REVIEW

A comprehensive catalogue of EQ-5D scores in chronic disease: results of a systematic review

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Abstract

Purpose Chronic diseases are associated with impaired health-related quality of life (HRQoL) outcomes. Comparison of HRQoL outcomes between different diseases and with the general population is of major importance to health economists, epidemiologists, clinicians, and policy makers. The aim of this systematic literature review was to develop a catalogue with EQ-5D scores in chronic non-communicable diseases, and to compare these scores with reference values from the general population.

Methods MEDLINE, Embase, and Web of Science were systematically searched independently by two reviewers. Studies were included if they reported mean EQ-5D index values for the adult population and if these scores were compared with the general population. The QualSyst tool for quantitative research was used for quality appraisal.

Results Two hundred and seven articles met the inclusion criteria. An extensive catalogue summarizes the EQ-5D scores in a wide variety of chronic diseases. Mean EQ-5D index values ranged between −0.20 and 1. Lower EQ-5D scores are reported in chronic diseases compared to the general population, specifically in neurological disorders. Most of the diseases demonstrate a substantial disutility, although a minority of diseases have equal or even higher index scores than the general population.

Conclusion A comprehensive, international catalogue has been developed to provide EQ-5D index scores for diverse chronic diseases compared with reference values based on the available literature. The catalogue gives a clear overview of the existing EQ-5D scores and can be rapidly accessed by researchers worldwide for different applications such as health economic evaluations, decision making, resource allocation, and other policy objectives. Future studies should focus on unexamined diseases and specific patient groups to expand the evidence base on HRQoL in chronic diseases.

Keywords Health-related quality of life · Utility · EQ-5D · Catalogue · Chronic disease · Cost-effectiveness analysis · Health economic evaluation · Systematic review

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Introduction

With an estimated 36 million deaths annually, chronic diseases remain the leading cause of mortality worldwide [1, 2]. Furthermore, chronic diseases are associated with a substantial burden of disease for the patients, their caregivers, and the society as a whole [3, 4]. The burden of disease is commonly assessed by disability-adjusted life years (DALYs) with more than half of the DALYs worldwide being caused by chronic diseases [4]. During the past decades, patients' health-related quality of life (HRQoL) has gained importance as a key health outcome indicator, specifically in chronically ill patients, due to improved care which contributes to the increase of lifespan [3]. HRQoL captures patients' self-perceived impact of a medical condition, its

symptoms and treatment referring to physical, mental, and social well-being, compared to what patients believe to be ideal [3, 5]. The number of studies exploring the relationship between chronic diseases and HRQoL is increasing. These studies show a significant decrease in HRQoL in chronic diseases and indicate HRQoL as an important predictor of mortality and morbidity [5–8].

Hence, in addition to mortality and morbidity, patients' HRQoL is of major concern to policy makers. HRQoL outcomes are often included in health economic evaluations when calculating quality-adjusted life years (QALYs) [9, 10]. QALYs combine the impact of a disease on both the quantity and quality of life [11]. To calculate QALYs, preference-based utility scores are required ranging from zero (death) to one (perfect health) [11–13]. These preference-based utilities can be derived from the widely used Euro-Qol Five Dimensions (EQ-5D) instrument. The EQ-5D is a standardized generic instrument for describing and valuing HRQoL. The instrument allows to calculate utility scores based on country-specific value sets or scoring algorithms, which reflect the preference for a health state of the general population in a specific country [14]. Compared to disease-specific HRQoL instruments, generic instruments can be used across different patient groups allowing comparison in HRQoL loss across diseases [15]. Some initiatives to summarize HRQoL data in a specific disease area have been established, but to date, a comprehensive overview of HRQoL data, particularly EQ-5D data in different chronic diseases across countries, is lacking [16].

A comparison of EQ-5D index scores can facilitate health economic evaluations and epidemiologic research. Therefore, the aim of this review is to develop a catalogue of EQ-5D index scores by systematically reviewing the currently available evidence on EQ-5D index scores across patients with chronic diseases, and to compare these scores with reference values from the general population. Developing a catalogue as such would be of major interest to researchers and decision makers in their search for useful EQ-5D data without the difficulty of primary data collection. The availability of a comprehensive and easy accessible EQ-5D catalogue will enable more efficient cost-effectiveness analysis, decision making, and resource allocation. This review does not aim to be applied in Global Burden of Disease context since decomposing patient-level burden to the underlying diseases or health states, presented by DALYs, is beyond the scope of this review [17].

Methods

The methodology as described in the Cochrane Handbook for Systematic Reviews of Interventions was used [18]. The protocol was registered on PROSPERO (https://www.crd. york.ac.uk/prospero) with the following registration number: CRD42018104110.

Search strategy

A systematic literature search was conducted until May 2019. To identify all relevant studies, three electronic databases were systematically searched: MEDLINE (using Pub-Med interface), Embase (using embase.com interface), and Web of Science.

Details of the search strategies are illustrated in Online Resource 1. The search strategy was peer reviewed by an information expert (NP) and evaluated using the Peer Review of Electronic Search Strategies (PRESS) checklist [19].

Study eligibility criteria

The following eligibility criteria were used:

(1) The population of interest had to have a medically confirmed or self-reported diagnosis of one or more non-communicable chronic diseases. Infectious diseases were excluded.
(2) The study had to include adults (≥ 18 years).
(3) The study had to evaluate preference-based utilities derived from the three-level (EQ-5D-3L) or five-level (EQ-5D-5L) version of the EQ-5D. The utilities had to be presented as means. Mapped utilities, for example derived from the 36-item Short Form Health Survey (SF-36), were excluded because they may not correspond with directly obtained EQ-5D scores.
(4) The study had to compare the EQ-5D index scores with those of the general or the healthy population. The former includes both healthy and unhealthy people, whereas the latter includes people without any disease.
(5) If no full text was available, the study was excluded.
(6) Abstracts and full texts in any other language than English were excluded.
(7) Only observational studies were recognized as appropriate. Experimental study designs were excluded.
(8) No restrictions by publication date were implemented.

Study selection

Study selection was performed using the web application Rayyan (https://rayyan.qcri.org). After removing duplicates, two independent reviewers (ER and LVW) were blinded from each other's decision and excluded irrelevant studies, based on title and abstract. Next, all full-text records of the remaining references were independently assessed by both reviewers. Disagreements were resolved by discussion and

if consensus could not be achieved, a third review author (DDS) was consulted.

Quality assessment

The QualSyst tool for quantitative research was used for quality appraisal [20]. This checklist consists of a 14-item scale with questions related to the research question, study design, sampling method, subject characteristics, outcome measures, sample size, statistical methods, estimate of variance, risk of bias/confounders, results, and conclusions. Three questions related to interventional study design were not considered. A summary score (%), ranging from zero (low quality) to 100 (high quality), was calculated for each study by one author (LVW). A minimum quality threshold for study inclusion was not determined, and hence studies were not excluded based on the quality assessment.

Data extraction

Data were extracted to develop a catalogue with the following information: disease, patient subgroup (e.g., disease stage), sample size, mean age, percentage men, EQ-5D score for the chronically ill patients and for the general and healthy population with corresponding standard deviation or standard error, country-specific scoring algorithm, EQ-5D version, disutility, country, and author. Diseases were grouped based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) classification [21]. When the corresponding ICD-10 class was not clearly indicated, the disease was categorized in the most appropriate disease group.
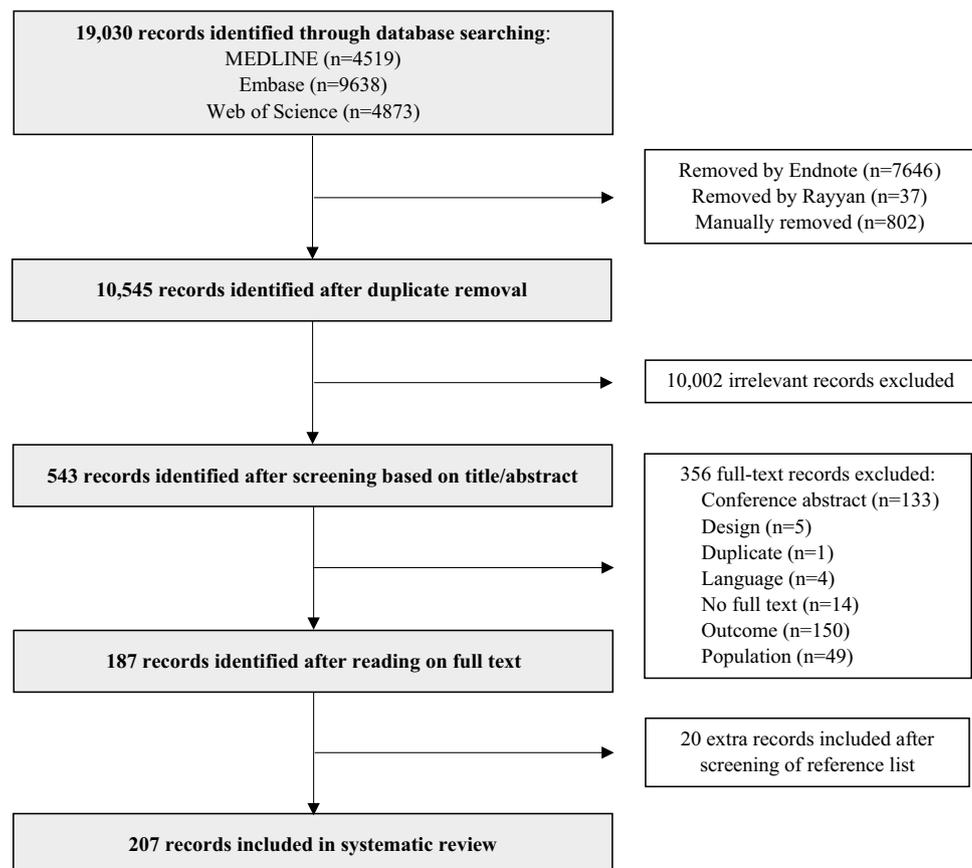
Disutilities demonstrate the impact of diseases in terms of 'loss' in EQ-5D. They reflect the difference between the EQ-5D scores of the general population and the patient population.

Results

Study selection

After deduplication, 10,545 articles were screened for relevance based on title and abstract, resulting in 543 articles. After reading full texts, 187 articles remained eligible for inclusion. Examining the reference lists resulted in 20 additional studies. In total, 207 studies were included. Figure 1 presents the flowchart of the literature search and study selection process.

Fig. 1 Flowchart of the literature search and study selection process

19,030 records identified through database searching:
MEDLINE (n=4519)
Embase (n=9638)
Web of Science (n=4873)

Removed by Endnote (n=7646)
Removed by Rayyan (n=37)
Manually removed (n=802)

10,545 records identified after duplicate removal

10,002 irrelevant records excluded

543 records identified after screening based on title/abstract

356 full-text records excluded:
Conference abstract (n=133)
Design (n=5)
Duplicate (n=1)
Language (n=4)
No full text (n=14)
Outcome (n=150)
Population (n=49)

187 records identified after reading on full text

20 extra records included after screening of reference list

207 records included in systematic review

Agreement between the two authors was determined using Cohen's Kappa statistic and resulted in an interrater reliability of 0.77. The quality assessment demonstrated considerable discrepancies in quality between studies. Overall, all studies appeared to have appropriate representations of the utility outcomes. Details of the quality assessment are illustrated in Online Resource 2.

Study characteristics

All studies found in this review were published between 1999 and 2019 and were conducted in various countries worldwide. Most of the studies were performed in Europe ($n = 121$), specifically in the UK ($n = 29$), followed by Korea ($n = 26$), the USA ($n = 17$), and China ($n = 13$). Study population varied in sample size ($n = 1$ to $n = 233,124$), gender (0% male to 100% male), and age (mean age = 21.4 to mean age = 82.0).

Most of the studies (87.4%) used the EQ-5D-3L, and only twenty-three (11.1%) used the EQ-5D-5L. Three studies (1.4%) did not mention the EQ-5D version that was used. The time trade-off scoring algorithm was used by 77.3% to obtain the EQ-5D value set, whereas only 1.9% used the VAS scoring algorithm. Four studies (1.9%) used a crosswalk index value set for the EQ-5D-5L. A substantial number of studies did not mention the scoring algorithm (18.8%). Moreover, a wide range of country-specific value sets was used. Utilities for the reference population were mostly extracted from the literature, which often resulted in different scoring algorithms between patients and reference population.

Synthesis of findings

The EQ-5D index scores for all available chronic diseases compared to their reference values are summarized as a catalogue available in Online Resource 3.

Overall, the highest EQ-5D score was reported in obesity with alcohol dependence and in lung cancer with chemotherapy (1.00), followed by alcohol abuse, diabetes, cancer, hypercholesterolaemia, and hypertension (0.97). The lowest EQ-5D score was reported in severe Alzheimer's disease (− 0.20) and multiple sclerosis (− 0.07). Likewise, the highest disutility was reported in severe Alzheimer's disease (− 1.05). In contrast, the lowest disutility was reported in non-small cell lung cancer with chemotherapy with a utility score 0.22 points higher than the general population.

Few studies (15.5%) used regression analysis to calculate disutilities, adjusted for several covariates. The majority of disutilities were calculated by the authors of this review because they were not mentioned in the original papers.

An overview per ICD-10 chapter of the lowest and highest mean EQ-5D scores and disutilities as they appeared in the original papers are provided in Table 1.

Table 1 Overview of the findings

Chronic disease chapter (ICD-10)	Number of studies	Mean EQ-5D range	Disutility range
Neoplasms	38	0.45 to 1.00	− 0.46 to + 0.22
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	4	0.65 to 0.92	− 0.07 to − 0.01
Endocrine, nutritional, and metabolic diseases	57	0.31 to 1.00	− 0.58 to + 0.11
Mental and behavioural disorders	46	0.11 to 0.97	− 0.68 to + 0.15
Diseases of the nervous system	41	− 0.20 to 0.92	− 1.05 to + 0.06
Diseases of the eye and adnexa	17	0.45 to 0.95	− 0.48 to + 0.01
Diseases of the ear and mastoid process	10	0.59 to 0.93	− 0.19 to − 0.00
Diseases of the circulatory system	50	0.30 to 0.97	− 0.66 to + 0.02
Diseases of the respiratory system	36	0.47 to 0.95	− 0.37 to + 0.03
Diseases of the digestive system	17	0.49 to 0.92	− 0.41 to + 0.01
Diseases of the skin and subcutaneous tissue	8	0.58 to 0.90	− 0.34 to − 0.00
Diseases of the musculoskeletal system and connective tissue	48	0.26 to 0.94	− 0.67 to + 0.10
Diseases of the genitourinary system	15	0.44 to 0.96	− 0.49 to + 0.01
Certain conditions originating in the perinatal period	1	0.84	− 0.09
Congenital malformations, deformations, and chromosomal abnormalities	5	0.19 to 0.92	− 0.67 to + 0.10
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	13	0.32 to 0.93	− 0.29 to + 0.08
Injury, poisoning and certain other consequences of external causes	7	0.37 to 0.88	− 0.49 to + 0.20

Neoplasms

EQ-5D scores ranged from 0.45 for palliative breast cancer and non-small cell lung cancer with severe adverse event to 1.00 for non-small cell lung cancer with chemotherapy. Disutilities ranged from −0.46 for colorectal cancer stage IV to +0.22 for non-small cell lung cancer with chemotherapy.

Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism

EQ-5D scores ranged from 0.65 for haematologic conditions to 0.92 for anaemia. Disutilities ranged from −0.07 for haematologic conditions to −0.01 for anaemia.

Endocrine, nutritional, and metabolic diseases

EQ-5D scores ranged from 0.31 for diabetes with maximal major amputation to 1.00 for obesity with alcohol dependence. Disutilities ranged from −0.58 for diabetes with maximal major amputation to +0.11 for male diabetic patients.

Mental and behavioural disorders

EQ-5D scores ranged from 0.11 for dementia to 0.97 for alcohol abuse. Disutilities ranged from −0.68 for unspecified mental conditions to +0.15 for dementia.

Diseases of the nervous system

EQ-5D scores ranged from −0.20 for severe Alzheimer's disease to 0.92 for epilepsy, convulsion, and Parkinson's disease. Disutilities ranged from −1.05 for severe Alzheimer's disease to +0.06 for relapsing–remitting multiple sclerosis.

Diseases of the eye and adnexa

EQ-5D scores ranged from 0.45 for visual dysfunction with comorbid stroke to 0.95 for age-related macular degeneration. Disutilities ranged from −0.48 for visual dysfunction with comorbid stroke to +0.01 for age-related macular degeneration.

Diseases of the ear and mastoid process

EQ-5D scores ranged from 0.59 for patients ≥ 75 years with hearing impairment to 0.93 for patients ≥ 60 years with hearing impairment. Disutilities ranged from −0.19 for deafness to −0.0 for ear disorder.

Diseases of the circulatory system

EQ-5D scores ranged from 0.30 for cerebral haemorrhage, cerebral infarction, and embolism to 0.97 for hypertension. Disutilities ranged from −0.66 for cerebral haemorrhage, cerebral infarction, and embolism to +0.02 for 1 year after acute coronary syndrome.

Diseases of the respiratory system

EQ-5D scores ranged from 0.47 for chronic airway obstruction to 0.95 for asthma. Disutilities ranged from −0.37 for chronic bronchitis, chronic obstructive pulmonary disease, and emphysema to +0.03 for chronic obstructive pulmonary disease without comorbidities.

Diseases of the digestive system

EQ-5D scores ranged from 0.49 for pancreatic disorder to 0.92 for ulcer. Disutilities ranged from −0.41 for liver cirrhosis/dysfunction to +0.01 for atrophic gastritis, Barrett oesophagus, and oesophagitis.

Diseases of the skin and subcutaneous diseases

EQ-5D scores ranged from 0.58 for chronic ulcer of skin to 0.90 for pimples. Disutilities ranged from −0.34 for skin disorder to −0.00 for psoriasis and (inflammatory) skin disorder.

Diseases of the musculoskeletal system and connective tissue

EQ-5D scores ranged from 0.26 for juvenile idiopathic arthritis to 0.94 for arthritis. Disutilities ranged from −0.67 for severe fibromyalgia to +0.10 for postmenopausal women with osteoporosis.

Diseases of the genitourinary system

EQ-5D scores ranged from 0.44 for renal failure with haemodialysis to 0.96 for chronic kidney disease stage one. Disutilities ranged from −0.49 for urinary incontinence to +0.01 for chronic kidney disease stage one.

Certain conditions originating in the perinatal period

The EQ-5D score was 0.84 for survivors of bronchopulmonary dysplasia with a disutility of −0.09.

Congenital malformations, deformations, and chromosomal abnormalities

EQ-5D scores ranged from 0.19 for tuberous sclerosis complex with generalized convulsive seizure to 0.92 for aortic anomalies. Disutilities ranged from −0.67 for tuberous sclerosis complex with generalized convulsive seizure to +0.10 isolated congenital aortic valve disease.

Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified

EQ-5D scores ranged from 0.32 for chronic neuropathic pain to 0.93 for not specified other chronic diseases. Disutilities ranged from −0.29 for dizziness with falls and pain to +0.08 for chronic non-neuropathic pain.

Injury, poisoning, and certain other consequences of external causes

EQ-5D scores ranged from 0.37 for 2 weeks after hip fracture to 0.88 for 12 months after wrist fracture. Disutilities ranged from −0.49 for 2 weeks after hip fracture to +0.20 for 12 months after wrist fracture.

The findings confirm the lower HRQoL in patients with chronic diseases compared to the general population. Most of the diseases demonstrate a substantial disutility, although a minority of diseases had equal or even higher index scores than the general population.

Discussion

To our knowledge, this is the first systematic review that provides a comprehensive overview of the available literature on EQ-5D index scores for a large variety of chronic diseases compared with reference values from the general population. The focus of this review lies on all chronic non-communicable disease chapters included in the ICD-10, which resulted in 207 included studies covering 308 different diseases. As a result, a large, international catalogue was developed with an extensive source of EQ-5D data. Since HRQoL has been prioritized as a key patient-reported outcome measure, the demand for these data is rising. This catalogue meets the rising demand from health economists for appropriate EQ-5D data that can be used in QALY calculations, but also from epidemiologists and policy makers to better understand the burden of chronic diseases [22, 23].

Our results confirm the substantial reduction in HRQoL associated with chronic diseases. Chronically ill patients have lower utility scores compared to the reference population. More specifically, patients with neurological disorders have the highest reduction in HRQoL, especially in

Alzheimer's disease. Moreover, the majority of studies focus on endocrine, nutritional, and metabolic diseases, mental and behavioural disorders, and diseases of the musculoskeletal and circulatory system.

A knowledge gap in the literature still exists for a few diseases, despite the fact that this review covers all chronic disease chapters in the ICD-10. For example, no data were available for cystic fibrosis, sleep apnoea, or specific types of cancer such as pancreatic cancer or bone cancer, although literature demonstrated their impact on HRQoL [24–28]. There is also little evidence about certain conditions originating in the perinatal period, diseases of the blood, and congenital malformations. Moreover, few studies reported on young adults whereas most studies focused on older populations. This can be explained by the fact that chronic diseases mainly occur in the elderly [29, 30]. Additionally, research originating from South America, Africa, and Australia is lacking.

In this review, substantial differences in index scores for similar disease conditions were observed. For example, an index score of −0.07 is reported for multiple sclerosis by one study, while another study reported a score of 0.90. This is also observed for dementia with scores ranging from 0.11 to 0.90. Possible explanations to these variations are differences in study quality and methodology such as population characteristics, disease severity, scoring algorithm, EQ-5D version, and random measurement error [31]. Furthermore, scores vary according to gender. Several studies stratify the scores by gender with men having higher scores. This result is also seen in the general population [32, 33]. A possible explanation can be found in women's extraversion when rating their health, resulting in more realistic scores than men [34]. Likewise, studies show that women have more comorbidities, and hence women's HRQoL is often more impaired than men.

This study has several major strengths. It is unique in its kind, since it is the first study that summarizes mean EQ-5D scores for a wide range of chronic diseases across countries addressing the rising demand for HRQoL data [22, 23]. In this regard, Sullivan et al. developed two high-quality catalogues with nationally representative preference-based HRQoL scores for chronic conditions [15, 31]. Despite their extensive work, the scope of Sullivan's work is still quite limited given its national character. In response, our study has included a large number of international studies in which every continent, except Antarctica, is represented with Europe, Asia, and North America having the largest number of studies. The majority of studies originate from the UK, Sweden, and Korea. This global spread results in an extensive source of data useful for researchers worldwide. Another strength is the broad range of chronic diseases. Most studies collected information on one particular disease, impeding comparison with other diseases [35].

In this view, our review can be regarded as innovative by including a large number of both common and rare diseases. Another strength is the inclusion of both EQ-5D versions, although a thorough comparability between both is not desirable due to differences in responses and valuation system. Therefore, the catalogue clearly mentioned the EQ-5D version to avoid misinterpretation. Currently, the EQ-5D-5L is already widely used, but yet the EQ-5D-3L will remain part of the evidence base for many years, specifically due to its value sets [36]. Furthermore, many studies were screened on full text to avoid the risk of inadequate exclusion since the majority of studies report index scores as a small secondary outcome. A final important strength is the inclusion of reference values in each study, which allows us to assess the impact of a given disease, since a sole index value without reference is difficult to interpret.

However, caution is needed when interpreting the results because of the heterogeneity in quality of the studies. In some studies, there is a lack of sample size information and demographic information, such as age and gender. In addition, most studies did not clearly state disease severity or stage, disease duration, whether or not the disease was self-reported, and whether or not they followed active treatment. The latter is very important to take into account since research showed that receiving treatment has a significant impact on patients' HRQoL [37]. Furthermore, other determinants such as socio-economic class, country of origin, and country of residence are worth to be mentioned as these can be a source of heterogeneity in the results. Due to practical restrictions, this review could not include all determinants in the catalogue.

Additionally, several studies have not reported which scoring algorithm was used. It is confirmed that the selection of scoring algorithm influences the index score [38]. Utility scores might differ substantially between countries because they reflect the preferences of the country of elicitation [39, 40]. This may confound comparison across studies or diseases [35]. Moreover, careful consideration is needed when interpreting the disutility values as some studies provide disutilities based on regression analysis, whereas for the majority a simple subtraction of the mean values was performed. A final caution is needed when interpreting the index scores in patients with dementia or with Alzheimer's disease. These scores are often filled in by proxy and may bias the patients' index scores. These findings underline the importance of investigating study characteristics and patients' demographic background to interpret results properly.

Another limitation is the lack of information about whether or not significant differences in EQ-5D index scores exist between chronically ill patients and the general population. The majority of studies did not perform statistics to investigate significance, and therefore only disutilities without details about the significance level were described.

Selecting studies based on reported significance level would have resulted in less included studies. Furthermore, there is a lack of information on whether or not the utilities are age-standardized. Hence, comparison between scores is difficult because the disease groups being compared may differ significantly with respect to demographic characteristics. Another limitation is the exclusion of median utilities. Although both are mathematically valid point estimates, the use of means is recommended by health economists [41]. Experimental studies were excluded because they are often not representative for a given disease group; however by excluding these, some useful findings could have been missed.

This review is limited to the EQ-5D because it is internationally recognized as the most widely used instrument for obtaining health utilities. Other valuable measures, such as the SF-36 or Health Utilities Index (HUI), were not included but can be of importance for health economic evaluations. However, caution is needed since literature confirms that outcomes of various instruments are not interchangeable [42].

In conclusion, this study is the first to provide a comprehensive overview of published EQ-5D index scores in chronic diseases. By making the catalogue publicly available, researchers will no longer have to collect primary EQ-5D data that can be used for different applications such as cost-effectiveness analysis, decision making, and resource allocation. To enlarge evidence on HRQoL in chronic diseases, further investigation on unexamined diseases is required and more attention to specific patient groups is essential.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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