

Supplementary File 3

Symptom burden in multimorbidity. A Danish population study.

Definition of Multimorbidity

In this article multimorbidity was defined in to steps

- 1) Selection of diagnoses
- 2) Grouping of diagnoses according to different systems of the body

Selection of diagnoses

By this definition of multimorbidity we aim to have a simple and clinically relevant definition that at the same time is able to embrace complexity. Therefore, the definition is organized according to clinical picture rather than disease etiology. Diagnoses are considered on the basis of the following criteria:

- Diagnoses with high prevalence in the Danish population. (Risk factors are not included because of the low completeness of this information in the registers)
- Diagnoses relevant for general practice
- Diagnoses causing severe loss of function and/or loss of quality of life
- Diagnoses combined with reduced life expectancy
- Diagnoses resulting in a considerable treatment burden for the patient
- Chronic conditions (e.g. conditions that "require ongoing management over a period of years or decades"(1)).

Congenital diseases are not included.

Grouping of diagnoses according to different systems of the body

To have multimorbidity, a patient has to have a least one diagnosis from each of two different groups of diagnoses. E.g., if a patient has asthma and COPD this patient is categorized as lung sick instead of multimorbid. This choice rests on the assumption that it is more complex from an organizational and physiological point of view if the patient suffers from diagnoses from different bodily systems. Furthermore, concordant conditions (conditions with overlapping pathophysiology and management) are intended to be gathered in the same group (2). However, diabetes and cardiovascular diseases which could be expected to share both pathophysiology and risk factors are distributed over two different groups because they after all have different clinical manifestations and different treatments. The grouping of diagnoses and count of bodily system morbidity instead of single diagnoses may better relate to the way health care is organized as well as to the complexity and burden of morbidity (3).

See table A below for the selected diagnoses and bodily systems.

Background for redefining multimorbidity

In the literature the variation in how to define multimorbidity is large and the lack of consensus is evident (4-6). Most studies on multimorbidity include diagnoses based on the argument that the

diagnoses are common (6). However, if only selecting diagnoses based on prevalence there would be a risk of excluding many relevant conditions. In some studies authors selected a limited number of diagnoses thoroughly (7), others included all chronic ICPC codes (8), or selected specific chronic diagnoses from ICPC (9, 10). Others selected all existing ICD-10 codes without further explanation (11) or let the diagnoses count for the chapter in the ICD-10 system they came from (12). Some authors used indices, mainly developed for comorbidity, e.g. Charlson Comorbidity Index (CCI) (13, 14) and Cumulative Illness Rating Scale (CIRS) (15-17).

We could have included all possible codes from the ICD-10 system. However, doing so would have resulted in some rather small groups of multimorbidity combinations and diagnoses of less importance in relation to prevalence and mortality. To use chapters from ICD-10 could be an option, but some chapters are difficult to apply to the above stated selection criteria. Furthermore, an already existing index could be used. However, CCI was primarily developed for studying one-year mortality and we prefer a broader pallet of diagnoses than they suggest. On the other hand, CIRS could be interesting because it takes severity in to account, nevertheless, this would require access to medical records that were not available in the present register study.

Tonelli et al. (18) suggested a panel of 30 conditions when doing research on multimorbidity and their recommendation was based on 40 conditions included in a Scottish study (7). Of notice, most diagnoses used in these two studies were also included in our study, with a few exceptions: connective tissue disorders, chronic pain, hypertension, severe constipation, transient ischemic attacks, diverticular disease of intestine, peripheral vascular disease, prostate disorders, chronic sinusitis, learning disability, bronchiectasis and viral hepatitis. The reason for not including these conditions is that some of them are acute rather than chronic, some of them are closely related to other conditions covered by our diagnosis groups, and the validity of the coding in the national registers is relatively low for some of the diagnoses mentioned above. In particular risk factors, like hypertension, are underreported, leading to low completeness and a larger underestimation of these conditions compared with others.

By this definition complexity can be grasped, and prevalent diseases with significant impact on patients' lives can be included, but without the need of including all possible ICD-10 codes.

Registers

The data was extracted from the following registers:

The Danish National Patient Registry (NPR) (19)

The Danish Psychiatric Central Research Register (PCRR) (20)

The Danish Cancer Register (CR) (21)

The registers contain information solely from the Danish hospital sector. Since we are interested in general medicine it would be optimal to use ICPC codes from primary care. However, there is no access to ICPC codes and there exist no registers validated for research with primary care data in Denmark yet.

All codes are based on International Classification of Diseases, 10th edition (ICD-10) and the earlier 8th edition (ICD-8). ICD is a well-established coding system used in 117 countries and translated into 40 languages. The coding system is based on the medical specialties and hence coded in 21

chapters. The coding system is reliable because of the long history, the many editions with continuous improvements and the involvement of medical experts (22). ICD-10 was introduced in Denmark 1 January 1994 and the present study contains both ICD-8 and ICD-10 diagnoses. NPR contains information on all inpatient care contacts in secondary care since 1977 and from 1995 also outpatient and emergency care contacts. Psychiatric diagnoses were included in NPR from 1995 (19). ICD-8 and ICD-10 are not comparable in every detail, and this has required a pragmatic approach when selecting diagnoses. In certain cases, one cannot distinguish between acute and chronic diagnoses in ICD-8, which sometimes leads to inclusion of the corresponding broader ICD-10 diagnoses with less relevant subcategories.

The validity and completeness of the registers vary. NPR constantly control data received from hospitals for incorrect codes and inconsistencies between sex and diagnoses in order to increase validity and completeness. Validation studies have shown variation in positive predictive value (PPV) between specialties and PPV showed to be higher when including three-number digits in ICD compared to five-number digits (23). In our definition of multimorbidity the three digit level is used as the highest level. Moreover, by using groups of conditions the need of high validity of some of the variables is reduced, e.g. whether atrial fibrillation is correctly coded as fibrillation or incorrectly as atrial flutter is of minor importance, since both conditions are included in the same diagnosis group: heart disease.

In our study we included diagnoses from a window ten years back in time from year 2000. Due to this choice some prevalent cases will be mistaken for being incident. The change from ICD-8 to ICD-10 in 1994 will probably lead to a higher number of incident cases around that year (23). Since 1994 is placed in the middle of our collection period a larger number of truly prevalent cases will probably be collected before 1994 and a larger number of cases falsely considered being incident in the year after. However, we do not necessarily consider prevalent cases less important than incident. Changes in diagnostic criteria and methods over time may also have affected how to interpret incidence (19).

For CR the validity is secured through daily control routines and yearly publications where checks for internal consistency are performed. Furthermore, the register uses several sources e.g. pathology to check their own information leading to high completeness of the register (21).

Validation studies on certain diagnoses have turned out well for PCRR (24, 25), but a systematic validation of the whole register has never been performed. There exist no private hospitals in Denmark for treating psychiatric patients therefore PCRR has high completeness. It has to be kept in mind, however, that the relatively large number of people treated for psychiatric diagnoses in primary care and at private practicing psychiatrists is not included in the register (20).

Diagnoses and organ systems included in the multimorbidity definition

	ICD-10	ICD-8
Lung diagnoses (LUNG)		
COPD	J44	490
Chronic bronchitis	J41-J42	491
Emphysema	J43	492
Asthma	J45-J46	493
Musculoskeletal diagnoses (MUSCULOSKELETAL)		

Rheumatic diagnoses / arthritis	L40.5, M05-M07	696.09, 712, 715
Arthrosis	M15-M17	713.00-09
Back diagnoses	M45, M47, M50-M51, M53-M54	712.49, 725, 728
Osteoporosis	M80-M82	723.09
Endocrine diagnoses (ENDO)		
Hypothyroidisme	E03	244
Hyperthyroidisme	E05	242
Diabetes	E10-E14	249-250
Mental health diagnoses (MENTAL HEALTH)		
Inclusion of all patients registered with a psychiatric diagnose in Psychiatric Central Register (except for patients having only Y - or Z-diagnoses) (26) and the following dementia and alcohol-related diagnoses from DNPR:		
Dementia	G30, G31.8-9, F00, F01, F02.0, F02.3, F03	290, 293
Alcohol	F10.1-F10.9	291, 303
Cancer (CANCER)		
All diagnoses from CR except C44, non-melanoma skin cancer.		
Neurological diagnoses (NEURO)		
Apoplexia cerebri (stroke)	I60-I64, I69	430-431, 433-434, 436-437
Multiple sclerosis	G35	340
Epilepsy	G40	345
Migraine	G43	346
Parkinson disease	G20	342
Gastrointestinal diagnoses (GASTRO)		
Dyspepsia	K30	536.90-91
Mb. Crohn and colitis ulcerosa	K50-K51	563
Colon irritabile	K58	564.19
Chronic liver disease	K70-K76	571-573
Chronic pancreatitis	K86.0, K86.1	577.10, 577.11, 577.19
Cardiovascular diagnoses (HEART)		
Ischemic heart disease	I20-I25	410-413
Heart failure and arrhythmia	I44.1-7, I45.2-9, I47-I50	427.09, 427.19, 427.23-24, 427.90-97, 428
Heart valve diagnoses	I05-I08, I34-I37	394-396, 397.00, 397.01, 424.00-19, 424.90-92
Genitourinary diagnoses (KIDNEY)		
Chronic kidney disease	N03-N05, N11-N12, N18-N19, Z49, Z99.2	581, 582, 583, 590.09, 590.15, 792
Urinary incontinence	N39.3-4	786.29
Endometriosis	N80	625.30-39

Diagnoses in sensory organs (SENSORY)		
Glaucoma	H40	375
Blindness and low vision	H54.0-54.3, H54.7	379.09, 379.19
Loss of hearing	H90.0, H90.2, H90.3, H90.5, H90.6, H90.8, H91	388, 389.09, 389.99
Psoriasis	L40	696.10, 696.19

Table A. In order to have multimorbidity the patient needs at least one diagnosis from two different bodily systems; for instance COPD from LUNG and multiple sclerosis from NEURO.

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