

Supplementary material: Process, content and considerations of the medical review and ratification regarding register-based definitions of chronic conditions

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Supplement to:

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1. Doctors and experts involved, contributions, objectives and the panel method used

The following doctors and medical experts contributed to the definitions and medical review of the definitions of the study:

- Søren Paaske Johnsen¹, PhD (co-author)*
- Charlotte Glümer², PhD (co-author)**
- Martin Bach Jensen³, PhD***
- Ib Rasmussen⁴ ****
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Contributions:

* All conditions, general epidemiological experience. See: <http://pure.au.dk/portal/da/spj@clin.au.dk>

** All conditions, public health and general epidemiological experience.

See: <https://www.regionh.dk/fcfs/medarbejdere/Sider/Charlotte-Gl-mer.aspx>

*** Conditions within M group.

See: [http://vbn.aau.dk/da/persons/martin-bach-jensen\(929fc31a-f5b6-45b8-b3ed-29bd2c4b4bf7\).html](http://vbn.aau.dk/da/persons/martin-bach-jensen(929fc31a-f5b6-45b8-b3ed-29bd2c4b4bf7).html)

**** Conditions within F group. See: <http://www.psykiater-aalborg.dk/kontakt.html>

***** Conditions related to treatment in general practice, including diabetes, and more.

See: www.laegejohnhyltoft.dk

***** Eye conditions within H group.

See: <http://www.labome.org/expert/denmark/aarhus/palnum/kaare-d-palnum-1226992.html>

***** Conditions within disease group A and B.

See: [http://vbn.aau.dk/da/persons/kaspar-rene-nielsen\(bc41abea-4b3e-473b-b7a6-8d2c7515f572\).html](http://vbn.aau.dk/da/persons/kaspar-rene-nielsen(bc41abea-4b3e-473b-b7a6-8d2c7515f572).html)

In addition, approx. 20 of the complex definitions were built upon existing definitions (see references in Table 1 in manuscript), and therefore many other medical specialists and doctors have contributed indirectly to the definitions.

The following experts contributed to the definitions by review, identifying literature, suggestions of data possibilities and others:

- Michael Falk Hvidberg⁸ (corresponding-author), MSc, PhD fellow, data manager and expert in health registers, e-mail: michael@falkhvidberg.dk
- Lars Holger Ehlers⁸ (co-author), PhD, professor,
- Karin Dam Petersen⁸ (co-author), DDS, PhD, associate professor,
- Anne Vingaard⁸ (co-author), PhD, assistant professor, epidemiological experience

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Objectives and the panel method

A medical expert panel was formed to review and ratify the register-based definitions. Their objectives were as follows:

- Selecting the ICD-10 codes of chronic conditions (see section 2 and 6)
- Ensuring grouping of the chronic conditions into clinically meaningful groups (see section 3 and 6)
- Ratifying the four overall inclusion times (see section 4) and assigning one of the four inclusion times to each of the chronic conditions (see section 4 and 6)
- Assessing conditions in need of complex definitions, reviewing and ratifying these (see section 5 and 6)

To archive consensus over the objectives, the used panel method was partly inspired by the Delphi method [1] and can be described as follows:

- I. **The panel of medical experts:** A medical panel of seven doctors, including a “core panel” of two doctors from the co-authors of the manuscript. The corresponding author acted as coordinator of the process.
- II. **Process and rounds:** The rounds were performed bilaterally, by meetings, phone and email, between the coordinator and each expert. The detailed contents of the process are further described in section 2 and 6. When conducted by personal meeting or phone, the main conclusions were incorporated into the manuscript for the next round, or for the external doctors not among the authors, and also by separate summary thereof by email. The contributions of the external experts were, however, finally reviewed and approved by the authors. At least six full rounds were carried out (many more if bilateral email correspondence and other communications are included).
- III. **Personal meetings:** Three bilateral personal meetings were carried out with the corresponding author and with Søren Paaske Johnsen, Ib Rasmussen and Martin Bach Jensen, respectively, as well as email correspondence including a summary of the discussed conclusions.
- IV. **Conference calls/email:** Several conference calls were held with Charlotte Glümer, Søren Paaske Johnsen, Ib Rasmussen, John Hyltoft and Kaare Dyre Palnum, as well as email correspondence including a summary of the discussed conclusions either in the form of a separate summary or by incorporation into the manuscript.
- V. **Questions:** A core of systematic questions were asked for each meeting or contact, including the option of further discussion and comments. Questions are further described in sections 2, 4-6.
- VI. **Anonymity:** Anonymity, as in the traditional Delphi method, was only partially ensured as the corresponding author handled the comments bilaterally, and by incorporating the comments into the manuscript mostly with anonymity. However, all participants knew each other by name, and some named comments for discussion were also implemented in the manuscript if asked for.
- VII. **Time of process:** The process started in late 2013 and finished in early 2016.

The contents of the process and steps are described in more detail in the following. Although the following steps also have been carried out as iterative processes, section 2 - 5 can largely be seen as consecutive steps.

2. Selecting the ICD-10 codes of chronic conditions

Choosing the chronic ICD codes and definition of chronicity

For an overview of the approximately 22,000 codes available in the ICD-10 classification, the clinically ratified 99-level disease categorization [2] was initially used, which includes all the ICD-10 codes grouped into 99 broad disease categories. Then, non-chronic conditions were excluded by the authors based on Hwang et al's definition of chronicity:

“We defined a person as having a chronic condition if that person's condition had lasted or was expected to last twelve or more months and resulted in functional limitations and/or the need for ongoing medical care.” [3,4]

The individual conditions were subsequently discussed at meetings, by email and by phone. The final choices of inclusion and categorization of the chronic conditions were confirmed by email after each meeting or contact – similarly to the form presented in the results section of the manuscript. Notably, the 99-level disease categorization was only used temporarily and the conditions were later expanded and grouped differently. This process is described in section 3.

As it is not possible to summarize the discussed points of all 199 groups of conditions, the final categorizations are shown in the Results section of the manuscript.

Discussed issues and choices

In general, communicable diseases, including most treatable viral and bacterial conditions, were initially excluded as they were often short term and/or not chronic by definition in terms of constituting any functional limitations lasting more than 12 months. This was also coherent with both the Hwang et al definition above and the WHO's definition of chronic or non-communicable diseases [5].

Obesity (E66) was discussed separately but excluded as it was considered a *health risk factor* rather than a chronic condition or disease in alignment with the other included chronic conditions. Including obesity would violate the present clinical distinction between diseases and health risks, and would thus also require the inclusion and definition of other health risk factors such as smoking, lack of exercise and drinking as chronic conditions. Additionally, not all obese people have co-morbidities or functional limitations. Thus, the inclusion of obesity was not recommended by the authors in line with the Danish National Board of Health [6].

Another principal issue discussed was how to categorize and handle conditions that are most likely to have the state of the condition changed or even cured by treatment, even though it is chronic by definition. As such, a condition may have lasted for more than 12 months, but when first reported in the national patient register (NPR) or medication register it may be cured soon after, which is applicable to several conditions in

Supplementary Table 1. For example, in the case of cataracts, hernias, shoulder or knee disorders, the conditions are expected to be fully cured. Consequently, a borderline chronic categorization was applied for these conditions.

Handling disputed conditions

When the medical expert panel was in dispute over whether an ICD-10 condition could be considered chronic according to Hwang's definition of chronicity, previous studies based on the same definition were taken into consideration [3,4]. The following conditions were discussed as borderline chronic by definition, but were included as they were either defined as chronic by related studies using the same definition, or most likely lasting for a minimum of 2 years by consensus among the medical panel experts:

Supplementary Table 1. Discussed borderline chronic conditions

No.	Somatic Conditions	ICD-10	Category	Definitions
76	Disorders of eyelid, lacrimal system and orbit(*)	H02– H06	Cat. IV	(DIAG)
79	Diseases of the eye lens (cataracts)*	H25–H28	Cat. IV	(DIAG)
18	Glaucoma*	H40–H42	Cat. III	Complex: (DIAG) and/or (MEDICINE2) including all prescriptions with ATC: S01E. Min. two prescriptions needed.
84	Disorders of the vitreous body and globe*	H43–H45	Cat. IV	(DIAG)
85	Disorders of optic nerve and visual pathways**	H47	Cat. IV	(DIAG)
86	Disorders of ocular muscles, binocular movement, accommodation and refraction**	H49–H50, H52	Cat. IV	(DIAG)
118	Varicose veins of lower extremities*	I83	Cat. IV	(DIAG)
24	Haemorrhoids*	I84	Cat. IV	Complex: (DIAG) and/or (MEDICINE2) including all prescriptions with ATC: C05A and indication code 63 (for haemorrhoids). Min. two prescriptions needed.
28	Ulcers*	K25–K27	Cat. IV	Complex: (DIAG) and/or (MEDICINE2) including all prescriptions with indication codes 003 (For ulcer) or 465 (against ulcer (helicobacter pylori eradication)). And/or ATC: A02BD. Only one prescription needed.
124	Inguinal hernia*	K40	Cat. IV	(DIAG)
125	Ventral hernia*	K43	Cat. IV	(DIAG)
140	Internal derangement of knee*	M230, M231, M233, M235, M236, M238	Cat. IV	(DIAG)
141	Derangement of meniscus due to old tear or injury*	M232	Cat. IV	(DIAG)
142	Internal derangement of knee, unspecified*	M239	Cat. IV	(DIAG)
143	Other specific joint derangements*	M24, except M240–M241	Cat. IV	(DIAG)
144	Other joint disorders, not elsewhere classified*	M25	Cat. IV	(DIAG)
156	Cervical disc disorders*	M50	Cat. IV	(DIAG)
157	Other intervertebral disc disorders*	M51	Cat. IV	(DIAG)
158	Other dorsopathies, not elsewhere classified*	M53	Cat. IV	(DIAG)
159	Dorsalgia*	M54	Cat. IV	(DIAG)
160	Disorders of muscles**	M60–M63, except M60.0	Cat. IV	(DIAG)
161	Synovitis and tenosynovitis **	M65	Cat. IV	(DIAG)
162	Disorders of synovium and tendon**	M66–68	Cat. IV	(DIAG)
163	Soft tissue disorders related to use, overuse and pressure(*)	M70	Cat. IV	(DIAG)
165	Shoulder lesions*	M75	Cat. IV	(DIAG)
166	Enthesopathies of lower limb, excluding foot*	M76	Cat. IV	(DIAG)
167	Other enthesopathies*	M77	Cat. IV	(DIAG)
171	Other soft tissue disorders, not elsewhere classified: pain in limb*	M796	Cat. IV	(DIAG)
175	Disorders of continuity of bone*	M84	Cat. IV	(DIAG)

* included in other studies. (*) partly included in other studies as some codes are convertible. ** not included in other studies. See conversion tool: <http://www.icd10codesearch.com/> and chronic conditions from existing studies [3,4].

For example, the following conditions were discussed as borderline chronic conditions and were *not* included as they were assessed as not being chronic on average by definition, and/or were not confirmed as chronic from existing studies [3,4]:

1. D50-53 (*)
2. E30 (*)
3. E36-64 **
4. E65-E67 (*) and **
5. E68-E69**
6. H00-H01, H10-H13, H19-H22, H33, H58-H59**
7. H15, H59 (*)
8. M00 **
9. M240-M241 *
10. M60.0 *
11. M833 **

* included in other studies. (*) partly included in other studies. ** not included in other studies. Further conditions were excluded as not being chronic although they are not listed here, as there was no doubt or detailed discussion thereof.

3. Grouping the selected chronic conditions into clinically meaningful disease groups

First criterion

The current study's division of conditions into groups was based on the WHO's existing clinical ICD-10 grouping [7]. The aim was to keep the conditions at a two-digit ICD-10 level (for example E10 or C56) if possible, or a three-digit level (for example I13.1) or more if medically suggested, as required by the involved doctors, or the clinically ratified definitions used from other studies. This was done where possible and clinically meaningful to ensure medical usefulness. Yet, when suggested by the medical experts or experts from the cited literature, several two or three digit ICD-10 codes were aggregated into one group to form a condition or related conditions. This was done for 57 groups of conditions (condition no. 1, 2, 6, 9-12, 15-16, 18, 20-23, 26-28, 30-32, 35, 39, 44-46, 48, 50, 64, 66, 68-69, 79-80, 84, 89, 99-100, 102, 106, 110-111, 117, 120A, 120, 132, 136, 145, 155, 160, 162, 170, 177, 182, 186, 190, 197).

Second criterion

As one of the objectives of this study was to create grouped conditions which could be applied on larger surveys of 50,000+ respondents, e.g. the national health profile surveys, more rare conditions were divided into larger groups containing a range of ICD-10 codes with the nearest clinically meaningful conditions. This was done so that none of the included conditions had less than 50 persons based on three pooled samples with a total of 56,988 persons (The National Health Surveys [8–10]). 39 conditions were joined due to the second criterion (condition no. 36-37, 49,51-53, 55-62, 71-76, 85-86, 104, 115, 119, 123, 131, 174, 176, 178-181, 185, 191, 193, 196, 198-199).

Exceptions of second criterion

A few conditions were considered of medical interest and not clinically meaningful to be joined with other chronic conditions without “indulging” the conditions, even though these did not fulfill the data requirement of a minimum of 50 persons. Thus, clinical coherence superseded the data requirements. This was the case for the following conditions:

Supplementary Table 2. Table of conditions with less than the required minimum of 50 persons for use in surveys

No.	Somatic Conditions	ICD-10	Category	n of test sample
6	Diabetes others	E12–E14	Cat. II	18
8	Cystic fibrosis	E84	Cat. I	4
34	Chronic viral hepatitis	B18	Cat. IV	17
35	HIV	B20-B24	Cat. I	14
52	Haemolytic anaemias	D55–D59	Cat. II	20
77	Corneal scars and opacities	H17	Cat. II	36
80	Disorders of the choroid and retina	H31-H32	Cat. I	37
100	AMI complex/other	I23–I24	Cat. III	30
146	Systemic lupus erythematosus	M32	Cat. I	46
147	Dermatopolymyositis	M33	Cat. I	15
148	Systemic sclerosis	M34	Cat. I	13
192	Fibromyalgia	M797	Cat. I	37
173	Osteoporosis in diseases classified elsewhere	M82	Cat. I	17
175	Disorders of continuity of bone	M84	Cat. IV	29
186	Mood (affective) disorders	F340, F348–F349, F38–F39	Cat. I	45
197	Mental retardation	F70–F79	Cat. I	46
198	Disorders of psychological development	F80–F89	Cat. I	46

4. Definition, expert ratification of the four categories of inclusion times - and cataloging of the conditions

Defining four categories of inclusion times

As many chronic conditions were not lifelong, a maximum inclusion time from the first report of the condition in registers was defined. This was needed as it is crucial that the condition exists – or the person has limitations from the condition and/or an ongoing medical need for treatment – at a chosen time of interest.

The use of different inclusion time window in our study differs from the approach used in most other register studies by differentiating into more categories of inclusion times and placing different chronic conditions into these by medical judgment. This approach was especially needed as this study involved more chronic and different conditions than most other studies as well as longer data time series.

The categories were initially proposed by the authors based on different existing studies as referenced and medical assessment where possible, as well as register experience and data possibilities; this was further reviewed and ratified by the involved doctors ensuring medical relevance and coherence of the included conditions. All authors approved the final categorization:

- *Category I: Stationary to progressive chronic conditions* (no time limit = inclusion time going back from the time of interest as long as valid data are available. In the current study, this starting point was defined by the introduction of ICD-10 diagnosis coding in Denmark in 1994).
- *Category II: Stationary to diminishing chronic conditions* (10 years of register inclusion time of diagnosis from the time of interest).
- *Category III: Diminishing chronic conditions* (5 years of register inclusion time of diagnosis from the time of interest).
- *Category IV: Borderline chronic conditions* (2 years of register inclusion time of diagnosis from the time of interest).

If the condition as a minimum was not recorded once within the inclusion times, it was not included.

The authors did recognize that the categorization is an average judgment that may vary across and within conditions, and that there might be exceptions from unique cases thereof. However, on average, we expected it to be the best solution at this time, and looked forward to further development thereof.

Medical cataloging of the chronic conditions into one of the four categories

Questions regarding the categorization of each condition were given to the medical experts as follows by email as well as being discussed at meetings, by phone or by email:

For the included diseases, how far do you by medical judgment suggest it is feasible to go back in the NHR register and include a patient – and still at a time of interest (for example 01/01/2013) be reasonably sure the patient still has the disease [based on the four categories shown previously]?

This was done iteratively as described earlier for each of the chronic conditions. Initially, the experts among the co-authors categorized the conditions by experience and/or based on existing research, which was done several times. However, for disease groups M (diseases of the musculoskeletal system and connective tissue) and F (mental disease), it was decided that external medical review and inputs from other specialists were needed and thus they were included in the process.

As each condition was assessed and discussed, a summary containing solely the categorization was incorporated into the manuscript by the corresponding author for comments and approval. The final categorization can be seen in the results section of the manuscript. All authors approved the final categorizations and definitions. The process was conducted separately with a separate summary for the external doctors as described in section 7.

Examples of the discussed conditions and considerations

As a detailed summary of all the discussions for each of the 199 grouped conditions is not possible, a selected summary of particularly difficult and/or generally representative discussed issues and corresponding considerations is provided below:

- Disease group C – Cancers (C00–99)
- Disease group E – Diabetes type 2 (E11)
- Disease group G – Migraine (G43), headache (G44) and epilepsy (G40–G41)
- Disease group H – Glaucoma (H40–H42), cataracts (H25–H28) and others
- Disease group K – Ulcers (K25–K27) and hernias (K40, K43)
- Disease group M – Different surgical conditions
- Disease group F – Anxiety disorders (F40–F41), depression (F32, F33, F34.1, F06.32), eating disorders (F50), personality disorders (F60)

In general, less severe conditions or conditions with a high variation of severity, clinical complexity or a debated diagnosis were especially difficult to categorize.

Cancers

With regard to several cancers, a 5- or 10-year inclusion time was discussed. A 5-year inclusion time was considered as this is often the curative clinical time limit. However, as most cancers do not actually dissolve completely, and often create long-lasting functional limitations/after-effects, a 10-year inclusion period was chosen for all cancers except for malignant other malignant neoplasms of the skin (C44), which had a 2-year inclusion time due to their minor severity. This was done in conformity with the definition of chronicity within the study. Notably, experts criticized a recent report for not using 10-year inclusion times in regard to some cancers [11].

Diabetes

With regard to type 2 diabetes, a 10-year inclusion time was preferred as the condition varies in severity and curability for some, but is a long-term condition for most. The definition is further described later. However, inclusion time was coherent with the Statens Serum Institute national diabetes algorithm [12,13]. Type 1 Diabetes was categorized as lifelong.

Migraine and headache

Migraine and headache are examples of conditions with a high variability of severity, clinical complexity and debated diagnosis that are not necessarily captured fully within registers. Despite agreement that there is no cure for migraine even though new promising treatments are emerging, a inclusion time of 10 years was decided, and a complex definition was created including medication. The concerns, however, regarded the clinical complexity, the possibility that the debated diagnosis might differ over time and misdiagnosis, and thus a lifelong categorization was rejected. On the other hand, shorter inclusion times were rejected due to the high severity that was expected when reported in the registers by either diagnosis or medication – even though it was recognized that less severe variation also exists, and they would most likely not be within the reports of registers if so. As the diagnosis of other headache syndromes was considered less severe than, for example, migraine, the inclusion time was set to 5 years.

Epilepsy

Epilepsy is another case of a clinically complex, debated diagnosis largely changed over time, and with high variability, that for a large part may also be cured or disappear, and for another part needs lifelong treatment of severe symptoms. Thus, inclusion times were set to 5 years including medication in coherence with another study [14]. It was then expected that the less severe or historically misdiagnosed cases were mostly excluded, and the severe cases were included as they were being treated within the inclusion period.

Other conditions of complex or often debated diagnosis

Other clinically complex or often debated diagnoses also had lower inclusion times for similar reasons to epilepsy although they were considered moderately severe conditions – for example:

Other non-infective gastroenteritis and colitis	K52	Cat III
Other functional intestinal disorders	K59	Cat III
Eating disorders	F50	Cat III
Depression	F32, F33, F34.1, F06.32	Cat III

Disease group H eye conditions

Cataracts and other disease group H conditions are examples of conditions that in recent years have become curable, although they may have lasted/developed over several years before being reported, and are expected to be cured shortly after the report in registers as this indicates that treatment is near. Thus, several H eye conditions were given a borderline inclusion time of 2 years. The same applies for ulcers and hernias in K group. However, many H eye conditions were found non-chronic and excluded as they were on average of shorter duration than 12 months, not constituting any functional limitations or were often curable (see examples in section 2). Another issue identified is that the variation of chronicity can be particularly high within H eye group conditions. As so, we do not expect all less severe conditions within the included conditions treated by the GP or private specialists to be chronic by definition. Some two digit conditions range from lifelong to curable (for example within H47, H49, or even H40-H42) – and were thus set to a cat III - as well as high variation of inclusion times is found between closely related disease codes (see conditions no. 85-86). Other conditions might range from *not* chronic to borderline chronic (for example H19-20, H33, H58-H59) and are as such not included. Moreover, some H group conditions also constitute difficulties as many less severe conditions of the outer eye, except squint surgery, are treated by GP's or private specialists not reporting to the NPR why the definitions should be used with caution in regards of for example H25–H28 or H49–H52. As some of these conditions are treated and often “cured” with for example glasses, they were also discussed as borderline conditions, but included as the conditions are consistent and needs ongoing treatment. Inner eye conditions, except cataracts, iridotomy and some selective laser trabeculectomy, are mostly treated at hospitals. Notably, many of the included ICD-10 codes include severe conditions treated in public or private hospitals reporting to the NPR and these are on average expected to be fairly representative captured.

Disease group M conditions

Disease group M is a large group of conditions with many of them treated surgically. However, high variability exists as many conditions are life-long, such as arthrosis, rheumatoid arthritis, systemic sclerosis, spondylosis, spinal osteochondrosis and others, although the severity also varies within these conditions. Yet, several other M conditions may generate major “functional limitation” for at least 12 months, but are perhaps naturally cured without treatment or cured surgically, such as internal derangement of the knee, derangement of the meniscus due to an old tear or injury, cervical disc disorders or dorsalgia and others. Thus many surgically treated H conditions were categorized as borderline conditions.

Disease group F conditions

With regard to disease group F anxiety disorders (F40–F41), depression (F32, F33, F34.1, F06.32), eating disorders (F50) and personality disorders (F60), an inclusion period of 2 or 5 years was considered. However, it was assessed that as the conditions were either reported in the registers by clinical diagnosis or medicine, they were more severe and of longer duration than the mainstream everyday interpretation of the terms anxiety or depression etc. For example, medications are often given over a longer period than 2 years.

In conclusion, the authors recognize that the categorizations are debatable. The categorizations used for this publication are thus based on the best medical judgment of the involved doctors at the present time. Future studies should *validate* and assess the results of the current study further; also as new treatments emerge.

5. Expert judgment of conditions in need of complex defined algorithms

Choice of complex definitions: medical and expert judgment of conditions in need of complex defined algorithms

An important part of the definitions was assessing both the possibilities and need for complex algorithms using several registers for “capturing” the condition. For each of the 199 conditions the following medical assessment was asked:

- *Can any of the diseases, in your opinion, not be solely identified by the NHR ICD-10 diagnosis codes, for example because they are diagnosed in the practice sector and therefore do not get a diagnosis code? We are aware that there may be validity problems with diagnosis codes, and you are welcome to point out areas with special problems.*

Complex algorithms of existing studies were used as inspiration and incorporated into the framework of the 4 categories and/or included medication indication codes in contrast to most previous studies. This was done for 22 of the total number of 35 complex conditions as seen and referenced in the result section of the manuscript:

1. Brain cancer (C71, C75.1–C75.3, D33.0–D33.2, D35.2–D35.4, D43.0–D43.2, D44.3–D44.5 (brain). C70, D32, D42 (brain membrane). C72, D33.3–D33.9, D43.3–D43.9 (cranial nerve, spinal cord))
2. Diabetes type 1 (E10)
3. Diabetes type 2 (E11)
4. Other diabetes (E12–14)
5. Cystic fibrosis (E84)
6. Dementia (F00, G30, F01, F02.0, F03.9, G31.8B, G31.8E, G31.9, G31.0B)
7. Schizophrenia (F20)
8. Depression (F32, F33, F34.1, F06.32)
9. Glaucoma (H40–42)
10. Aortic and mitral valve disease (I05, I06, I34, I35)
11. Ischaemic heart diseases (I20–I25)
12. Heart failure (I11.0, I13.0, I13.2, I42.0, I42.6, I42.7, I42.9, I50.0, I50.1, I50.9)
13. Stroke (I60, I61, I63–I64, Z501 (rehabilitation))
14. Respiratory allergy (J30, except J30.0)
15. Chronic lower respiratory diseases (J40–J43, J47)
16. COPH (J44, J96, J13–J18)
17. Asthma (J45–J46)
18. Inflammatory polyarthropathies and ankylosing spondylitis (M05–M14, M45)
19. Rheumatoid arthritis (M05, M06, M07.1, M07.2, M07.3, M08, M09)
20. Inflammatory polyarthropathies except rheumatoid arthritis (M074–M079, M10–M14, M45)
21. Osteoporosis (M80–M81)
22. Chronic renal failure (N18)

Thus, all the above conditions had other doctors involved in the review than in the current study.

Thirteen other conditions had complex definitions constructed based on both diagnosis and medicine and were incorporated into the framework of the 4 categories as seen in the results section of the manuscript:

1. Diseases of the thyroid (E00–E04, E06, E07)
2. Thyrotoxicosis (E05)
3. Disorders of lipoprotein metabolism and other lipidaemias (E78)
4. Bipolar affective disorder (F30–F31)
5. Obsessive compulsive disorder (OCD) (F42)
6. Hyperkinetic disorders (ADHD) (F90)
7. Parkinson’s disease (G20, G21, G22, F02.3)
8. Epilepsy (G40–G41)
9. Migraine (G43)
10. Ménière’s disease (H810)
11. Haemorrhoids (I84)
12. Ulcers (K25–K27)
13. Psoriasis (L40)

To avoid false positives, the use of minimum two prescriptions was recommended as a rule of thumb when medicine was applied to the definitions - with the exception of conditions such as ulcer where only one prescription is needed for treatment. The complex conditions were constructed as the conditions were often treated in primary care or by private specialists and were often less severe conditions not included in hospital diagnosis.

Summary of considerations of selected complex conditions

Selected considerations and issues of the four major types of chronic conditions as defined by the WHO, cardiovascular diseases, cancers, chronic respiratory diseases and diabetes [5], are briefly summarized in the following along with considerations and issues of three other major prevalent conditions, arthritis, depression and anxiety.

Cardiovascular conditions

As most cardiovascular conditions are diagnosed at hospitals, including non-complex definitions, the main use of experts was related to the combinations of ICD-10 codes of the conditions and inclusion times. The combinations of ICD-10 codes used are close to existing referenced literature, but were categorized by expert experience among the authors. With regard to stroke, the definitions had more diagnoses included than in the referenced reports as change was expected in future The Danish Clinical Registries (TDCR) definitions and recommendations. Aortic and mitral valve diseases, hypertensive diseases and ischaemic heart diseases were considered less severe than stroke and heart failure and thus had shorter inclusion times. As high blood pressure was mainly treated in primary care, medicine was included in the definition as defined and referenced.

Cancers

As most cancers are clearly defined by ICD-10 codes, only brain cancer had a complex definition constructed, which was done as referenced in the manuscript. With regard to inclusion times, see the previous section, as cancers are mostly not defined as complex except for brain cancer.

Chronic respiratory diseases

As existing studies using complex definitions with medication and services did not differentiate among chronic lower respiratory diseases, this was altered in the current study distinguishing between COPH (J44, J96, J13–J18) and other less severe chronic lower respiratory diseases (J40–J43, J47). Future studies should assess the *validity* thereof as it cannot be ruled out that the medication and service algorithms include overlapping conditions, especially as the services are not disease-specific. In order to minimize the problem, the service criteria were only applied for COPD as the service criteria were initially developed for COPH and indication codes and disease-specific medicine were applied. However, at this time, the definitions cannot differentiate further between different levels and severities of COPH. Moreover, contrary to another referenced study [15], COPD is not an exclusion criterion for asthma or other respiratory disease definitions as, for example, COPD and asthma often coexist. Moreover, patients were excluded among chronic lower respiratory diseases if the medicine was prescribed for COPD or asthma. This was done as the medication is often given across the different conditions. Finally, we used longer inclusion periods than other studies as the chronic respiratory diseases were considered lifelong.

The use of longer inclusion periods in general were properly also due to the increased data possibilities compared to other studies.

Diabetes

With regard to diabetes, it was decided not to use the commonly used Diabetes Register [16] mainly for three reasons. Firstly, it cannot differentiate between type 1 and type 2 diabetes. Secondly, the Diabetes Register will no longer be updated. Thirdly, it was important to create “economical” and effective definitions that could be used by researchers and health-care planners without a separate application for the Diabetes Register – or other disease-specific registers related to other conditions (see references in the table of the complex definitions in the manuscript for different registers and databases of different conditions). Furthermore, the same “basic” registers as is the foundation of the Diabetes Register (NPR, medicine, GP services) and several criteria and algorithms like the Diabetes Registers (for example bloodsucker measurements (BS) and foot therapy) were applied. Notably, the inclusion criteria of patients with 5 yearly BS were discussed in a new validation of the Diabetes Register regarding the risk of including false positive patients [17] due to the number of BS having increased. However, according to the GPs of the expert panel, 5 yearly BS are most likely not given to anyone other than diabetics at this time in private practice. Earlier studies did, however, show the high predictability of the BS [17]. However, we recommend that the risk of false positives is considered and assessed in the future.

The category of Diabetes others (E12–14) was also discussed, but it was decided to separate it as also defined as mutually exclusive to E10-E11 within the ICD-10, differentiated by clinical experts in the TDCR definitions [18] ensuring “clean” categories of type 1 and 2 diabetes. The same approach was also adopted, for example, for Osteoporosis others (M82) so that Osteoporosis (M80–M81) was also kept “clean”.

Arthritis

Similar lower respiratory diseases, most existing complex algorithms of inflammatory polyarthropathies and ankylosing spondylitis are not differentiated. As rheumatoid arthritis was often of special interest, two revised complex algorithms based on existing research were proposed (condition no. 30 and 31) using indication codes. However, as several medications are still overlapping, and as indication codes are first used from 2004 and have around roughly around a quarter of the yearly missings registrations, there is a possible overlap of conditions. Thus future studies should validate the definitions. However, an exclusion criterion for rheumatoid arthritis indication codes at any time was used for *inflammatory polyarthropathies except rheumatoid arthritis* to minimize a possible problem. Also, the used medication is validated in other studies or by medical experts.

Depression and anxiety

Depression and anxiety are examples of common, mainstream, everyday defined conditions, which, in particular, are expected to vary in severity. And as depression is often treated in primary care, the use of medication is crucial. However, as depression medication is often used for different conditions, indication codes of depression were applied. In contrast to depression, it was not possible to differentiate between different anxiety conditions using medications, although this was desirable in the pursuit of including less severe cases.

Considerations in use of hospital procedure codes within complex definitions

The use of hospital procedure codes besides medication was also considered for some conditions such as, for example, hernia and diabetes, but rejected as a rule of thumb for several reasons. One problem with relying on hospital procedure codes in general would be that we do not include the less severe conditions that are not treated yet, or at all, with a specific procedure. Moreover, some procedures might be used across conditions, making it impossible to identify a specific condition, such as, for example, in the case of procedures for high blood pressure. But just as importantly, every procedure code is to be accompanied by a diagnosis code in hospital care, thus we do not expect any real gain using procedure codes in regard to the scope of the study. In addition, register procedure codes are not available within primary care, and neither is the procedure codes used in Denmark based on a widely international classification as the used ICD-10 and ATC classification. However, we recognize the usefulness of procedure codes if the aim is to identify a subgroup of patients, such as, for example, *active hospital-treated* patients, e.g. chronic renal failure as referenced in the manuscript, or plain activities of, for example, hernia, heart surgeries or others within hospital care. This is, however, beyond the scope of the current study. Nevertheless, we cannot rule out that a few definitions can be further improved using procedure codes or others, such as, for example, a new study that suggests using procedure codes in regard to diabetes [17], although this study

also recognized that the gain is limited, if any. Future studies could explore and assess the possible gain in including procedure codes within, for example, diabetes or hernias in complex algorithms.

Future subjects of complex conditions

The following conditions were discussed and could be recommended for complex algorithms in future studies as they were often treated in primary care, by private specialists and with high variation of severity including many less severe patients, but this could not be done appropriately at this time due to data limitations:

Supplementary Table 3. Conditions recommended for complex algorithms in future studies

No.	Conditions	ICD-10	Category	Definitions
65	Other headache syndromes	G44	Cat. III	(DIAG)
67	Sleep disorders	G47	Cat. III	(DIAG)
76	Disorders of eyelid, lacrimal system and orbit	H02–H06	Cat. IV	(DIAG)
79	Diseases of the eye lens (cataracts)	H25–H28	Cat. IV	(DIAG)
84	Disorders of the vitreous body and globe	H43–H45	Cat. IV	(DIAG)
85	Disorders of optic nerve and visual pathways	A: H46, H48 and B: H47	A: Cat. I B: Cat. III	(DIAG)
86	Disorders of ocular muscles, binocular movement, accommodation and refraction	A: H49 and B: H50, H52 and C: H51	A: Cat. III B: Cat. IV C: Cat. I.	(DIAG)
90	Otosclerosis	H80	Cat. II	(DIAG)
91	Other diseases of the inner ear	H83	Cat. II	(DIAG)
92	Conductive and sensorineural hearing loss	H90	Cat. II	(DIAG)
93	Other hearing loss and other disorders of ear, not elsewhere classified	H910, H912, H913, H918, H930, H932, H933	Cat. II	(DIAG)
94	Presbycusis (age-related hearing loss)	H911	Cat. II	(DIAG)
95	Hearing loss, unspecified	H919	Cat. II	(DIAG)
96	Tinnitus	H931	Cat. I	(DIAG)
97	Other specified disorders of ear	H938	Cat. II	(DIAG)
133	Polyarthrosis [arthrosis]	M15	Cat. I	(DIAG)
134	Coxarthrosis [arthrosis of hip]	M16	Cat. I	(DIAG)
135	Gonarthrosis [arthrosis of knee]	M17	Cat. I	(DIAG)
136	Arthrosis of first carpometacarpal joint and other arthrosis	M18–M19	Cat. I	(DIAG)
186	Mood (affective) disorders	F340, F348-F349, F38-F39	Cat. I	(DIAG)
187	Phobic anxiety disorders	F40	Cat. II	(DIAG)
188	Other anxiety disorders	F41	Cat. II	(DIAG)
192	Eating disorders	F50	Cat. III	(DIAG)

6. External expert review of selected disease groups and inclusion times

Process of external medical experts

As a part of the final rounds of review and ratification, it was decided to include external medical experts, besides the co-authors, for ICD-10 disease groups A, B, F, H and M.

As each condition was assessed and discussed, a written summary only containing the categorization was sent back for information and verification. Afterwards, the suggestions and comments were incorporated into the manuscript for final approval by the authors. The process and several discussions and considerations of the external reviewed conditions are also described in previous sections on earlier pages.

The questions in summary

The questions regarding categorization to the doctors were as follows or similar and sent by email as well as being discussed at meetings, by phone or by email:

- 1) *Do you define the enclosed diseases as “chronic” based on the following definition of chronic*?*
- 2) *For the included diseases, how far do you by medical judgment suggest it is feasible to go back in the NHR register and include a patient – and still at a time of interest (for example 01/01/2013) be reasonably sure the patient still has the disease [based on the four categories shown previously]?*
- 3) *Can any of the diseases, in your opinion, not be solely identified by the NHR ICD-10 diagnosis codes, for example because they are diagnosed in the practice sector and therefore do not get a diagnosis code? We are aware that there may be validity problems with diagnosis codes, and you are welcome to point out areas with special problems.*
- 4) *Other comments? For example, if you think that the groupings should be changed.*

* See page 4.

7. Examples of impact from using complex definitions – and selected prevalences comparisons to other literature

Examples of impact from using complex definitions

As seen in

Supplementary Table 4, there are major differences for several conditions with and without a complex definition – varying from approximately 3 times to 24 times differences, the latter seen for ulcers. However, the differences narrows as the severity increases and specialized treatment is needed as seen for bipolar affective disorder. Yet, there is still a difference that might be explained by patients treated by private specialists or perhaps diagnosed earlier than the inclusion period and afterwards treated in primary care. The case of ADHD, however, is somehow different as many patients are diagnosed below the age of 16 at hospitals, but as the population and many studies do not include patients below the age of 16, prescribed medicine is needed.

Supplementary Table 4. Examples of impact using complex algorithms

No.	Name of condition	ICD-10 code/definition	Category	Full population estimates for Denmark	
				<i>N</i>	<i>Per cent</i>
-	Hypertensive diseases *	I10–I15	Cat. III	316,037	6.9
21	Hypertensive diseases**	I10–I15 and/or prescribed medicine	Cat. III	1,060,043	23.3
-	Ulcers*	K25–K27	Cat. IV	6,702	0.1
28	Ulcers**	K25–K27 and/or prescribed medicine	Cat. IV	157,379	3.5
-	Psoriasis*	L40	Cat. I	15,232	0.3
29	Psoriasis**	L40 and/or prescribed medicine	Cat. I	65,469	1.4
-	Depression*	F32, F33, F34.1, F06.32	Cat. III	91,534	2.0
12	Depression**	F32, F33, F34.1, F06.32 and/or prescribed medicine	Cat. III	454,933	10.0
-	Bipolar affective disorder*	F30–F31	Cat. II	6,427	0.1
11	Bipolar affective disorder**	F30–F31 and/or prescribed medicine	Cat. II	22,669	0.5
-	ADHD*	F90	Cat. I	15,453	0.3
14	ADHD**	F90 and/or prescribed medicine	Cat. I	42,908	0.9

*Not complex defined condition. ** Complex defined condition. Full Denmark population estimates based on a sample of N= 4,555,439 citizens aged 16 or more on 1st January 2013.

Selected prevalences of different categories comparisons to other literature

Supplementary Table 5. Examples of prevalence of conditions in different inclusion categories

No.	Name of condition	ICD-10 code/definition	Category	Full population estimates for Denmark	
				<i>N</i>	<i>Per cent</i>
4	Diabetes type 1**	E10 and/or prescribed medicine	Cat. I	23,062	0.5
5	Diabetes type 2**	E11 and/or prescribed medicine	Cat. II	242,176	5.3
63	Sclerosis*	G35	Cat. I	13,284	0.3
16	Epilepsy**	G40–G41 and/or prescribed medicine	Cat. III	61,695	1.4
17	Migraine**	G43 and/or prescribed medicine	Cat. II	149,866	3.3
79	Diseases of the eye lens (cataracts)*	H25–H28	Cat. IV	68,009	1.5
18	Glaucoma**	H40–H42 and/or prescribed medicine	Cat. III	67,310	1.5
96	Tinnitus*	H931	Cat. I	40,124	0.9
23	Stroke**	I60, I61, I63–I64, Z501 (rehabilitation)	Cat. II	72,606	1.6
124	Inguinal hernia*	K40	Cat. IV	25,032	0.5
125	Ventral hernia*	K43	Cat. IV	7,941	0.2
9	Dementia**	F00, G30, F01, F02.0, F03.9, G31.8B, G31.8E, G31.9, G31.0B and/or pres. medicine	Cat. I	36,803	0.8

* Not complex defined condition. ** Complex defined condition. Full Denmark population estimates based on a sample of N= 4,555,439 citizens aged 16 or more on 1st January 2013.

Supplementary Table 5 includes selected conditions of different severity and both complex and non-complex conditions.

Diabetes

As mentioned in the manuscript, the number of included patients differs across methods. For example, self-reported prevalence of diabetes is usually a little lower, around 5.2 per cent, than in the current study (5.8 per cent – 0.5+5.3) [19]. Compared to other Danish register studies using the national Diabetes Register, there was a total of 247,570 living with diabetes in 2012 since 1996 [20]. This is largely identical to the frequencies of the current study's total of 264,642 patients (23,062+241,580). In comparison, another new study also based on the national Diabetes Register and thus similar definitions identifies more patients, 306,624, by the end of 2011 [21]. The differences among the studies might be explained by the fact that the last mentioned study includes patients from 1977 [22] and not “only” 1996. Notably, there are still minor differences across the studies; some might be explained by minor differences in the definitions, and different versions of the NPR, as they have been revised by the Statens Serum Institute, which in fact may explain the differences in estimates of other conditions, but more importantly there is no final agreement on inclusion times. We argue that if a type 2 diabetic is identified in the register before the 10 years of interest, and is not included later by medicine criteria or others, there is a chance of recovery so that the patient is not chronic by the definition of the current study – or even misdiagnosis – which is why a 10-year inclusion time has been preferred in line with the Statens Serum Institute [12,13]. As a newer study implies a risk of up to 20 per cent false positive included in the national Diabetes Registers [17], this might be even more important. Finally, the Diabetes Registers do not differentiate between type 1 and 2, contrary to the definition of the current study. Studies also show that around 10 per cent of all diabetics have type 1 [23], which is consistent with the results of the current study when taking into account that the current study has not included patients under the age of 16.

Multiple sclerosis

With regard to multiple sclerosis (MS), one study identified 11,236 Danish patients alive by the end of 2004 with a diagnosis of MS [24]. However, 1,889 were evaluated as possible cases. The study further showed an increasing trend of 28.3 patients per 100,000 inhabitants from 2000 to 2005, equivalent to approximately 1,500 patients in 5 years. Thus, we should expect around 3,000 more patients in 2015, which is around the identified prevalence in the current study. This is closely confirmed by the Sclerosis Treatment Register with approximately 12,500 patients [25].

Migraine and tinnitus

Migraine and tinnitus are selected as examples of less severe conditions with high variation, often not treated at hospitals and conditions with no treatment or self-treatment. Thus, registers will most likely include the severe patients. For example, other studies show much higher self-reported (thus different methods) prevalence of both migraine/headache (14.5 per cent) and tinnitus (12.1 per cent) than the current study [19]. With regard to migraine, studies often include headaches too and use varying time inclusion criteria different to the current study, thereby making comparisons difficult; bearing this in mind, the prevalence of solely migraine is identified as around 10 per cent [26]. However, differences in definition might also influence results; for example, “chronic headache” only shows a prevalence of around 2 per cent in other studies [26].

A review of tinnitus found studies ranging from a prevalence of 3 to 30 per cent [27], suggesting high variability in methods and definitions. Thus, estimates of migraine and tinnitus in the current study should be used with caution and solely as representatives of more severe cases of the conditions. However, as chronic conditions were defined as having “functional limitations” and/or in need of “on going treatment”, the included conditions might not be wrong by definition, but should not be used as an estimate of the full disease population in regards of both migraine and tinnitus.

Cataracts, glaucoma and eye and ear conditions

In addition to other less severe conditions, the prevalence of cataracts in the current study is much lower than the self-reported 4.1 per cent [19]. Cataracts and other eye and ear conditions may be treated by GP's or private specialists not reporting to the NPR, and no medicine to identify the condition was found, which is why these estimates could be underestimated and should be used with caution. However, one exception is glaucoma, which had medicine included in the definition. A recent study estimated a slightly higher prevalence of glaucoma of 1.7 per cent in 2011 compared to 1.5 per cent in the current study, which is also slightly higher than previous studies [28]. One explanation could be differences in algorithm, for example the current study's use of a minimum of two prescriptions compared to only one prescription needed in the referenced study. However, in attempt to avoid false positives, the use of one only prescription is in general not recommended for the purpose of current study. In addition, including

ATC: S01EC might also include some false positive patients with idiopathic intracranial hypertension, but excluding S01EC was expected to exclude many more patients with glaucoma and ATC: S01EC was thus included coherent with another study [28].

Epilepsy

Epilepsy is an example of a complex disease with historically varying inclusion criteria as well as different severity and polarized patients ranging from lifelong affected to fully cured. Thus, the inclusion period was set to 5 years in line with another study [14] as lifelong patients would still be included due to the need for ongoing medication, but we would have cured or excluded misdiagnoses after 5 years. However, contrary to older studies, medication with indication codes of epilepsy was also included in pursuit of including less severe conditions not identified by hospital diagnosis. In addition, hospital diagnosis was found to have low validity, although it was able to identify “general trends” [14]. The use of medicine has more than doubled the prevalence compared to an older study of 2002 [14]. Future studies should both explore the validity of the indication codes and report on the primary sector and the new increased prevalence.

Stroke

The prevalence of stroke is slightly higher than in a self-reported study in 2013 that reported a prevalence of around 1.1 per cent [19]. Also, a literature review comparing stroke prevalence and incidence across countries showed varying prevalence across countries indicating the impact of different methods and definitions [29]. Therefore, it is difficult to assess the “true” value of stroke in comparison. However, a recent Danish study found 93,266 patients by the end of 2012, based on the NPR, living with stroke using 10-year inclusion times [20]. The slightly higher number in the current study might be explained by the use of more ICD-10 codes (I60–I69) than in the current study. Yet, the current study included ICD-10 codes coherent with the definition of medical experts of the TDCR [23,30] and therefore is expected to be of higher medical precision as the two studies have different medical aims.

Dementia

With regard to dementia, a new Danish study found 32,373 patients not including medicine by the end of 2012 based on registers [20], which is fairly close to the prevalence in the current study when both differences in inclusion time and use of medicine are taken into account. Also, the frequencies are quite similar to another regional Danish study [15].

However, other studies show both varying and higher estimates, varying by up to 40–50 % across studies [31,32]. This might be explained by the extrapolation of foreign studies, differences in method (surveys), the inclusion of mild dementia, regional estimates or guessed estimates.

Hernias

In Denmark, approximately 13,027 hernia surgeries are performed yearly, including 8,842 inguinal and 4,185 ventral hernia surgeries based on procedure codes [33]. When the two-year inclusion time in the present study is considered, and the fact that the prevalence of Supplementary Table 5 is based on diagnosis, we expect higher frequencies in the present study as not all those diagnosed are treated.

8. Supplementary references

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