for each *j* year were re-proportioned to obtain the combined disability weights (*DW_combj*), following the multiplicative approach described in Hilderink et al. [11] For each year, the proportion of time lived with disability was calculated as the product of the complement to 1 of the weights of each co-occurring i disease: *(1-DW1)*(1-DW2)*....*(1-DWi)*. The combined disability weight for each year was obtained by subtracting the above product from 1 (i.e., the maximum disability weight indicating death): *DW_combj = 1-(1-DW1j)*(1-DW2j)*....*(1-DWij)*, where *j* indicates the *j-th* year (with *j* ranging between 1 and the duration of the least recent disease).

Then, adding up the combined disability weights of each year yielded the number of years lived with disability by the individual chronic patient, due to multimorbidity: $yld=\Sigma jDW\_combij$.

Finally, we calculated the disability weight fraction of a specific disease (*dwfi*), as follows: $dwfi = (\Sigma jDWij/\Sigma ijDWij)$. The disability weight attributable to each disease (*dwai*), re-proportioned to the combined disability weight of the coexisting health conditions (*yld*), was obtained as follows: *dwai = dwfi*yld*. The two metrics *dwfi* and *dwai* are measures of the burden of each chronic condition in a multimorbid patient.

As an example, consider a patient with three chronic conditions in 2022: dementia, diagnosed three years earlier, heart failure, present for two years, and CKD, with onset in the last year. This is a chronic patient since 2020. In 2020 the patient suffered from dementia, which was treated with drug therapy. According to the disease severity criteria, dementia was assigned a mild severity level, associated with a DW of 0.069, i.e. 6.9% of the patient's healthy life was impaired due this disease. In 2021, the patient presented with heart failure requiring hospitalisation (DW = 0.072), while still affected by a mild dementia (DW = 0.069). Thus, in 2021 the combined disability weight, *DW_combj*, was 1-(1-0.069)*(1-0.072) = 1-(0.931*0.859) = 0.20, i.e. the two conditions together compromised 20% of the patient's healthy life. In 2022, the patient's clinical condition worsened due to a diagnosis of CKD, requiring at least three dialysis procedures per year (DW = 0.104). In the same year, heart failure got worse, requiring two hospitalisations (DW = 0.179), while dementia was still treated pharmacologically (DW = 0.069). Therefore, the patient's overall disability in 2022 was calculated as follows: *DW_combj* = 1-(1-0.069)*(1-0.179)*(1-0.104) = 0.685, i.e. the 3 chronic conditions impaired 68.5% of the patient's healthy life. In total, over the three-year period 2020–2022, the patient lost about 1 year (yld = 0.069 + 0.20 + 0.685 = 0.954) of healthy life (see Fig. 1 for details of the calculation of yld, dwfi and dwai).

Calculation of years of life lost due to premature death (yll)

The calculation of the yll component involved a record-linkage of the deceased chronic patients under study with the regional mortality register (REM) and a subsequent record-linkage by age and gender with the ER ISTAT lifetables, reporting estimates of the age- and sex-specific life expectancy of the residents. For each deceased patient, yll was thus calculated as the difference between the actual and expected age of death.

Calculation of disability-adjusted life years (dalys)

For chronic patients who died during 2022, the calculation of dalys resulted from the sum of the yll and the yld metrics.

Application of BoD methodology: endpoints of the study

In the present study, we applied the BoD methodology to assess the impact of chronic diseases and multimorbidity at progressive levels of analysis:

General health status of the population with chronic disease under study. The impact of individual chronic diseases and their respective diagnostic categories was assessed at the population level by calculating the DALYs (and their YLD and YLL components), obtained from the sum of the dalys (and their yld and yll components) of each patient, standardised per 1,000 inhabitants, by both age (5-year groups) and sex. The DWFs of the individual chronic diseases and categories were also calculated to show their relative contribution in the total YLD, again by age and sex. Population-level DWFs for individual chronic diseases are obtained by dividing the DWAs for each disease, obtained as the sum of each patient's disease-specific dwas, by the total population YLDs (obtained as the sum of each patient's ylds). DWAs were estimated by adding the relative disease-specific dwas at the patient level.

Burden of chronic disease categories. The eleven chronic disease categories were ranked according to their DALYs. In addition, the DWAs for individual pathologies were calculated to assess their specific contribution within each chronic disease category. The percentage of YLD attributable to the number of comorbidities within each diagnostic category was also determined.

Burden of individual chronic diseases. The burden of each disease is expressed both as the total YLD of the study population suffering from that disease and as DWAs.

As expressed in terms of YLD, the burden of each disease includes the disability due to other concomitant diseases. Additionally, the DWFs of the comorbidities that make up the YLD of each individual chronic disease can be calculated to provide information on the overall picture of the patient's multimorbidity. Four single chronic disease examples are provided.

Patient clinical complexity. Since the yld metric is highly informative of the patient's chronic disease history, it can be considered a summary indicator of the severity of the individual's health condition. To test the ability of the patient's yld to accurately predict adverse outcomes such as a death event, a logistic analysis was carried out with death as a dichotomous dependent variable and yld as a covariate. The goodness-of-fit of the logistic model was tested using the C statistic, representing the area under the ROC curve. Finally, we explored the informative power of yld and the number of concomitant pathologies as indicators of the patient's disease-related disability. The number of comorbidities at the individual patient level was plotted against individual yld and this relationship was tested using Kendall's correlation coefficient.

Comparison with the GBD standard estimates. To highlight the differences between the two methodological approaches, GBD estimates of the corresponding YLDs for the Emilia-Romagna region, available on the IHME website [23], were compared with the YLDs estimated by the new method, using a cross-sectional perspective, i.e. without considering the cumulative disease burden over the previous 10 years. Since the most recent GBD estimates refer to the year 2021, also the new method was applied to 2021 regional data. For each pathology, two different YLD metrics were estimated: the first was obtained as the sum of the DWi, without adjustment for multimorbidity; the second was derived from the sum of the DWAi, with adjustment for multimorbidity.

Uncertainty intervals

The 95% Uncertainty Interval (UI95%) of each estimated metric is based on the UI95% of the DWi and is obtained by applying the same calculation procedures used for the DWi, both to their lower UI (DW_LUI_i) and upper UI (DW_UUI_i) values. Thus, for example, the lower and the upper UI95% values of DW_combj were obtained as follows: DW_combj_LUI_j = 1-(1-DW_LUI_1j)*(1-DW_LUI_2j)*…….*(1-DW_LUI_ij) and DW_combj_UUI_j = 1-(1-DW_UUI_1j)*(1-DW_UUI_2j)*…….*(1-DW_UUI_ij), where i indicates the disease and j indicates the j-th year (with j ranging between 1 and the duration of the least recent disease).

Results

Prevalence of chronic diseases in the regional population

Prevalent chronic diseases among the 2022 ER population are reported by sex in Table 1.

In 2022, 1,617,138 ER residents had at least one out of the 30 identified chronic conditions, representing 36.4% of the overall regional population. Most chronic disease cases were females (39.9%). People with two or more chronic conditions were 695,464, representing 15.6% of

Table 1 Prevalent chronic diseases by sex in the ER population in 2022

ER population (2022)	Females	Males	All
	2,281,321	**2,164,134**	**4,445,455**
	N (%)	**N (%)**	**N (%)**
Age			
0–19	362,009 (8.2)	386,149 (9.9)	748,158 (9.0)
20–39	444,192 (18.6)	462,206 (13.9)	906,398 (16.2)
40–59	682,410 (37.0)	669,743 (27.8)	1,352,153 (32.4)
60+	792,710 (68.9)	646,036 (64.7)	1,438,746 (67.0)
Chronic disease			
Diabetes	134,037 (5.9)	160,342 (7.4)	294,379 (6.6)
Thyroid disease	282,630 (12.4)	61,891 (2.9)	344,521 (7.7)
Obesity	13,838 (0.6)	8,940 (0.4)	22,778 (0.5)
Ischemic heart disease	36,391 (1.6)	76,564 (3.5)	112,955 (2.5)
Cardiac arrhythmias	56,291 (2.5)	62,031 (2.9)	118,322 (2.7)
Heart failure	36,042 (1.6)	30,979 (1.4)	67,021 (1.5)
Peripheral vascular disease	48,329 (2.1)	46,478 (2.1)	94,807/4 (2.1)
Other cardiovascular diseases	4,948 (0.2)	7,636 (0.4)	12,584 (0.3)
Asthma	47,452 (2.1)	49,571 (2.3)	97,023 (2.2)
Chronic obstructive pulmonary disease (COPD)	59,390 (2.6)	57,854 (2.7)	117,244 (2.6)
Interstitial lung disease	2,255 (0.1)	2,976 (0.1)	5,231 (0.1)
Chronic kidney disease (CKD)	17,746 (0.8)	28,080 (1.3)	45,826 (1.0)
Chronic hepatitis/Cirrhosis	59,667 (2.6)	93,051 (4.3)	152,718 (3.4)
Crohn's/ulcerative colitis	21,578 (0.9)	26,757 (1.2)	48,335 (1.1)
Gastro-oesophageal disease	18,743 (0.8)	19,948 (0.9)	38,691 (0.9)
Cerebrovascular disease	69,925 (3.1)	48,715 (2.3)	118,640 (2.7)
Motor-neuron disease	33,178 (1.5)	32,452 (1.5)	65,630 (1.5)
Multiple sclerosis	401 (0.0)	496 (0.0)	897 (0.0)
Epilepsy	4,460 (0.2)	2,274 (0.1)	6,734 (0.2)
Anoxic encephalopathy	177 (0.0)	311 (0.0)	488 (0.0)
Alzheimer's disease and other dementias	38,981 (1.7)	20,597 (1.0)	59,578 (1.3)
Parkinson's disease	17,820 (0.8)	17,207 (0.8)	35,027 (0.8)
Depression	197,946 (8.7)	87,881 (4.1)	285,827 (6.4)
Psychosis, schizophrenia, and bipolar disorder	44,886 (2.0)	33,780 (1.6)	78,666 (1.8)
Neoplasms	16,208 (0.7)	15,878 (0.7)	32,086 (0.7)
Vision impairment	172,819 (7.6)	135,616 (6.3)	308,435 (6.9)
Hearing impairment	74,100 (3.2)	60,927 (2.8)	135,027 (3.0)
Gout	2,549 (0.1)	2,513 (0.1)	5,062 (0.1)
Rheumatic disease	29,608 (1.3)	16,194 (0.7)	45,802 (1.0)
Other musculoskeletal disorders	141,087 (6.2)	84,474 (3.9)	225,561 (5.1)
Chronic disease population (2022)	**910,675 (39.9)**	**706,463 (32.6)**	**1,617,138 (36.4)**
Number of diseases per patient			
1	509,066 (22.3)	412,608 (19.1)	921,674 (20.7)
2	218,777 (9.6)	154,528 (7.1)	373,305 (8.4)
3	97,298 (4.3)	69,737 (3.2)	167,035 (3.8)
> 3	85,534 (3.7)	69,590 (3.2)	155,124 (3.5)

the ER population. Thyroid disease and diabetes were the most prevalent conditions, accounting for 7.7% and 6.6% of cases in the regional population, respectively. Depression also showed a high prevalence (6.4%). In 2022, 50,380 deaths among chronic disease patients were recorded, representing 3.1% of the total prevalent cases.

Additional File 1, Supplementary Table 5 shows the frequencies of the 11 chronic disease categories among the study population (i.e. patients with chronic conditions, $N = 1,617,138$) by sex and age groups. The most frequent category was represented by metabolic diseases (37.7%), followed by musculoskeletal conditions (24.4%), psychiatric disorders (20.1%) and neoplasms (19.1%). The frequencies of these pathologies were much higher among older people, who also presented age-related conditions,

such as neurological, respiratory, and cardiovascular diseases.

Health status of the study population with chronic conditions

Figure 2 shows DALYs and DWFs for the chronic disease categories under study by age group in the study population. These results are also reported for individual chronic diseases in Additional File 1, Supplementary Table 6. With increasing age, DALYs also increased, and the relative contribution of different chronic disease categories (DWAs) varied across age groups (Fig. 2A). In the first years of life (0–4 years group), YLL explained more than half of the DALYs. In the subsequent ages, YLD represented the predominant component of DALYs, exceeding 1,000 years of healthy life lost from the age of 60 and reaching over 1,900 years of healthy life lost among the over 95s. Respiratory diseases, especially Ashma, explained about a third of the YLD among children aged 0–4 years (DWF = 29.6%, 95% Uncertainty Interval (UI) 17.1–45.8%)), while neurological disorders, first of all epilepsy, were the main contributors to YLD in the 5–19 age group (with a peak among those aged 10–14, DWF equal to 40.7% (95% UI 27.2–55.5%) (Fig. 2B and Supplementary Table 6). In the subsequent ages up to 64 years, psychiatric disorders, first psychosis, schizophrenia and bipolar disorders, had a prominent role, with DWA up to 354.8 (95% UI 250.1–463.0) in 50–54 age group. The DWFs of neoplasms, gastrointestinal/liver diseases, and metabolic disorders increased from 30 years old and reached more than 30% between 65 and 79 years of age. Cardiovascular, metabolic, and musculoskeletal conditions also showed increased DWFs and from the age of 65 onwards, in combination with neurological disorders, accounted for the largest portion of YLD. Notably, the DWF of depression was significant regardless of age, and its relative weight did not increase as a function of age (Additional File 1 and Supplementary Table 7). Depression explained 6.2% (95% UI 4.4–8.2%) of the estimated disability among adolescents (age group 15–19), 8.3% (95% UI 5.8–11.4%) to 13.7% (95% UI 9.4–19.4%) among those aged 20–49 and 14.4% (95% UI 9.9–20.2%) in the 55–59 age group. Excluding disability from other chronic conditions, the relative burden of depression did not increase with increasing age.

Figure 3 shows the DALYs and DWFs for the chronic disease categories under study by sex and age group in the study population. These results are also reported for individual chronic diseases in Additional File 1, Supplementary Tables 8–11. DALYs among females were higher than among males in most age groups.

Considering psychiatric disorders, psychosis, schizophrenia and bipolar disorders explained about 40% of the YLD calculated for males aged between 20 and 40, whereas the corresponding DWF among females was around 25%. On the other hand, the DWF of depression was higher among females than among males, and this difference became more marked from age 40 onwards (on average 16.5 vs. 10%) (Additional File 1, Supplementary Tables 9 and 11). It should be noted that the burden attributable to the individual diseases and categories, although comparable in the two groups in terms of DWFs, was in absolute number of years higher for females than for males.

Burden of chronic disease categories

Figure 4 shows the ranking of DALYs associated with chronic disease categories per 1,000 patients, with their relative YLD and YLL components. For each category, the YLD directly attributable to the individual diseases included in the category is displayed. The YLD (in percentage) attributable to the presence of 1, 2 or more comorbidities in the same patient is also highlighted.

Patients with neurological diseases had the highest BoD, with 3,522.1 (95% UI 2,836.8-4200.1) DALYS per 1,000 patients, of which 38% were attributable to concomitant diseases and 28% to premature death (YLL component). Alzheimer's disease and other dementias were the diseases with the greatest impact on the disability of neurological patients (YLD = 1,041.4, 95% UI 871.1-1,197.9)). Patients with CKD and those with stroke showed a similar BoD, with 3,353 (95% UI 2,744.5 -3,978.7) and 3,160 (95% UI 2,640.7-3,692.0) DALYs, respectively, mostly attributable to concomitant pathologies (47% and 52%, respectively) and with the largest fraction of YLL (34% and 39%, respectively). Comorbidities accounted for the majority of DALYs in most of the chronic disease categories. However, they played a marginal role in the composition of BoD of patients with neoplasms (23%) and psychiatric diseases (28%).

Burden of individual chronic diseases

Figure 5 shows that multimorbidity-related disability can also be broken down to the single-disease level. Four examples of chronic diseases with a high impact in terms of patient burden are presented: COPD (Fig. 5A), dementias (Fig. 5B), depression (Fig. 5C) and heart failure (Fig. 5D). The YLD for each of these diseases was subdivided into fractions of disability (DWFs) attributable to both the index disease itself and the various comorbidities. For comparison, their frequency is also given in brackets. The YLD of patients with COPD was mainly attributable to comorbidities (77.7%, 95% UI 69.9–84.7%), including neoplasms (15.8%, 95% UI 12.4–22.2%), depression (10.9%, 95% UI 7.8–14.3%), and psychosis, schizophrenia, and bipolar disorders (9%, 95% UI 6.7–10.5%). A similar pattern was found for patients with Alzheimer's disease and other dementias. However,

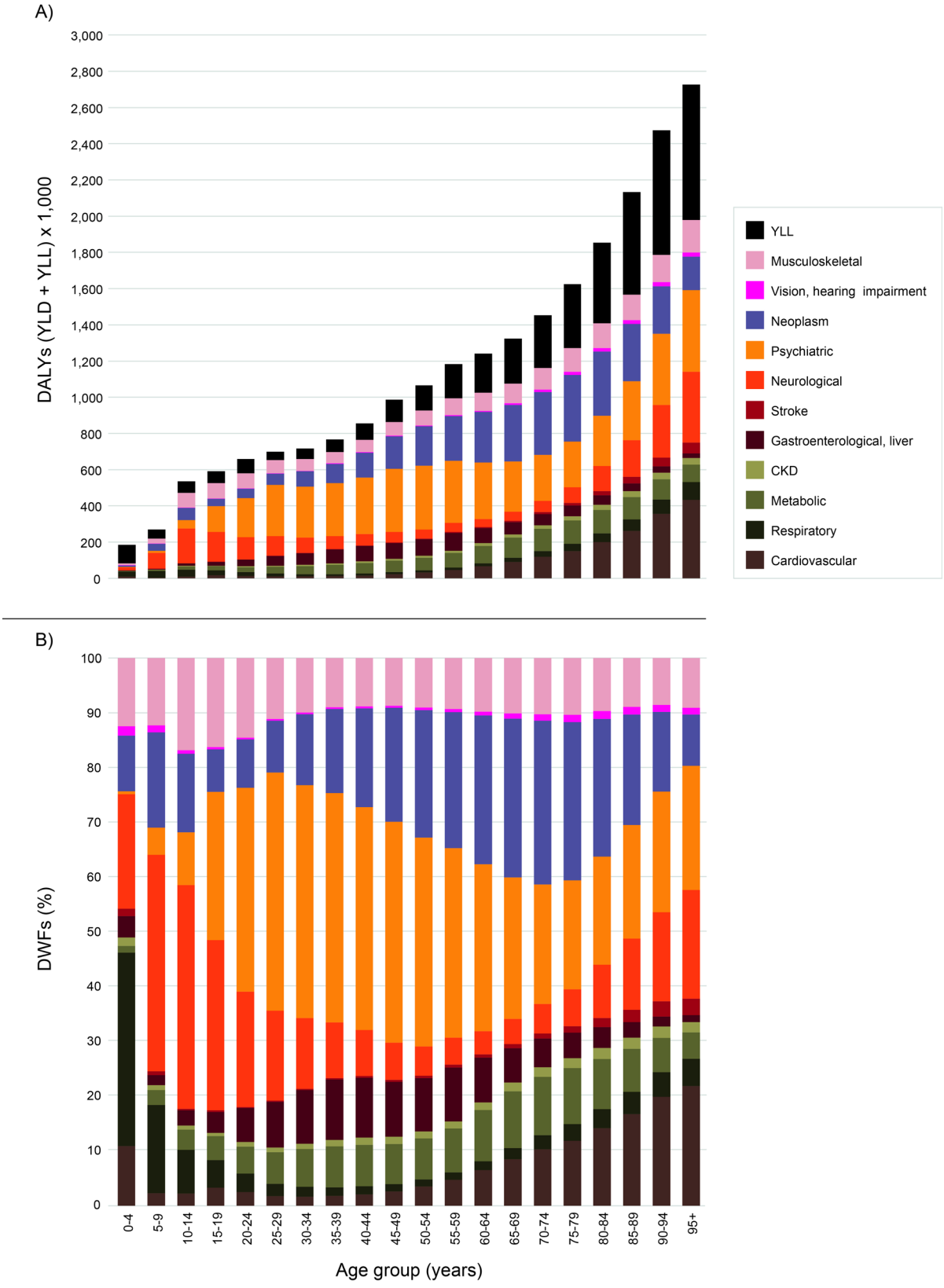

Fig. 2 DALYs per 1,000 inhabitants (**A**) and DWFs (**B**) of chronic disease categories, by age group
(**A**) DALYs are indicated as YLD + YLL. Each chronic disease category is reported as DWA, i.e. Disability Weight attributable to the category, reproportioned to the overall YLD component
(**B**) Each chronic disease category is reported as DWF, i.e. Disability Weight Fraction of the overall YLD component

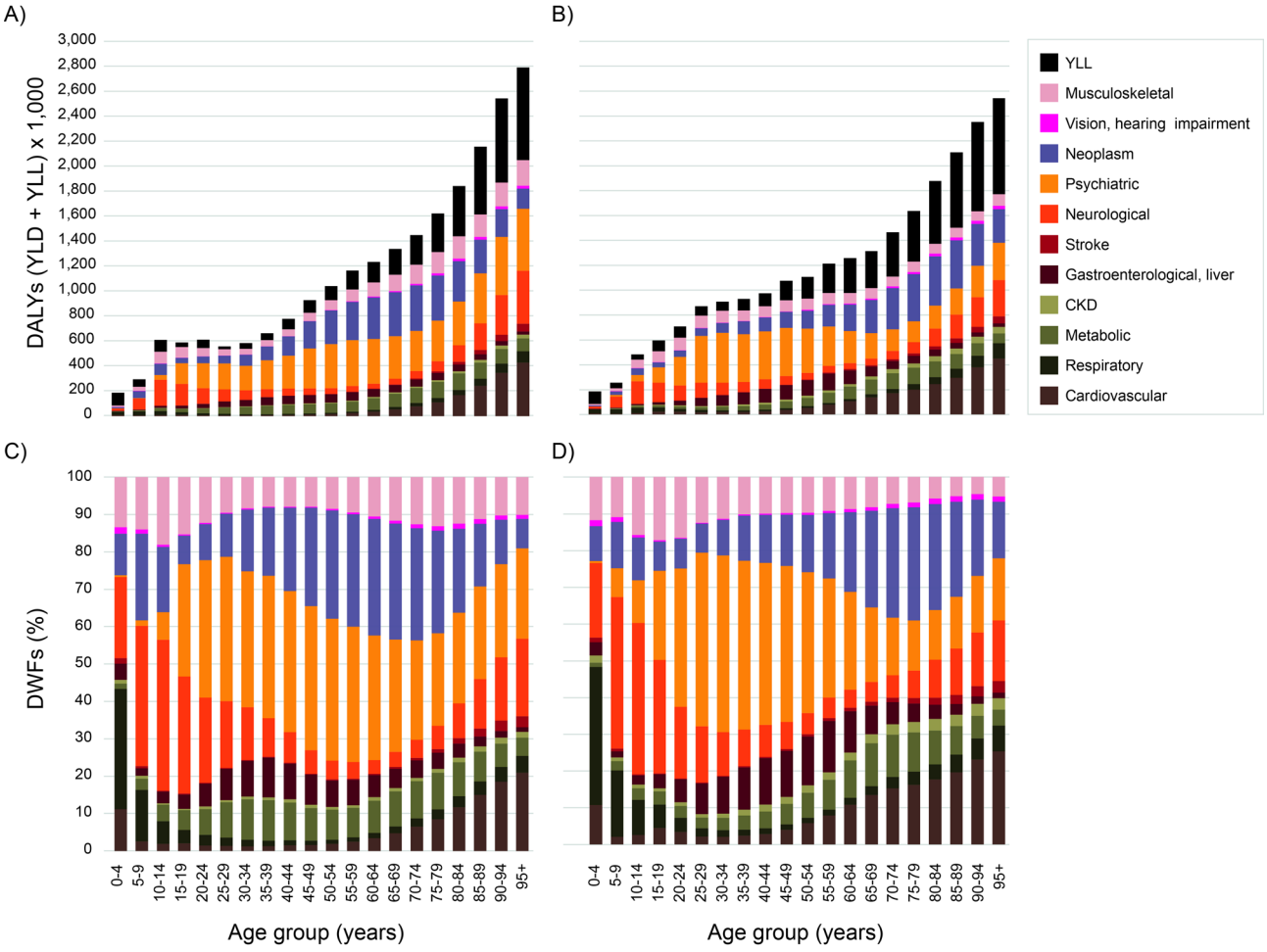

Fig. 3 DALYs per 1,000 inhabitants by age group in females (**A**) and males (**B**); DWF of each chronic disease category by age group in females (**C**) and males (**D**)

(**A**) and (**B**) DALYs are indicated as YLD + YLL. Each chronic disease category is reported as DWA, i.e. Disability Weight attributable to the category, reproportioned to the overall YLD component

(**C**) and (**D**) Each chronic disease category is reported as DWF, i.e. Disability Weight fraction of the overall YLD component

the DWF of dementias was quite significant (27.3%, 95% UI 19.7–33.5%), as was that relating to two very frequent comorbidities: psychosis, schizophrenia and bipolar disorder (16.6%, 95% UI 12.6–19.2%), and depression (10.7%, 95% UI 7.8–13.6%). In contrast, depression itself was the main cause of disability (56.2%, 95% UI 39.1–77.4%) of depressed patients, with comorbidities explaining less than half of their YLD. Finally, heart failure showed a more heterogeneous picture. Approximately 88% of YLD of patients with heart failure was explained by comorbidities, with cardiac arrhythmia playing a relevant role (13.7%, 95% UI 9.8–17.4%), in combination with neoplasms (10.7%, 95% UI 7.4–13.6%), depression (8.9%, 95% UI 6.5–11.1%) and COPD (7.2%, 95% UI 5.2–8.9%)).

Patient clinical complexity

Figure 6A shows the predictive power of yld tested against the probability of mortality. As the yld increased, the mortality rate also increased, with yld alone explaining 77.9% of the risk of death (Area Under the Roc Curve = 0.7795). This finding confirms that yld can be considered an indicator of patient complexity. The probability of death varied between 1.5% (95% CI 1.5%-1.5%) and 78.9% (95% CI 78.0%-79.4%), at the lowest and highest yld values, respectively. With yld values above 2, the increase in the probability of death per yld unit increase became exponential: from 4.4% (95% CI 4.4%-4.5%) to 7.5% (95% CI 7.4%-7.6%) and then to 12.5% (95% CI 12.3%-12.6%), 20% (95% CI 19.7%-20.3%) and so forth. yld and the number of coexisting long-term conditions were correlated (Kendall's correlation coefficient = 0·45 $p < 0.0001$). Figure 6B shows that, as the number of comorbidities increased, the percentage of patients with high disability also increased. However, the two measures were not interchangeable indicators for disability. For example, 79.9% of patients with 3 concomitant

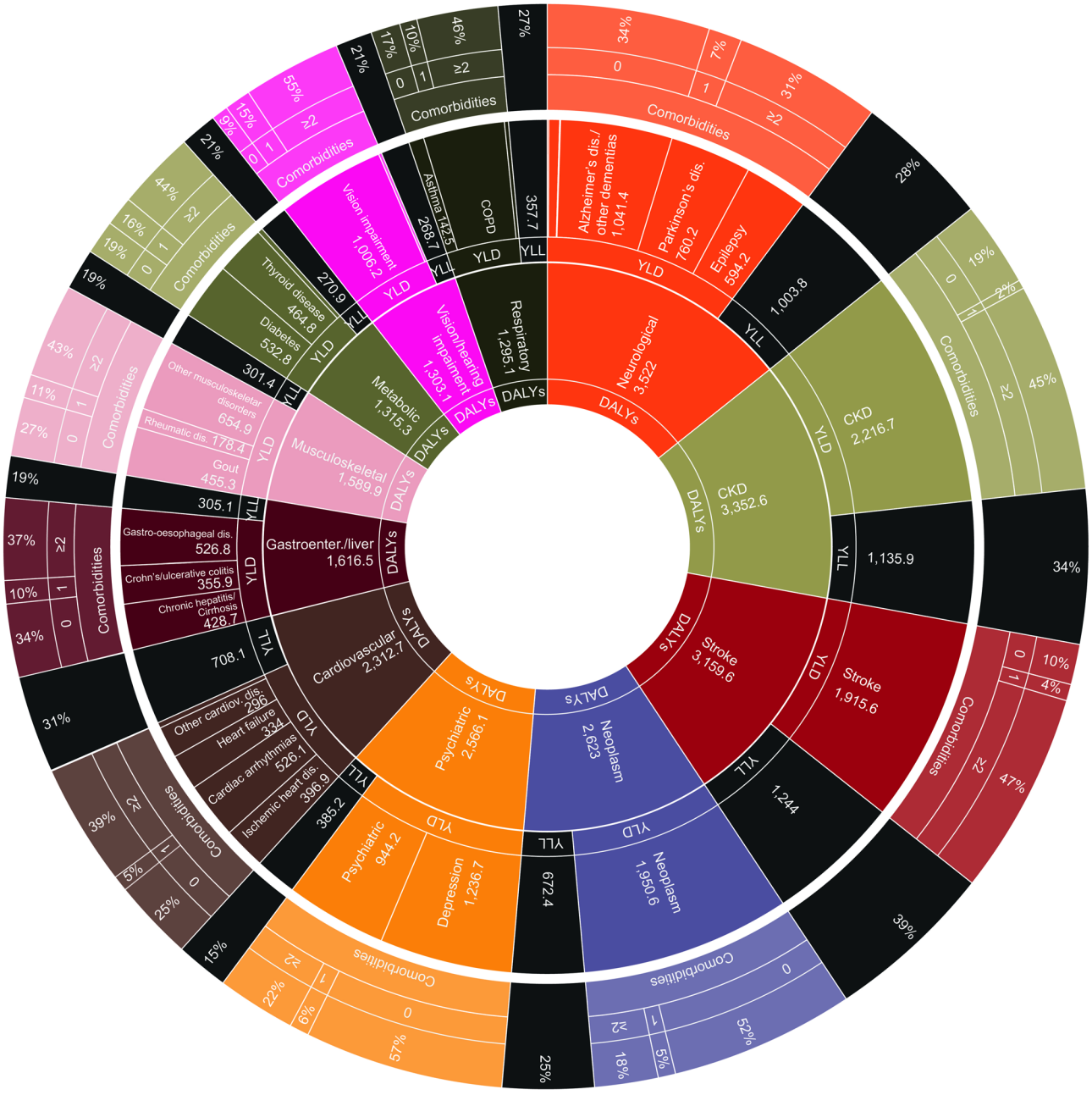

Fig. 4 DALYs (and their YLD and YLL components) for the 11 chronic disease categories included in the study
From the innermost to the outermost circle:
- Ranking of DALYs for the 11 diagnostic categories;
- YLD component (broken down into DWAs associated with the individual chronic diseases included in the diagnostic category) + YLL component for each diagnostic category;
- Proportion (%) of YLD explained by comorbidities (0, 1, 2 or more)
DALYs = Disability-Adjusted Life Years; YLD = Years Lived with Disability; DWA = Disability Weight Attributable to single chronic diseases; YLL = Years of Life Lost due to premature death

pathologies and 69% of patients with 4 comorbidities showed low yld values (below 2). On the other hand, 3.5% of those with one single chronic disease displayed a medium-high disability of more than 2 yld.

Comparison between the new method and GBD estimates

The performance of the new method was evaluated by comparing its estimates with those produced by the standard GBD methodology. To enable this comparison, a cross-sectional perspective was adopted, excluding the

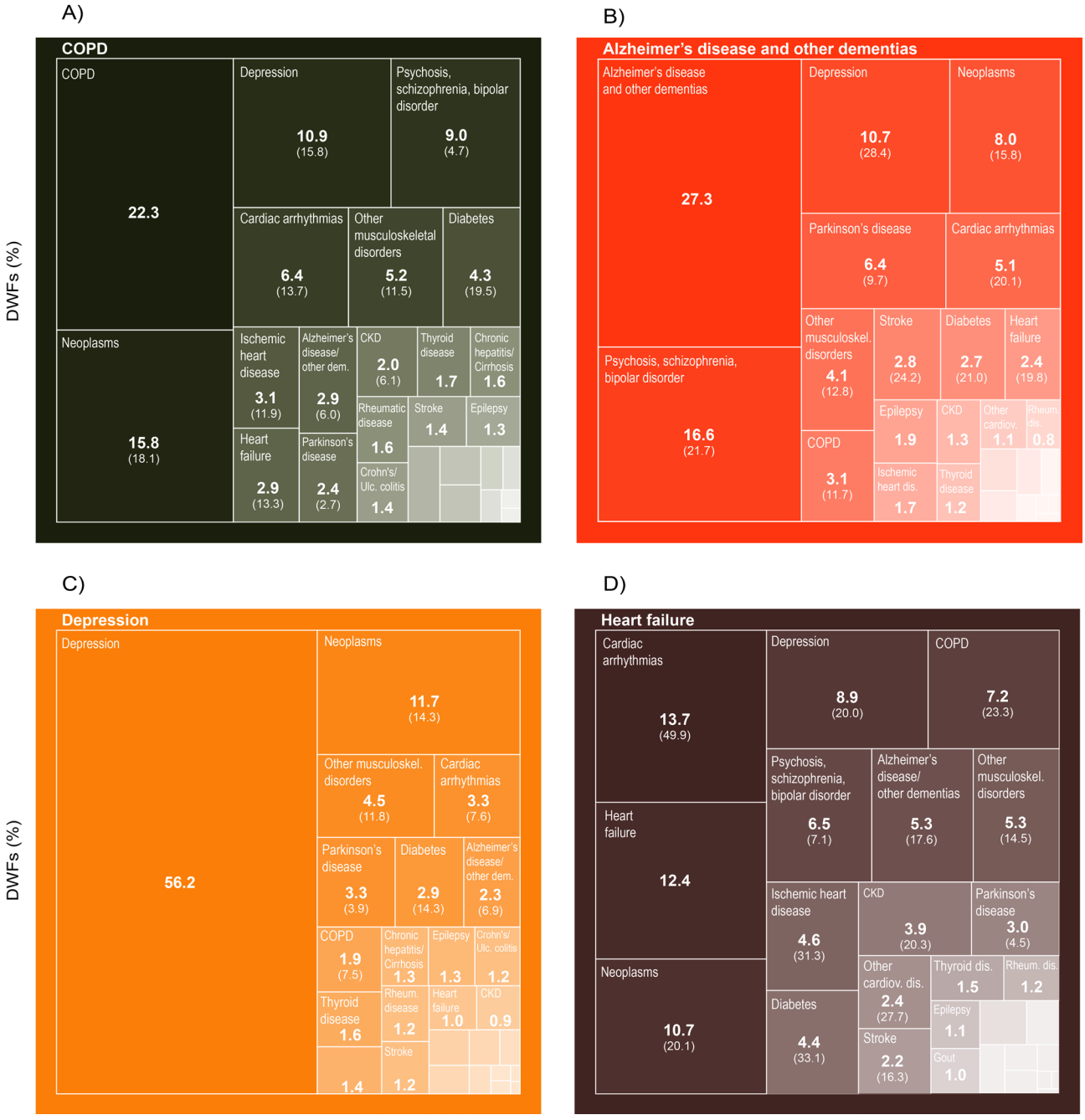

Fig. 5 Composition of YLD of 4 example chronic diseases: COPD (**A**); Alzheimer's disease and other dementias (**B**); Depression (**C**); Heart failure (**D**) Numbers are DWFs (%) of concomitant diseases, accompanied by their frequency (in brackets). Colour intensity indicates the degree of disability attributable to the individual disease and varies according to the DWF (concomitant diseases with the lowest values are not shown)

cumulative burden of disease over the previous 10 years. For each pathology, the YLD estimates were compared across three approaches: (1) the standard GBD method, (2) the new method without adjustment for multimorbidity and (3) the new method with adjustment for multimorbidity.

As Fig. 7 shows, the total YLD estimated by the GBD method were higher (88.8, UI95% 60.6–124.1) than those derived from the new method (79.1, UI95% 54.3–110.9)), even though not significantly. The largest differences were found in musculoskeletal diseases, partly due to the exclusion of certain pathologies which were instead considered by the GBD. In contrast, the YLD estimated by the new method for neoplasms and cardiac arrhythmias were higher than those calculated by the GBD method, likely due to the inclusion of cancers with uncertain

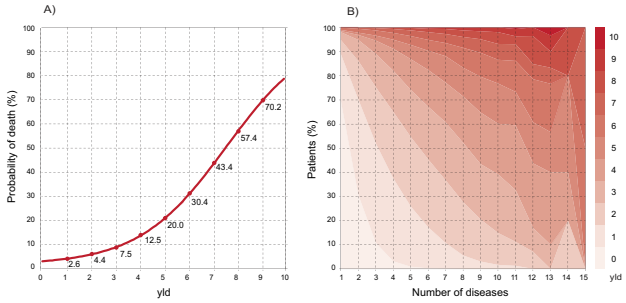

Fig. 6 (**A**) Relation between yld and probability of mortality (with death = 1; 95% confidence limits); (**B**) Relation between yld and number of pathologies

behaviour and heart conduction disorders in their respective categories. Other differences, such as those for depression, were mainly attributable to discrepancies in the number of prevalent cases. In the case of diabetes, only the DW of uncomplicated diabetes was applied in our study, since the additional DWs associated with renal and/or cerebrovascular complications considered by the GBD were instead included in the YLD computed for their respective disease categories (for details see Supplementary Tables 4, 12 and 13).

Finally, when adjusting for multimorbidity, the total YLD were further reduced, as they were no longer calculated by summing the single-disease YLDs but instead derived from the sum of the corresponding DWAs. However, the uncertainty intervals indicate that this difference was not statistically significant compared to the other two approaches.

Discussion

To our knowledge, this is the first population-based study estimating the BoD combining the GBD metrics with real-world healthcare data derived from administrative databases. We reported on a novel replicable method to quantify the BoD of patients with chronic conditions, which takes into account the progression of multimorbidity over time. The metrics adopted in this methodology are the same as those introduced by the GBD study, which aims to offer a perspective on health loss worldwide, through aggregated indicators of the burden of more than 300 conditions and pathology sequelae [24]. However, the effort of this study was to adapt the GBD metrics to the clinical complexity of patients with one or multiple chronic conditions, in order to provide accurate estimates of the relative contribution of each disease to the burden of multimorbidity at the individual patient level. The assumption underlying this work is that these estimates would be valuable to better understand the care needs of these patients and to optimise public health strategies and interventions.

This study shows that patient-centred BoD metrics may offer a detailed evaluation of disability due to chronic diseases in a specific patient population and represent an effective tool for identifying subgroups of patients with similar disease burden and healthcare needs. Such stratification would have significant practical implications for health policy, enabling the development of more tailored, efficient and equitable interventions that better reflect the complex realities of multimorbidity and focus resources on those groups most at risk of poor outcomes or high health care utilisation. It would also promote proactive population health management by supporting early identification of at-risk individuals and enabling preventive strategies to reduce long-term burden. Importantly, this tool will be made available at the level of individual regional districts, enabling local health authorities to monitor the evolving needs of patients with chronic conditions in real time and with a high degree of granularity. This capability will strengthen care coordination and support more adaptive planning and allocation of territorial health services. Having a measure of the burden of multimorbidity available at the individual patient level aligns with the principles of integrated care, which call for coordinated, continuous, and person-centred pathways aimed at preventing avoidable complications, reducing inappropriate hospital admissions, and improving overall quality of life. This is particularly relevant in light of the ongoing transition from a hospital-centred model to a more community and home-based healthcare system, designed to bring care closer to people's living environments, and to address the complex, long-term needs of patients with multiple chronic diseases. For example, leveraging Italy's territorial health infrastructure, care coordination can be informed by data on the burden of multimorbidity to provide regular follow-ups with dedicated healthcare professionals and seamless communication among primary care providers, specialists, and social services, ensuring continuous, patient-centred assistance close to home. Our analysis explored different levels of potential application of this method. At a more general level, the aggregation of data estimated from individual patients provided useful information on the health status of the population under study in terms of DALYs and DWFs and their composition by age group and sex. Two key aspects of disability emerged: first, the

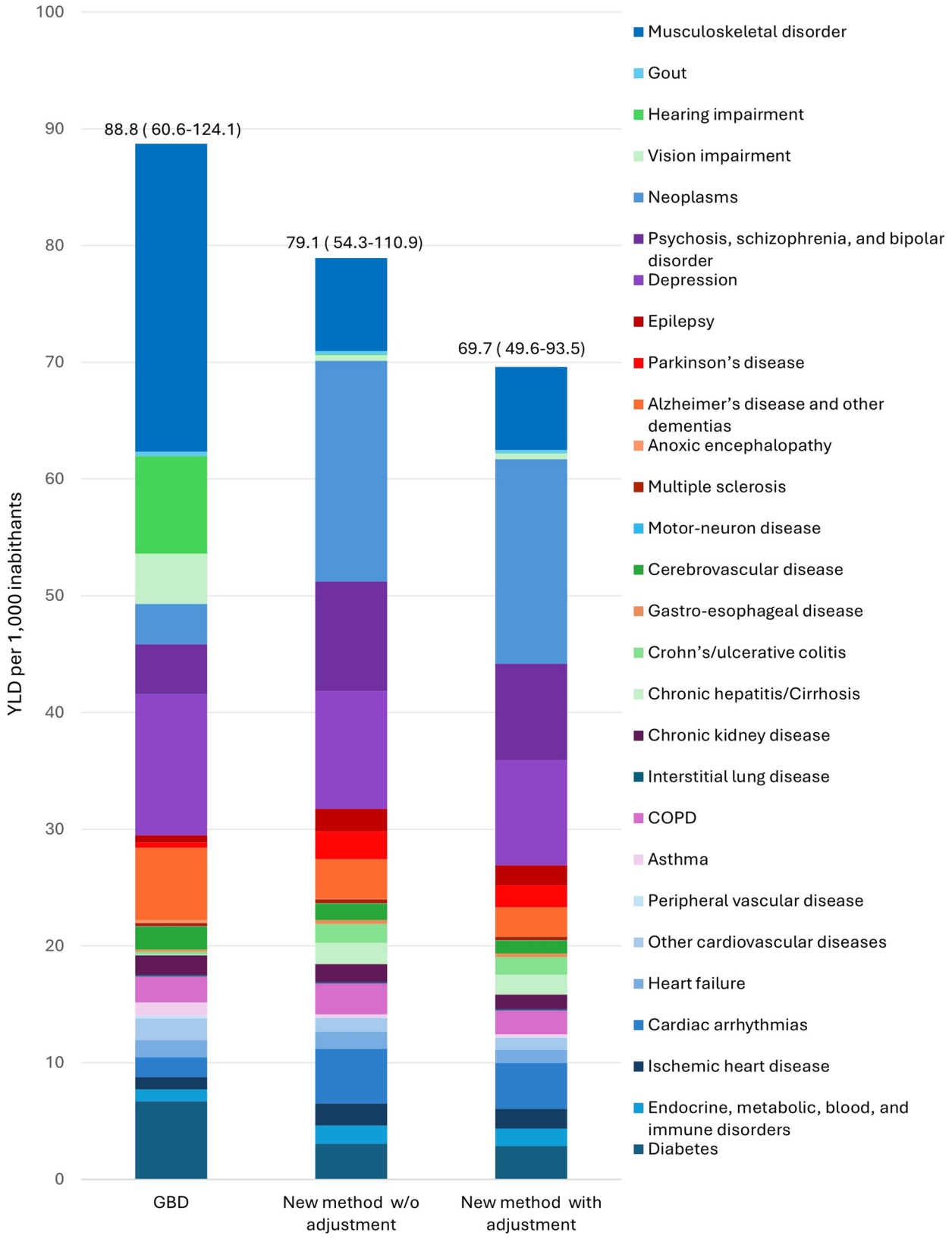

Fig. 7 Comparison between GBD and new method estimates, in a cross-sectional perspective

chronic disease categories leading to health loss changed with age: neurological and psychiatric conditions had a great impact on disability among younger groups, while cancer and cardiovascular diseases were more relevant among older people. Second, DALYs were consistently higher in females than in males across almost all ages, echoing the findings of studies on gender health disparities [25, 26].

From a disease-centred perspective, the aggregated DALYs of individual patients were used to rank, by disability and mortality, the chronic disease categories that have the greatest impact on the health of the study population. For instance, the YLD components highlighted that neurological, oncological, and psychiatric diseases were the most disabling for the population, even when assessed within the patient's comorbidity picture. In contrast, the high disability of patients with CKD or stroke could be mainly explained by coexisting conditions, such as cardiovascular diseases, which are known to be strongly associated with both diseases [27, 28]. In addition, CKD and stroke presented the highest number of years of life lost due to premature death (YLL), indicating that they often represent the end result of complications associated with a number of comorbidities and risk factors.

The YLD component of each chronic disease can be further explored to assign specific disability weights to individual comorbidities present at the patient level. These estimates provide useful insights into the different patterns of multimorbidity which, for the same number of diseases, can result in varying clinical trajectories and care needs, and consequently lead to very different treatment approaches and health outcomes [14, 29, 30]. For example, the composition of disability associated with heart failure was very heterogeneous. Heart failure accounted for only a small fraction (12.3%) of the disease burden of patients suffering from it, while several other diseases contributed more. Notably, despite their high frequency in the study population (49.9%), cardiac arrhythmias contributed with a modest fraction (13.7%) to the disability of patients with heart failure. These results emphasize the significance of employing patient-centred estimates: these can provide crucial insights into multimorbidity that might otherwise be overlooked by a less detailed approach. For example, using GBD-like metrics based on aggregated disease data, 88% of the disability of heart failure patients would not be captured or explained. Instead, having this information is essential for organising care pathways tailored to the needs of these patients.

Ultimately, the yld metric derived from this method was suggested as a valuable composite measure of a patient's clinical complexity, as it considers the concurrent chronic conditions, their duration, and severity. We propose it as a potential predictor of adverse health outcomes, including mortality, as it has proven to be explaining alone 77.9% of chronic patient mortality. It is important to note that the yld metric can include conditions that, while contributing significantly to disability, are not inherently life-threatening, such as lower back pain. Hence, if taken alone, the yld of these conditions is unlikely to be associated with a high risk of death. However, within the context of multimorbidity, i.e. when they coexist with more severe or life-threatening diseases, their contribution to overall disability may still play a role, albeit limited, in increasing the risk of mortality. This result also addresses the much-debated issue of defining the concept of multimorbidity. While the number of chronic diseases is widely accepted as a key determinant of the burden of multimorbidity, increasing evidence suggests that the nature, severity and progression of each condition also play a crucial role in defining patient complexity [31]. The correlation between yld and the number of chronic conditions supported this hypothesis: yld proved to be a more informative indicator of the patient's level of disability, as a high number of comorbidities did not necessarily correspond to a high yld and vice versa.

A recent systematic review highlighted that, although a number of European studies have estimated the BoD at an individual level using DWs, there is scant research with a multimorbidity adjustment approach [7]. In the few findings addressing the issue, comorbidity was adjusted assuming the same independent multiplicative method [11] used here. However, most of them referred to a selected cohort of patients with a specific chronic condition and a defined age group [32, 33] and have based their estimates on self-reported data obtained from surveys, in some cases supplemented with information from administrative sources or disease registries [12, 33].

The comparison with the GBD estimates required to apply the new method from a cross-sectional perspective, leaving out information on the clinical history of patients. Differences observed in this comparison stemmed partly from the selection criteria used for the diagnostic categories and partly from discrepancies in disease prevalence estimates. Regarding the first point, the meticulous preparatory work carried out with the panel of clinical experts involved in defining the criteria for the disease disability levels highlighted the need to revise some diagnostic categories considered by the GBD. For example, it was recommended to include cancers with uncertain behaviour within the neoplasm category and to classify cardiac conduction disorders under cardiac arrhythmias. About the discrepancies observed in prevalence estimates, these reflect broader challenges in the estimation process. In this regard, the Italian GBD Initiative Network (https://www.italian-gbd-initiative.it/)

has been collaborating for several years with the Institute for Health Metrics and Evaluation to enhance the accuracy of Italian GBD estimates by flagging issues related to data reliability and consistency and providing updated data sources.

As highlighted by the comparison, the statistical non-significance of the differences found between the estimates deriving from the new method applied from a cross-sectional perspective and the GBD ones confirms the consistency of the criteria used to define the levels of disability, based on the regional health databases. Furthermore, the new approach addresses key limitations of the standard GBD methodology, specifically, the over-simplification of multimorbidity and the lack of a longitudinal perspective on patients' clinical histories. In the comparison presented here, these limitations have been shown to impact YLD metrics, which remain overestimated when conventional GBD methods are used, a crucial point to consider for rankings and for comparisons with YLL estimates. By seeking to overcome these issues, the new method yields more context-specific and clinically coherent estimates of disease burden. This, in turn, contributes to a more nuanced understanding of population health needs and supports more informed public health planning and resource allocation.

We acknowledge that this study has potential limitations. The first limitation is intrinsic to the nature of administrative databases. These sources of information may be affected by selection biases, as they likely do identify more severe cases, while underestimating the prevalence of mild disease cases [34, 35]. Second, although multimorbidity is central to our BoD measures, this method does not address dependent comorbidity, which refers to coexisting diseases with common causal pathways being related one each other or to one disease increasing the risk of another [36]. The combined DWs simply reflect the co-presence of two or more chronic diseases with different severity levels in a given time period. Third, we mapped the severity levels of the chronic diseases to the GBD DWs with the support of a panel of expert clinicians [37]. This approach increased the accuracy in estimating the disease severity distribution based on the use of different types of healthcare services, allowing asymptomatic patients to be excluded and diseases with the greatest potential impact on disability to be identified more precisely across the study population [38]. However, empirical research has shown that the mapping criteria are dependent on the panel composition [39]. Another limitation of this method concerns the reference period for reconstructing patients' clinical histories, which may affect the estimation of the burden of disease and multimorbidity. In this study, a 10-year period was used, but this may vary depending on the availability of administrative data, potentially underestimating the burden in patients with longer clinical histories. Finally, this method was applied to sub-national data, focusing on a small subset of 30 chronic diseases, selected based on their relevance to health needs and impact on patients' quality of life within the studied population. While we emphasize the flexibility of this approach in adapting to available healthcare administrative data, we advise caution in generalizing these results to other chronic patient populations.

Conclusions

This study attempts to respond to the need of quantifying the burden of chronic disease and mainly of multimorbidity, which is a priority in health research [14]. The patient-centred BoD estimates obtained for an entire well-defined patient population through the methodology described here are valuable indicators for the size and composition of specific clusters of patients with complex healthcare needs. From a health policy perspective, this information can serve to define priority areas for intervention to evaluate and improve current, often suboptimal, management strategies.

Abbreviations

ATC	Anatomic Therapeutic Chemical
BoD	Burden of Disease
CKD	Chronic Kidney Disease
COPD	Chronic obstructive pulmonary disease
DALYs[§]	Disability-Adjusted Life Years
DW_combi	Combined Disability Weight
DWAi[§]	Disability Weight Attributable to disease i
DWFi[§]	Disability Weight Fraction attributable to disease i
DWs	Disability Weights
ER	Emilia-Romagna
GBD	Global Burden of Disease
ICD9-CM	International Classification of Diseases 9th Revision, Clinical Modification
IHME	Institute for Health Metrics and Evaluation
ISTAT	National Institute of Statistics
YLD[§]	Years Lived with Disability
YLL[§]	Years of Life Lost due to premature death

§ if lowercase, indicates the corresponding metric estimated at the patient level

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12963-025-00404-x.

Supplementary Material 1

Author contributions

F.D. conceptualised this study, conducted all data analyses, interpreted results and prepared the first draft of the manuscript and finalised it based on comments from other authors; L.C. interpreted results and prepared the first draft of the manuscript and finalised it based on comments from other authors. All other authors were members of the expert panel defining criteria for attributing disease severity levels, contributed with comments on the first draft, and approved the manuscript for publication.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Data availability
The datasets for this study are held securely in coded form by the Regional Authority for Health and Welfare. Current privacy legislation prohibits making health datasets available to the public. The full dataset creation plan and underlying analytic code are available from the authors upon request, with the understanding that the syntax might rely upon coding templates or macros that are unique to the Regional Health Service and are therefore inaccessible or might require modification.

Declarations

Ethics approval and consent to participate
Ethical review and approval were waived in accordance with the ER Regulation, which states that anonymised administrative data can be used for relevant public interest objectives, i.e. for planning, management, evaluation and quality improvement of healthcare [40].

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 16 September 2024 / Accepted: 15 July 2025
Published online: 31 July 2025

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