

Informal caregiving in COPD: a systematic review of instruments and their measurement properties

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Highlights

- Thirty-five instruments assessed the impact of COPD on informal caregivers;
- Psychological status/mood, burden and quality of life were the most common domains;
- Measurement properties of instruments have been poorly studied in this population;
- An improved understanding of the measurement properties of instruments is needed.

Abstract

Background: Increasing symptoms and activity restriction associated with COPD progression greatly impact on the lives of their informal caregivers, who play a vital role in maintaining their health. An understanding of this impact is important for clinicians to support caregivers and maintain a viable patient environment at home. This systematic review aimed to identify the instruments commonly used to assess informal caregiving in COPD and describe their measurement properties in this population.

Methods: Searches were conducted in PubMed, Scopus, Web of Science, CINAHL and PsycINFO and in references of key articles, until November 2016. Instruments used to assess the impact of COPD on caregivers were identified and their properties described. Quality of studies was rated using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist. Quality of the measurement properties of instruments was rated as 'positive', 'negative' or 'indeterminate'.

Results: Patients cared for, had moderate to very severe COPD and the sample of caregivers ranged from 24-406. Thirty-five instruments were used in fifty studies to assess caregivers' psychological status and mood (9 instruments), burden/distress (12 instruments), quality of life (5 instruments) or other (9 instruments). Eighteen studies assessed the measurement properties of 21 instruments, most commonly hypothesis testing (known validity) and internal consistency. Study quality varied from 'poor' to 'fair' and with many properties rated as 'indeterminate'.

Conclusions: Although several instruments have been used to assess the impact of COPD on caregivers, an increased understanding of their properties is needed before their widespread implementation.

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Introduction

Chronic obstructive pulmonary disease (COPD) affects 210 million people worldwide^{1,2}. Pulmonary rehabilitation is recognized internationally as the standard of care and professional societies have recently published updated guidelines and policy statements³⁻⁶ that summarize the evidence of its effectiveness and detail the challenges of patient access and capacity. However, the rising symptom burden, restriction in activities and psychological sequelae experienced by the patient also impact increasingly on their family members and other informal caregivers⁷⁻¹⁰. Recent narrative reviews have found that caring for a person with COPD is a stressful experience with unique challenges related to the specificities of the disease, although positive aspects, such as improved self-worth, have also been reported^{8,10}. Given the clinical as well as the economic implications of informal care, which in the US has been associated with a cost in excess of 3 billion dollars per year¹¹, the awareness of the overall experience of caregivers is fundamental to support them in their caregiving role⁸⁻¹⁰. An important component of addressing this issue is the selection of the most appropriate tool to measure the (negative and positive) impact of COPD on informal caregivers¹². Therefore, we undertook this systematic review to identify the instruments used to assess informal caregiving in COPD and describe their measurement properties if assessed in this population. Such information will guide clinicians on the aspects of caregiving most in need of support.

Methods

Search strategy

Searches in the Cochrane Library, the COSMIN list of systematic reviews of measurement properties database and the International Prospective Register of Systematic Reviews (PROSPERO) were conducted prior to the development of this review to exclude the existence of similar reviews/protocols. Since no similar studies were found, the systematic review protocol was registered at PROSPERO (ref. CRD42016041401).

A systematic literature search was performed in the electronic databases PubMed, Scopus, Web of Science, CINAHL and PsycINFO, from their inception until July 21st 2016. Additional searches were performed in weekly automatic updates retrieved from the databases until the end of November 2016. The search strategy contained a combination of terms in the title/abstract/keywords (Table A.1). The electronic search was supplemented by hand searching the references of key articles⁷⁻¹⁰. This search strategy was developed with the advice of a librarian with expertise in health sciences.

Eligibility criteria

This systematic review was reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines¹³. Eligible studies had to state in the objectives, methods or rationale that they were focused on assessing informal caregiving in COPD and include a self-administered assessment instrument. Instruments could be used to evaluate the negative (e.g., burden), positive (e.g., satisfaction) or both aspects of caregiving, e.g., caregiver burden/distress, psychological status and mood or health-related quality of life. Informal caregivers were defined as people who provided unpaid care on a regular basis to a person with COPD¹⁴, and could include spouses, siblings or other family members, friends or neighbors. Studies involving caregivers of patients with diseases other than COPD were also eligible if they had a subgroup of COPD caregivers. All original quantitative studies applying, testing or developing an instrument were eligible (e.g., cross-sectional, cohort, non-randomized/randomized controlled trials, case studies).

Studies with a mixed-methods design and interventional studies were included if quantitative data were available. Searches were restricted to studies published in English, Spanish and Portuguese. Qualitative studies, magazines, news, electronic resources and reports, theses, dissertations, abstracts, editorials and systematic reviews were excluded, although their references were searched for relevant articles. Studies that involved only formal caregivers, assessed patients' perspective of caring, and/or investigated other aspects of caregiving (e.g., caregivers' needs and expectations) were excluded.

Selection of articles

Two reviewers (JC and AM) independently performed the initial screening of articles based on type of publication and relevance for the scope of the review, according to their title and abstract. Then, the full-text of each potentially relevant article was screened for content to decide its eligibility. The level of inter-rater agreement was calculated using the Cohen's kappa statistic, considering the following cut-off points¹⁵: slight agreement (≤ 0.20), fair agreement (0.21–0.40), moderate agreement (0.41–0.60), substantial agreement (0.61–0.80) and almost perfect agreement (≥ 0.81).

Data extraction and synthesis

One researcher extracted the data from the included studies and the other authors checked for accuracy and completeness of data. Data extraction was performed using a pre-developed and standardized form to guarantee the consistency of extracted data concerning:

1. Instrument characteristics: name and abbreviation, original reference, life domain/construct, number of items, rating system, score range (total scale and/or subscales), practical burden (i.e.,

administration time and ease of scoring) and costs. When information was lacking, we searched for the original reference;

2. Country and study population in which the measurement properties of the instrument were assessed (e.g., age, gender, patient-caregiver relationship, COPD severity), as well as the sample size;

3. Identification of the measurement properties of instruments used to assess caregivers of patients with COPD. According to the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) checklist, the following measurement properties could be identified:

1. Validity – content validity, construct validity (i.e., hypotheses testing, structural validity, cross-cultural validity), and criterion validity (i.e., concurrent validity, predictive validity);

2. Reliability – internal consistency, reliability, measurement error;

3. Responsiveness.

Definitions of the measurement properties are described elsewhere¹⁶.

Methodological quality of studies

The COSMIN checklist (<http://www.cosmin.nl/>) was used to evaluate the quality of studies assessing the measurement properties of instruments. The checklist includes nine boxes with standards for the different measurement properties. Boxes were completed for each measurement property of each instrument described in each study. Each item of the boxes was rated on a 4-point rating scale ('excellent', 'good', 'fair' and 'poor') based on specific criteria. The overall score for the methodological quality of a study was determined for each measurement property separately by taking the lowest score of any item in the box ('*worst score counts*'). A detailed description of the boxes and scoring can be found in Mokkink et al.¹⁷. Assessment of the quality of studies was performed by two reviewers independently (JC and AM). In case of disagreement, a third reviewer was consulted. This procedure was also conducted to assess the quality of the measurement properties of instruments.

Quality of the measurement properties of instruments

The quality of the measurement properties of instruments was assessed using the rating system proposed by Terwee et al.¹². For each measurement property, one or more criteria was used to define a 'positive' (+), 'indeterminate' (?) or 'negative' (-) rating depending on the design, methods and outcomes of the studies.

Results

Study selection

The literature search provided a total of 1407 records. After duplicates were removed, 884 records were screened for content through title and abstract. From these, 817 were excluded. The full-text of 67 articles was then screened for eligibility and 17 articles were excluded (Figure 1). Reasons for exclusion were the following: studies did not use an instrument to assess caregivers or provided no information about the instrument (n=9), had a qualitative design (n=1) or were not relevant (n=7). In total, 50 articles were included, all published in English except one (Spanish)¹⁸. Most articles were published after 2000 (44 articles), with half of them (25 articles) being published in the last five years (i.e., 2012-2016). Studies were conducted in Europe (n=23), North (n=14) and South (n=2) America, Asia (n=8) or Oceania (n=3). Thirty-three of the 50 included studies had a cross-sectional design. The remaining studies were longitudinal (8 studies¹⁹⁻²⁶), interventional (8 studies²⁷⁻³⁴) or case studies (1 study³⁵). Inter-rater agreement regarding study selection was substantial (kappa=0.78). Disagreements were resolved by consensus.

Instruments

Table 1 presents the list of instruments found and their characteristics according to their life domain/construct. Thirty-five instruments were used to assess caregivers' psychological status and mood (9 instruments), burden/distress (12 instruments), health-related quality of life (5 instruments), or other domains (9 instruments). None of the instruments was designed to be specific to caregivers of patients with COPD.

Regarding psychological status and mood, the most used instrument was the Hospital Anxiety and Depression Scale which assesses symptoms of anxiety and depression (10 studies^{20,21,27,36-42}). The long and short versions were both used for two of the instruments: the Center for Epidemiological Studies Depression Scale⁴³⁻⁴⁷ and the Profile of Mood States^{47,48}. Another instrument, the Symptom Checklist-90, was used in its original⁴⁹ and revised^{26,50} forms. Most instruments assessing psychological status and mood required approximately 5-10 minutes to administer and had a recall period of a week. Scoring consisted of the sum of items in 4 instruments (*'easy scoring'*) or required the use of a simple (*'moderate scoring'*) or complex (*'complex scoring'*) formula (5 instruments).

Instruments used to assess burden/distress varied across the literature, although the most commonly used was the Zarit Burden Interview (11 studies^{18,22,35,44,46,51-56}) followed by the Caregiver Burden Scale (4 studies^{19,40,57,58}). Two of the instruments aimed to evaluate the subjective distress associated with a specific life event, such as a patient's stay at an intensive

care unit (Impact of Event Scale^{20,21}; Peritraumatic Dissociative Experiences Questionnaire²¹). All instruments had an easy scoring system consisting of the sum of the items, except one with no scoring information (Family Burden Questionnaire⁵⁹). Administration time varied from 5 to 30 minutes although one instrument required 90 minutes (Family Burden Questionnaire)⁵⁹.

Caregivers' quality of life was assessed with generic health-related quality of life instruments. The most used instrument was the Medical Outcomes Study Questionnaire 36-Item Short Form (6 studies^{29,30,40,57,58,60}). The European Quality of Life Questionnaire was either used in its full (i.e., 5 dimensions and a visual analogue scale [VAS] 0-100%)⁴² or short (VAS only)^{26,50} version. The recall period and the scoring system varied among instruments (Table 1). Administration time ranged from 5 to 20 minutes.

Other domains, assessed in the studies, comprised both the negative and positive aspects of caregiving (Caregiver Reaction Assessment^{25,47,61,62}; Family Appraisal of Caregiving Questionnaire for Palliative Care^{23,63}), disability due to the partner's disease (COPD Disability Index⁵⁰, which was a modified version of the Pain Disability Index), objective and subjective health status (Health Perceptions Questionnaire Form II – only the Current Health subscale was used⁴⁸), low back pain prevalence and impact (Nordic low back pain questionnaire⁶⁰), psychosocial impact of the illness (Psychosocial Adjustment to Illness Scale – Self-Report^{32,33}), loneliness (revised UCLA Loneliness scale^{43,64}), spiritual wellbeing (Functional Assessment of Chronic Illness Therapy 12-item Spiritual Well-Being Scale⁴⁷) and life satisfaction (Life Satisfaction Index-A⁶⁵).

Measurement properties of instruments

Only 18 studies assessed the measurement properties of 21 instruments, although none was specifically designed for this purpose. Seven instruments aimed to assess caregivers' psychological status and mood, 5 burden/distress, 4 quality of life domain and 5 other domains. Informal caregivers included in these studies were mostly female and patients' spouses^{26,33,36,38-41,43,48-50,52,64}. Sample sizes ranged from 25⁴⁸ to 406⁶¹. Caregivers' mean age ranged from 48 to 67 years. When reported, COPD severity was frequently moderate to very severe according to the GOLD¹ criteria (5 studies)^{26,41,48-50}. Four studies included patients at all COPD grades^{33,38,39,57}.

Table 2 presents the sample characteristics and country in which the instruments were applied, as well as the results for the methodological quality of studies and quality of the measurement properties of instruments. Studies assessed content validity (1 study), hypothesis testing (also known as 'known validity', 20 studies), internal consistency (21 studies), and/or test-retest reliability (2 studies) of the instruments in COPD caregivers. No information on criterion validity, structural validity, agreement or responsiveness was available. Inter-rater agreement regarding

the quality of studies and quality of the measurement properties of instruments was substantial ($\kappa > 0.76$).

Methodological quality of studies

Only one study assessed the content validity of an instrument, the Caregiver Reaction Assessment⁶¹. The study was rated as 'poor' mainly because it did not assess the relevance of items in the study population but only considered the professionals' views through the content validity index (CVI)⁶⁶.

Studies assessing hypothesis testing of instruments were classified as 'fair' (11 studies) or 'poor' (9 studies). Their common weaknesses included the lack of formulation of hypotheses and of description of missing items, and the use of a comparator that measures another construct. Correlations between the instruments and comparators are provided in Table A.2.

Studies assessing internal consistency were rated as 'fair' (6 studies) or 'poor' (15 studies). These low ratings were attributable to the fact that none of the studies checked for the unidimensionality of the instrument and information on missing items and how these were handled was not provided. All studies assessing internal consistency presented the Cronbach's alpha (values are presented in the Table A.2).

Studies assessing test-retest reliability of two instruments, the Carers' Assessment of Difficulties Index³⁸ and the European Quality of Life Questionnaire VAS²⁶, were classified as 'poor'. The low quality of studies was attributable to the lack of information on missing items and procedures (i.e., number of measurements, independence of administration, time interval, stability of the target population and testing conditions).

Quality of the measurement properties of instruments

Content validity of the Caregiver Reaction Assessment was classified as negative ('-') because the target population was not involved in the validation process. Hypothesis testing, internal consistency and test-retest reliability were rated as indeterminate ('?') for all instruments. The decisive factors for these results were the absence of factor analysis (internal consistency) and specific hypotheses (hypothesis testing), and the lack of information on the methodologies used (test-retest reliability).

Discussion

This systematic review provided a comprehensive overview regarding the instruments used to assess the impact of COPD on informal caregivers, examining all aspects of caregiving including mood, quality of life and wellbeing. Half of the included studies were published in the last five years which emphasizes the increasing awareness of the need to assess and support informal caregivers as part of the COPD management plan. Despite the large number of instruments in use, studies describing their measurement properties are few and have been of poor quality.

The 35 instruments identified assessed domains of psychological status and mood, burden/distress and quality of life. Qualitative studies have shown that caregivers identify changes in various dimensions of their lives (e.g. emotional, social and financial dimensions) as a result of caring for a person with COPD⁶⁷⁻⁷⁰. These findings are related to the life domains identified in this review. Most instruments explored the negative impacts of caregiving with only two addressing both the positive and negative impacts of caring for a person with COPD, the Caregiver Reaction Assessment^{25,47,61,62} and the Family Appraisal of Caregiving Questionnaire for Palliative Care^{23,63}).

Many of the instruments in this review have also been used among the healthy elderly or those with other chronic conditions^{71,72} such as heart failure⁷³, cancer⁷⁴ or other palliative care conditions⁷⁵. Although it is likely that there are more similarities than differences on the caregiver impact in populations with different diagnostic categories, a common requirement is that the measurement properties of instruments used have to be adequately described in the population of interest^{12,16}. Measurement properties were described in only 21 of the 35 instruments identified in this report. Samples in which the instruments were tested were comprised mostly of women, which reflects the dominance of the female gender and is in keeping with the wider caregiving literature¹⁴. Studies assessing the measurement properties of instruments were of low quality possibly because they were not specifically designed for this purpose. Only one study assessed the content validity of an instrument (Caregiver Reaction Assessment)⁶¹. Assessment of content validity is a fundamental step when testing an existing instrument in a population that differs from the original population for which it was developed¹⁷. None of the studies described explicitly formulated hypotheses regarding the expected correlations between instruments, without which there is a high risk of bias¹². In studies evaluating internal consistency, factor analysis was absent although it is fundamental to check for the unidimensionality of the instrument⁷⁶. Alternatively, newer statistical methods such as the Rasch analysis, could be used as recently highlighted by the COSMIN group⁷⁷. Studies assessing test-retest reliability did not describe the number of measurements, the time intervals or the testing conditions.

There were a number of study limitations. The search criteria did not include multiple languages, which may have led to the exclusion of potentially relevant studies. In the absence of validation, cultural differences may affect the use of instruments outside the country in which it was originally developed. Most of the included studies did not mention the type or extent of caregiving provided to patients with COPD which would likely influence the experience of caregivers⁷⁸. Instruments used to assess informal caregiving in COPD were included even if they were not specifically developed for caregivers. Generic instruments measure items that may be unrelated to informal caregiving; however, their inclusion was necessary to address the absence of summarized information on instruments most frequently used to assess informal caregiving in COPD and to avoid reporting bias (i.e., the authors making a determination of which instruments qualify and which do not). Our categorization of instruments into domains/constructs was not standardized. Whereas the categorization we selected is commonly used, clinicians choosing an instrument must be sure they are measuring the dimension(s) of the construct they are specifically interested in. Furthermore, given that some of the instruments identified in the review capture multi domains, their psychometric properties may not reflect specifically the caregiver domain in which they were included. Finally, broader dimensions of support, e.g. social and financial services, were not the topic of this review.

Whereas in the absence of information and better methodological quality assessment,¹⁷ one cannot conclude that the instruments identified were inadequate, a better knowledge of their validity, reliability and responsiveness as well as their ease of administration, acceptability and interpretability would greatly assist clinicians in selecting the most appropriate to the circumstances in which the impact of caring for patients with COPD is being assessed.

Conclusions

There is increasing interest in informal caregiving in COPD among clinicians and investigators as the prevalence of severe disease continues to rise and is associated with a substantial health, social and economic impact. Although a large number of instruments have been used to assess the impact of COPD on informal caregivers, their measurement properties have been poorly studied. An improved understanding of the measurement properties will assist clinicians selecting the most suitable instrument for the target population based on the study purpose and available resources and delivering optimal caregiver support.

References

1. Global Strategy for the Diagnosis Management and Prevention of COPD. *Global Initiative for Chronic Obstructive Lung Disease (GOLD)*. Available from: <http://www.goldcopd.org/>. 2017.
2. World Health Organization. *Action plan of the Global Alliance against Chronic Respiratory diseases, 2008-2013*. Geneva: WHO Library Cataloguing-in-Publication Data; 2008.
3. American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR). *Guidelines for Pulmonary Rehabilitation Programs*. 3rd ed. USA: Human Kinetics; 2011.
4. Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society Statement on Pulmonary Rehabilitation. *American journal of respiratory and critical care medicine*. 2006;173(12):1390-1413.
5. Rochester CL, Vogiatzis I, Holland AE, et al. An Official American Thoracic Society/European Respiratory Society Policy Statement: Enhancing Implementation, Use, and Delivery of Pulmonary Rehabilitation. *American journal of respiratory and critical care medicine*. 2015;192(11):1373-1386.
6. Spruit MA, Singh SJ, Garvey C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *American journal of respiratory and critical care medicine*. 2013;188(8):e13-64.
7. Bryant J, Mansfield E, Boyes AW, Waller A, Sanson-Fisher R, Regan T. Involvement of informal caregivers in supporting patients with COPD: a review of intervention studies. *International journal of chronic obstructive pulmonary disease*. 2016;11:1587-1596.
8. Cruz J, Marques A, Figueiredo D. Impacts of COPD on family carers and supportive interventions: a narrative review. *Health & Social Care in the Community*. 2017;25(1):11-25.
9. Grant M, Cavanagh A, Yorke J. The impact of caring for those with chronic obstructive pulmonary disease (COPD) on carers' psychological well-being: a narrative review. *Int J Nurs Stud*. 2012;49(11):1459-1471.
10. Nakken N, Janssen DJA, Van Den Bogaart EHA, et al. Informal caregivers of patients with copd: Home sweet home? *European Respiratory Review*. 2015;24(137):498-504.
11. Langa KM, Fendrick AM, Flaherty KR, Martinez FJ, Kabeto MU, Saint S. Informal caregiving for chronic lung disease among older americans*. *Chest*. 2002;122(6):2197-2203.
12. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol*. 2007;60(1):34-42.
13. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med*. 2009;6(7):e1000097.

14. Bastawrous M. Caregiver burden—A critical discussion. *International Journal of Nursing Studies*. 2013;50(3):431-441.
15. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. *Biometrics*. 1977;33(1):159-174.
16. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *Journal of Clinical Epidemiology*. 2010;63(7):737-745.
17. Mokkink LB, Terwee CB, Patrick DL, et al. *COSMIN checklist manual*. Consensus-based Standards for the selection of health Measurement Instruments (COSMIN);2012.
18. Godoy-Ramírez AM, Pérez-Verdún MÁ, Doménech-Del Rio A, Prunera-Pardell MJ. Caregiver burden and social support perceived by patients with chronic obstructive pulmonary disease. *Revista de Calidad Asistencial*. 2014;29(6):320-324.
19. Appleton S, Adams R, Porter S, Peacock M, Ruffin R. Sustained improvements in dyspnea and pulmonary function 3 to 5 years after lung volume reduction surgery. *Chest*. 2003;123(6):1838-1846.
20. Azoulay E, Kouatchet A, Jaber S, et al. Noninvasive mechanical ventilation in patients having declined tracheal intubation. *Intensive Care Medicine*. 2013;39(2):292-301.
21. De Miranda S, Pochard F, Chaize M, et al. Postintensive care unit psychological burden in patients with chronic obstructive pulmonary disease and informal caregivers: A multicenter study. *Critical care medicine*. 2011;39(1):112-118.
22. Garlo K, O'Leary JR, Van Ness PH, Fried TR. Burden in caregivers of older adults with advanced illness. *Journal of the American Geriatrics Society*. 2010;58(12):2315-2322.
23. Nakken N, Spruit MA, Wouters EFM, Schols J, Janssen DJA. Family caregiving during 1-year follow-up in individuals with advanced chronic organ failure. *Scandinavian Journal of Caring Sciences*. 2015;29(4):734-744.
24. Papaioannou AI, Tsirikla S, Bartziokas K, et al. Collateral damage: Depressive symptoms in the partners of COPD patients. *Lung*. 2014;192(4):519-524.
25. Sautter JM, Tulsy JA, Johnson KS, et al. Caregiver experience during advanced chronic illness and last year of life. *Journal of the American Geriatrics Society*. 2014;62(6):1082-1090.
26. Vaske I, Thone MF, Kuhl K, et al. For better or for worse: a longitudinal study on dyadic coping and quality of life among couples with a partner suffering from COPD. *Journal of Behavioral Medicine*. 2015;38(6):851-862.

27. Farquhar MC, Prevost AT, McCrone P, et al. The clinical and cost effectiveness of a Breathlessness Intervention Service for patients with advanced non-malignant disease and their informal carers: mixed findings of a mixed method randomised controlled trial. *Trials*. 2016;17.
28. Figueiredo D, Cruz J, Jácome C, Marques A. Exploring the Benefits to Caregivers of a Family-Oriented Pulmonary Rehabilitation Program. *Respiratory Care*. 2016;61(8):1081-1089.
29. Hughes SL, Weaver FM, Giobbie-Hurder A, et al. Effectiveness of team-managed home-based primary care: A randomized multicenter trial. *Journal of the American Medical Association*. 2000;284(22):2877-2885.
30. Kenealy TW, Parsons MJG, Rouse APB, et al. Telecare for Diabetes, CHF or COPD: Effect on Quality of Life, Hospital Use and Costs. A Randomised Controlled Trial and Qualitative Evaluation. *Plos One*. 2015;10(3).
31. Kwok T, Lum CM, Chan HS, Ma HM, Lee D, Woo J. A randomized, controlled trial of an intensive community nurse-supported discharge program in preventing hospital readmissions of older patients with chronic lung disease. *Journal of the American Geriatrics Society*. 2004;52(8):1240-1246.
32. Marques A, Gabriel R, Jacome C, Cruz J, Brooks D, Figueiredo D. Development of a family-based pulmonary rehabilitation programme: an exploratory study. *Disability and Rehabilitation*. 2015;37(14-15):1340-1346.
33. Marques A, Jacome C, Cruz J, Gabriel R, Brooks D, Figueiredo D. Family-Based Psychosocial Support and Education as Part of Pulmonary Rehabilitation in COPD A Randomized Controlled Trial. *Chest*. 2015;147(3):662-672.
34. Utens CMA, van Schayck OCP, Goossens LMA, et al. Informal caregiver strain, preference and satisfaction in hospital-at-home and usual hospital care for COPD exacerbations: Results of a randomised controlled trial. *International Journal of Nursing Studies*. 2014;51(8):1093-1102.
35. Sorocco KH, Bratkovich KL, Wingo R, Qureshi SM, Mason PJ. Integrating care coordination home telehealth and home based primary care in rural Oklahoma: a pilot study. *Psychological services*. 2013;10(3):350-352.
36. Al-Gamal E. Quality of Life, Anxiety and Depression among Patients with Chronic Obstructive Pulmonary Disease and their Spouses. *Issues in Mental Health Nursing*. 2014;35(10):761-767.
37. Al-Gamal E, Yorke J. Perceived breathlessness and psychological distress among patients with chronic obstructive pulmonary disease and their spouses. *Nursing and Health Sciences*. 2014;16(1):103-111.

38. Figueiredo D, Gabriel R, Jacome C, Cruz J, Marques A. Caring for relatives with chronic obstructive pulmonary disease: how does the disease severity impact on family carers? *Aging & Mental Health*. 2014;18(3):385-393.
39. Jácome C, Figueiredo D, Gabriel R, Cruz J, Marques A. Predicting anxiety and depression among family carers of people with Chronic Obstructive Pulmonary Disease. *International Psychogeriatrics*. 2014;26(7):1191-1199.
40. Lee E, Lum CM, Xiang YT, Ungvari GS, Tang WK. Psychosocial condition of family caregivers of patients with chronic obstructive pulmonary disease in Hong Kong. *East Asian Archives of Psychiatry*. 2010;20(4):180-185.
41. Meier C, Bodenmann G, Mörgeli H, Jenewein J. Dyadic coping, quality of life, and psychological distress among chronic obstructive pulmonary disease patients and their partners. *International Journal of COPD*. 2011;6(1):583-596.
42. Nakken N, Spruit MA, van den Bogaart EHA, et al. Health Status and Morbidities in Resident Relatives of Patients With COPD. *Journal of the American Medical Directors Association*. 2016;17(3).
43. Keele-Card G, Foxall MJ, Barron CR. Loneliness, depression, and social support of patients with COPD and their spouses. *Public health nursing (Boston, Mass.)*. 1993;10(4):245-251.
44. Schreiner AS, Morimoto T, Arai Y, Zarit S. Assessing family caregiver's mental health using a statistically derived cut-off score for the Zarit Burden Interview. *Aging and Mental Health*. 2006;10(2):107-111.
45. Unger DG, Jacobs SB. Couples and chronic obstructive airway diseases: the role of gender in coping and depression. *Women's health (Hillsdale, N.J.)*. 1995;1(3):237-255.
46. Washio M, Inoue i, Kiyohara C, et al. Depression among caregivers of patients with Chronic Obstructive Pulmonary Disease. *International Medical Journal*. 2003;10:255-259.
47. Burton AM, Sautter JM, Tulskey JA, et al. Burden and well-being among a diverse sample of cancer, congestive heart failure, and chronic obstructive pulmonary disease caregivers. *Journal of Pain and Symptom Management*. 2012;44(3):410-420.
48. Ross E, Graydon JE. The Impact on the Wife of Caring for a Physically Ill Spouse. *Journal of Women and Aging*. 1997;9(4):23-35.
49. Cossette S, Lévesque L. Caregiving tasks as predictors of mental health of wife caregivers of men with chronic obstructive pulmonary disease. *Research in Nursing & Health*. 1993;16(4):251-263.
50. Kühl K, Schürmann W, Rief W. Mental disorders and quality of life in COPD patients and their spouses. *International Journal of COPD*. 2008;3(4):727-736.

51. Badr H, Federman AD, Wolf M, Revenson TA, Wisnivesky JP. Depression in individuals with chronic obstructive pulmonary disease and their informal caregivers. *Aging and Mental Health*. 2016;1-8.
52. Cain CJ, Wicks MN. Caregiver attributes as correlates of burden in family caregivers coping with chronic obstructive pulmonary disease. *Journal of Family Nursing*. 2000;6(1):46-68.
53. Fried TR, Bradley EH, O'Leary JR, Byers AL. Unmet desire for caregiver-patient communication and increased caregiver burden. *Journal of the American Geriatrics Society*. 2005;53(1):59-65.
54. Goris S, Kilic Z, Elmali F, Tutar N, Takci O. Care Burden and Social Support Levels of Caregivers of Patients with Chronic Obstructive Pulmonary Disease. *Holistic Nursing Practice*. 2016;30(4):227-235.
55. Takata S, Washio M, Moriwaki A, et al. Burden among caregivers of patients with chronic obstructive pulmonary disease with long-term oxygen therapy. *International Medical Journal*. 2008;15(1):53-57.
56. Wicks MN. A test of the Wicks family health model in families coping with chronic obstructive pulmonary disease. *Journal of Family Nursing*. 1997;3(2):189-212.
57. Cedano S, Bettencourt AR, Traldi F, Machado MC, Belasco AG. Quality of life and burden in carers for persons with chronic obstructive pulmonary disease receiving oxygen therapy. *Rev Lat Am Enfermagem*. 2013;21(4):860-867.
58. Pinto RA, Holanda MA, Medeiros MMC, Mota RMS, Pereira EDB. Assessment of the burden of caregiving for patients with chronic obstructive pulmonary disease. *Respiratory medicine*. 2007;101(11):2402-2408.
59. Tsara V, Serasli E, Voutsas V, Lazarides V, Christaki P. Burden and coping strategies in families of patients under noninvasive home mechanical ventilation. *Respiration*. 2006;73(1):61-67.
60. Synnot A, Williams M. Low back pain in individuals with chronic airflow limitation and their partners--a preliminary prevalence study. *Physiotherapy research international : the journal for researchers and clinicians in physical therapy*. 2002;7(4):215-227.
61. Hsiao PC, Chu CM, Sung PY, Perng WC, Wang KY. Differences in COPD patient care by primary family caregivers: An age-based study. *PLoS ONE*. 2014;9(9).
62. Wang KY, Sung PY, Yang ST, Chiang CH, Perng WC. Influence of family caregiver caring behavior on COPD Patients' self-care behavior in Taiwan. *Respiratory Care*. 2012;57(2):263-272.
63. Janssen DJA, Spruit MA, Wouters EFM, Schols J. Family Caregiving in Advanced Chronic Organ Failure. *Journal of the American Medical Directors Association*. 2012;13(4):394-399.

64. Kara M, Mirici A. Loneliness, depression, and social support of Turkish patients with chronic obstructive pulmonary disease and their spouses. *Journal of nursing scholarship : an official publication of Sigma Theta Tau International Honor Society of Nursing / Sigma Theta Tau.* 2004;36(4):331-336.
65. Sexton DL, Munro BH. Impact of a husband's chronic illness (COPD) on the spouse's life. *Research in nursing & health.* 1985;8(1):83-90.
66. Rubio DM, Berg-Weger M, Tebb SS, Lee ES, Rauch S. Objectifying content validity: Conducting a content validity study in social work research. *Social Work Research.* 2003;27(2):94-104.
67. Hasson F, Spence A, Waldron M, et al. Experiences and Needs of Bereaved Carers during Palliative and End-of-Life Care for People with Chronic Obstructive Pulmonary Disease. *Journal of Palliative Care.* 2009;25(3):157-163.
68. Gabriel R, Figueiredo D, Jacome C, Cruz J, Marques A. Day-to-day living with severe chronic obstructive pulmonary disease: towards a family-based approach to the illness impacts. *Psychology & Health.* 2014;29(8):967-983.
69. Lindqvist G, Albin B, Heikkila K, Hjelm K. Conceptions of daily life in women living with a man suffering from chronic obstructive pulmonary disease. *Primary health care research & development.* 2013;14(1):40-51.
70. Simpson AC, Young J, Donahue M, Rocker G. A day at a time: caregiving on the edge in advanced COPD. *International journal of chronic obstructive pulmonary disease.* 2010;5:141-151.
71. Deeken JF, Taylor KL, Mangan P, Yabroff KR, Ingham JM. Care for the caregivers: a review of self-report instruments developed to measure the burden, needs, and quality of life of informal caregivers. *Journal of Pain and Symptom Management.* 2003;26(4):922-953.
72. Van Durme T, Macq J, Jeanmart C, Gobert M. Tools for measuring the impact of informal caregiving of the elderly: A literature review. *International Journal of Nursing Studies.* 2012;49(4):490-504.
73. Harkness KI, Tranmer JE. Measurement of the Caregiving Experience in Caregivers of Persons Living With Heart Failure: A Review of Current Instruments. *Journal of Cardiac Failure.* 2007;13(7):577-587.
74. Tanco K, Park JC, Cerana A, Sisson A, Sobti N, Bruera E. A systematic review of instruments assessing dimensions of distress among caregivers of adult and pediatric cancer patients. *Palliative and Supportive Care.* 2016:1-15.
75. Hudson PL, Trauer T, Graham S, et al. A systematic review of instruments related to family caregivers of palliative care patients. *Palliative Medicine.* 2010;24(7):656-668.

76. Tavakol M, Dennick R. Making sense of Cronbach's alpha. *International Journal of Medical Education*. 2011;2:53-55.
77. Mokkink LB, Prinsen CA, Bouter LM, Vet HC, Terwee CB. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) and how to select an outcome measurement instrument. *Brazilian journal of physical therapy*. 2016;20(2):105-113.
78. Adelman RD, Tmanova LL, Delgado D, Dion S, Lachs MS. Caregiver burden: a clinical review. *Jama*. 2014;311(10):1052-1060.
79. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Archives of general psychiatry*. 1961;4:561-571.
80. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement*. 1977;1(3):385-401.
81. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). *Am J Prev Med*. 1994;10(2):77-84.
82. Lovibond PF, Lovibond SH. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy*. 1995;33(3):335-343.
83. Nordtug B, Holen A. Similarities and differences in caring burden of home dwellers with partners suffering from chronic obstructive pulmonary disease or dementia. *Home Health Care Management and Practice*. 2011;23(2):93-101.
84. Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. *Psychol Med*. 1979;9(1):139-145.
85. Yesavage JA, Sheikh JI. 9/Geriatric Depression Scale (GDS). *Clinical Gerontologist*. 1986;5(1-2):165-173.
86. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta psychiatrica Scandinavica*. 1983;67(6):361-370.
87. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: Validity of a Brief Depression Severity Measure. *Journal of General Internal Medicine*. 2001;16(9):606-613.
88. McNair DM, Lorr M, Droppleman LF. *Profile of Mood States*. San Diego, California: Educational and Industrial Testing Service; 1981.
89. Cella DF, Jacobsen PB, Orav EJ, Holland JC, Silberfarb PM, Rafla S. A brief POMS measure of distress for cancer patients. *J Chronic Dis*. 1987;40(10):939-942.

90. Derogatis LR, Rickels K, Rock AF. The SCL-90 and the MMPI: a step in the validation of a new self-report scale. *The British journal of psychiatry : the journal of mental science*. 1976;128:280-289.
91. Elmståhl S, Malmberg B, Annerstedt L. Caregiver's burden of patients 3 years after stroke assessed by a novel caregiver burden scale. *Archives of Physical Medicine and Rehabilitation*. 1996;77(2):177-182.
92. Robinson BC. Validation of a Caregiver Strain Index. *Journal of Gerontology*. 1983;38(3):344-348.
93. Nolan MR, Grant G, Keady J. *Assessing carer's needs: A practitioner's guide*. Brighton: Pavilion Publications; 1998.
94. Kosberg JI, Cairl RE. The Cost of Care Index: A Case Management Tool for Screening Informal Care Providers. *The Gerontologist*. 1986;26(3):273-278.
95. Fadden G. *The relatives of patients with depressive disorders: a typology of burden and strategies of coping*. London: Institute of Psychiatry, University of London; 1984.
96. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: A Measure of Subjective Stress. *Psychosomatic Medicine*. 1979;41(3):209-218.
97. Montgomery RJV, Gonyea JG, Hooyman NR. Caregiving and the Experience of Subjective and Objective Burden. *Family Relations*. 1985;34(1):19-26.
98. Marmar CR, Weiss DS, Metzler TJ, Delucchi K. Characteristics of emergency services personnel related to peritraumatic dissociation during critical incident exposure. *The American journal of psychiatry*. 1996;153(7 Suppl):94-102.
99. Nordtug B, Krokstad S, Holen A. Personality features, caring burden and mental health of cohabitants of partners with chronic obstructive pulmonary disease or dementia. *Aging and Mental Health*. 2011;15(3):318-326.
100. Greene JG, Smith R, Gardiner M, Timbury GC. Measuring behavioural disturbance of elderly demented patients in the community and its effects on relatives: a factor analytic study. *Age and Ageing*. 1982;11(2):121-126.
101. Chapman J, Reeder L, Massey FJ, et al. Relationships of stress, tranquilizers, and serum cholesterol levels in a sample population under study for coronary heart disease. *American Journal of Epidemiology*. 1966;83(3):537-547.
102. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the Impaired Elderly: Correlates of Feelings of Burden. *The Gerontologist*. 1980;20(6):649-655.
103. Zarit S, Orr N, Zarit J. *The hidden victims of Alzheimer's disease: Families under stress*. New York: New York University Press; 1985.

104. Richardson J, Iezzoni A, Khan MA, Maxwell A. Validity and Reliability of the Assessment of Quality of Life (AQoL)-8D Multi-Attribute Utility Instrument. *The Patient*. 2014;7(1):85-96.
105. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual Framework and Item Selection. *Medical Care*. 1992;30(6):473-483.
106. Ferrans CE, Powers MJ. Quality of life index: development and psychometric properties. *ANS. Advances in nursing science*. 1985;8(1):15-24.
107. Development of the World Health Organization WHOQOL-BREF Quality of Life Assessment. *Psychological Medicine*. 1998;28(3):551-558.
108. Given CW, Given B, Stommel M, Collins C, King S, Franklin S. The caregiver reaction assessment (CRA) for caregivers to persons with chronic physical and mental impairments. *Research in Nursing & Health*. 1992;15(4):271-283.
109. Pollard CA. Preliminary Validity Study of the Pain Disability Index. *Perceptual and Motor Skills*. 1984;59(3):974.
110. Kuhl K, Schurmann W, Rief W. [COPD disability index (CDI) - a new instrument to assess COPD-related disability]. *Pneumologie (Stuttgart, Germany)*. 2009;63(3):136-143.
111. Cooper B, Kinsella GJ, Picton C. Development and initial validation of a family appraisal of caregiving questionnaire for palliative care. *Psychooncology*. 2006;15(7):613-622.
112. Ware JE. Scales for measuring general health perceptions. *Health services research*. 1976;11(4):396-415.
113. Neugarten BL, Havighurst RJ, Tobin SS. The Measurement of Life Satisfaction. *Journal of Gerontology*. 1961;16(2):134-143.
114. Kuorinka I, Jonsson B, Kilbom A, et al. Standardised Nordic questionnaires for the analysis of musculoskeletal symptoms. *Applied Ergonomics*. 1987;18(3):233-237.
115. Derogatis LR. The psychosocial adjustment to illness scale (PAIS). *J Psychosom Res*. 1986;30(1):77-91.
116. Russell D, Peplau LA, Cutrona CE. The revised UCLA Loneliness Scale: concurrent and discriminant validity evidence. *Journal of personality and social psychology*. 1980;39(3):472-480.

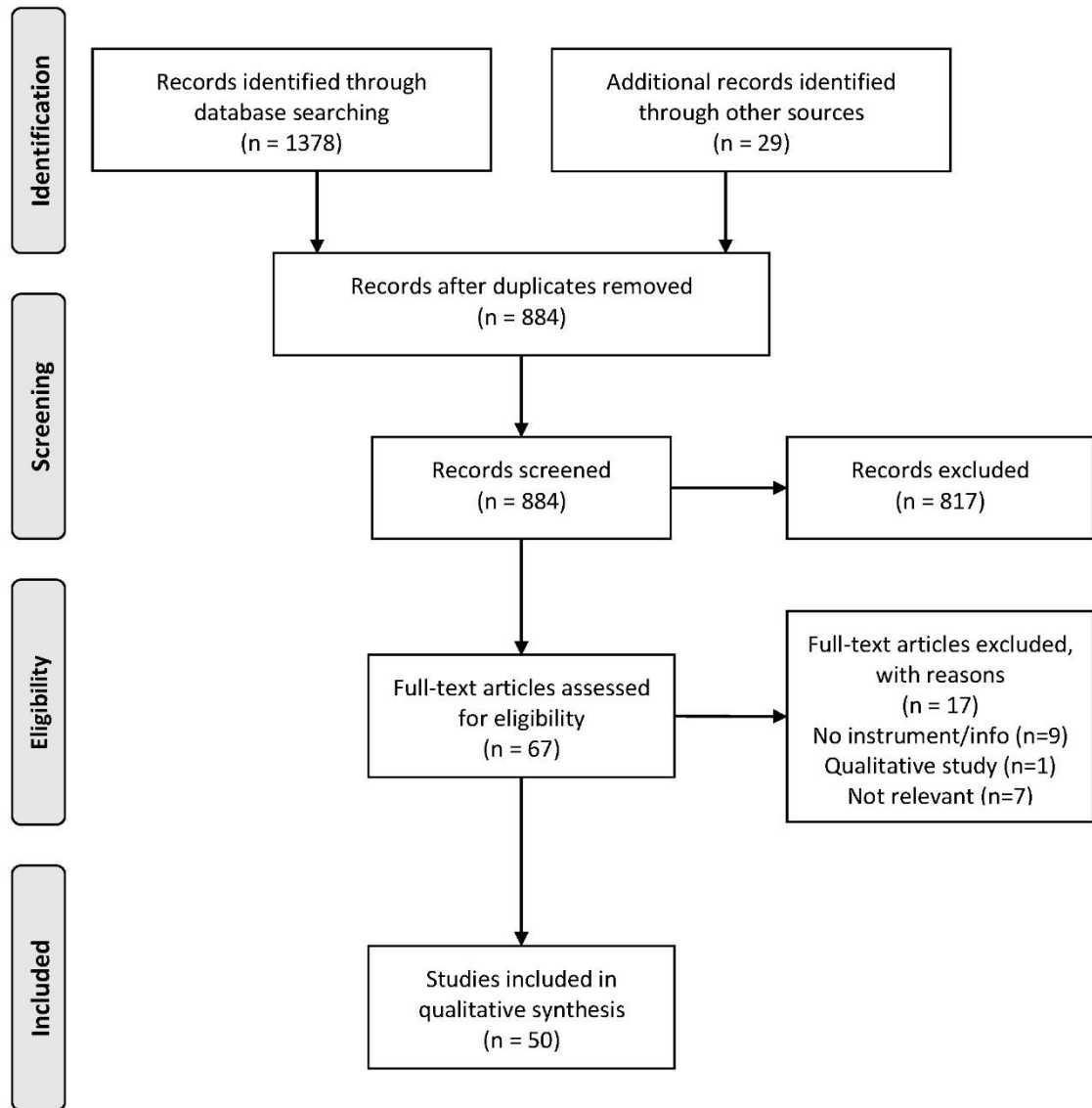


Figure 1. PRISMA flow diagram.

Table 1. Characteristics of the instruments used to assess the impact of COPD on informal caregivers (ordered per life domain/construct).

Instrument name and abbreviation	References		Description			Practical burden		Cost	Measurement properties
	Studies using the instruments	Original ref.	# items, rating system	Possible range scores	Recall period	Time to administer	Ease of scoring*		
<i>Psychological status and mood</i>									
Beck Depression Inventory (BDI)	Kara, 2004 ⁶⁴ Papaioannou, 2014 ²⁴	Beck, 1961 ⁷⁹	21 items 4-point scale	0-63	Last week	5-10 min	Easy	Not free	Internal consistency, hypothesis testing
Center for Epidemiological Studies Depression Scale (CESD)									
- Original version	Keele-Card, 1993 ⁴³ Schreiner, 2006 ⁴⁴ Unger, 1995 ⁴⁵ Washio, 2003 ⁴⁶	Radloff, 1977 ⁸⁰	20 items 4-point scale	0-60	Last week	5-10 min	Easy	Free	Internal consistency
- Short-form	Burton, 2012 ⁴⁷	Andresen, 1994 ⁸¹	10 items 4-point scale	0-30	Last week	5-10 min	Easy	Free	No
Depression Anxiety and Stress Scales (DASS-21)	Figueiredo, 2016 ²⁸	Lovibond, 1995 ⁸²	21 items 4-point scale	Subscales: Depression (0-42) Anxiety (0-42) Stress (0-42)	Last week	5 min or less	Moderate	Free	No
General Health Questionnaire (GHQ-28)	Nordtug, 2011 ⁸³	Goldberg, 1979 ⁸⁴	28 items 4-point scale	0-84 Subscales: Somatic symptoms (0-21) Anxiety and insomnia (0-21) Social dysfunction (0-21) Severe depression (0-21)	-----	5 min or less	Moderate	Not free	No

Geriatric Depression Scale (GDS) short-form	Lee, 2010 ⁴⁰ Schreiner, 2006 ⁴⁴	Yesavage, 1986 ⁸⁵	15 items yes/no	0-15	Last week	5-10 min	Easy	Free	Hypothesis testing
Hospital Anxiety and Depression Scale (HADS)	Al-Gamal, 2014 ³⁶ Al-Gamal, 2014 ³⁷ Azoulay, 2013 ²⁰ De Miranda, 2011 ²¹ Farquhar, 2016 ²⁷ Figueiredo, 2014 ³⁸ Jácome, 2014 ³⁹ Lee, 2010 ⁴⁰ Meier, 2011 ⁴¹ Nakken, 2016 ⁴²	Zigmond, 1983 ⁸⁶	14 items 4-point scale	Subscales: Anxiety (0-21) Depression (0-21)	Last week	5 min or less	Moderate	Free	Internal consistency, hypothesis testing
Patient Health Questionnaire (PHQ-9)	Badr, 2016 ⁵¹	Kroenke, 2001 ⁸⁷	9 items 4-point scale	0-27	Last 2 weeks	5 min or less	Easy	Free	Internal consistency, hypothesis testing
Profile of Mood States (POMS)									
- Original version	Ross, 1997 ⁴⁸	McNair, 1981 ⁸⁸	65 items 5-point scale	0-200 Subscales: Anger (0-48) Confusion (0-28) Depression (0-60) Fatigue (0-28) Tension (0-36) Vigour (0-32)	Last week	5-20 min	Moderate	Free	Hypothesis testing
- Brief POMS	Burton, 2012 ⁴⁷ (anxiety subscale used)	Cella, 1987 ⁸⁹	11 items 5-point scale	0-44	Last week	NA	Easy	Free	No
Symptom Checklist-90 (SCL-90)	Original Cossette, 1993 ⁴⁹ Revised (SCL-90-R) Kühl, 2008 ⁵⁰	Derogatis, 1976 ⁹⁰	90 items 5-point scale	Subscales: Depression (0-4) Obsession-compulsion (0-4) Somatization (0-4)	Last week	12-15 min	Complex	Not free	Internal consistency, hypothesis testing

Vaske, 2015 ²⁶

Anxiety (0-4)
 Hostility (0-4)
 Interpersonal sensitivity (0-4)
 Phobic anxiety
 Paranoid ideation
 Psychoticism
 (not all subscales were used
 in studies)
 Global Severity Index
 Positive Symptom Distress
 Index
 Positive Symptom Total

<i>Burden/distress</i>									
Caregiver Burden Scale (CBS)	Appleton, 2003 ¹⁹ Cedano, 2013 ⁵⁷ Lee, 2010 ⁴⁰ Pinto, 2007 ⁵⁸	Elmståhl, 1996 ⁹¹	22 items 4-point scale	22-88 Subscales: General strain (8-32) Isolation (3-12) Disappointment (5-20) Emotional involvement (3-12) Environment (3-12)	-----	NA	Easy	Free	Hypothesis testing
Caregiver Strain Index (CSI)	Utens, 2014 ³⁴	Robinson, 1983 ⁹²	13 items yes/no	0-13	-----	5 min or less	Easy	Free	No
Carers' Assessment of Difficulties Index (CADI)	Figueiredo, 2014 ³⁸ Figueiredo, 2016 ²⁸ Jácome, 2014 ³⁹	Nolan, 1998 ⁹³	30 items 4-point scale	0-90 Subscales: Carer-dependent relationships (0-21) Reactions to caregiving (0-21) Physical demands of caring (0-18) Restricted social life (0-12) Poor family support (0-6) Poor professional support (0-6) Financial consequences (0-6)	-----	Approximately 25 min	Easy	Free	Internal consistency, Hypothesis testing and test-retest reliability

Cost of Care Index (CCI)	Kwok, 2004 ³¹	Kosberg, 1986 ⁹⁴	20 items 4-point scale	20-100 Personal and social restrictions (4-16) Physical and emotional health (4-16) Value (4-16) Care recipient as provocateur (4-16) Economic (4-16)	-----	20-30 min	Easy	Free	No
Family Burden Questionnaire	Tsara, 2006 ⁵⁹ (modified version)	Fadden, 1984 ⁹⁵	95 items	Objective and subjective burden on: - employment issues - household management - financial issues - social relations	NA	90 min	NA	NA	No
Impact of Event Scale (IES)	Azoulay, 2013 ²⁰ De Miranda, 2011 ²¹	Horowitz, 1979 ⁹⁶	15 items 4-point scale	0-75 Subscales: Intrusion (0-35) Avoidance (0-40)	Last week	NA	Easy	Free	No
Montgomery's Burden scale	Hughes, 2000 ²⁹	Montgomery, 1985 ⁹⁷	22 items 5-point scale	Subscales: Objective burden (9-45) Subjective burden (13-65)	-----	15-20 min	Easy	Free	No
Numeric rating scale (NRS) for caregiver distress due to patient's breathlessness	Farquhar, 2016 ²⁷	-----	-----	0-10	-----	5 min or less	Easy	Free	No
Peritraumatic Dissociative Experiences Questionnaire (PDEQ)	De Miranda, 2011 ²¹	Marmar, 1996 ⁹⁸	10 items 5-point scale	10-50	During/after traumatic stress exposure	Approximately 5 min	Easy	Free	No
Relative Stress Scale (RSS)	Nordtug, 2011 ⁹⁹ Nordtug, 2011 ⁸³	Greene, 1982 ¹⁰⁰	15 items 5-point scale	0-60 Subscales:	-----	NA	Easy	Free	Hypothesis testing

	Ross, 1997 ⁴⁸			Personal distress scale (0-24) Life upset scale (0-20) Negative feelings scale (0-16)						
Subjective Stress Scale	Cossette, 1993 ⁴⁹ Sexton, 1985 ⁶⁵	Chapman, 1966 ¹⁰¹	4 items 4-point scale	4-16	-----	NA	Easy	Free	Internal consistency, hypothesis testing	
Zarit Burden Interview	Badr, 2016 ⁵¹ Cain, 2000 ⁵² Fried, 2005 ⁵³ Garlo, 2010 ²² Godoy-Ramírez, 2014 ¹⁸ Goris, 2016 ⁵⁴ Schreiner, 2006 ⁴⁴ Sorocco, 2013 ³⁵ Takata, 2008 ⁵⁵ Washio, 2003 ⁴⁶ Wicks, 1997 ⁵⁶	Zarit, 1980 ¹⁰² Zarit, 1985 ¹⁰³	22 items 5-point scale	0-88	-----	NA	Easy	Free/ Not free	Internal consistency	
<i>Health-related quality of life</i>										
Assessment of Quality of Life with 8 dimensions (AQoL-8D)	Nakken, 2016 ⁴²	Richardson, 2014 ¹⁰⁴	35 items 5-point scale	35-175 Dimensions (psychometric score): Independent living (4-20) Relationships (7-35) Mental health (8-40) Coping (3-15) Pain (3-15) Senses (3-15) Self-worth (3-15) Happiness (4-20)	-----	About 5 min	Easy	Free	No	
European Quality of Life										

Questionnaire (EuroQol) - EuroQol-5 Dimensions (EQ-5L-5D)	Nakken, 2016 ⁴²	EuroQol Group EQ- 5D™	5 items 5-point scale	EQ-5D-5L profile EQ-5D-5L index (based on normative data) Domains: Mobility (1-5) Self-care (1-5) Usual activities (1-5) Pain/Discomfort (1-5) Anxiety/Depression (1-5)	Present	NA	Complex	Free/ Not free	No
- VAS 0-100%	Kühl, 2008 ⁵⁰ Vaske, 2015 ²⁶	EuroQol Group EQ- 5D™	-----	0-100%	Present	NA	Easy		Hypothesis testing, test- retest reliability
Medical Outcomes Study Questionnaire 36- Item Short Form (SF-36)	Cedano, 2013 ⁵⁷ Hughes, 2000 ²⁹ Kenealy, 2015 ³⁰ Lee, 2010 ⁴⁰ Pinto, 2007 ⁵⁸ Synnot, 2002 ⁶⁰	Ware, 1992 ¹⁰⁵	36 items Scores differ among items	Subscales: Physical functioning (0-100) Role limitations due to physical problems (0-100) General health perceptions (0-100) Vitality (0-100) Social functioning (0-100) Role limitations due to emotional problems (0-100) General mental health (0- 100) Health transition (0-100) Physical and mental component summary scores	Past 4 weeks	5–10 min	Complex	Free or not free	Hypothesis testing
Quality of Life Index – Generic version (QLI-G)	Al-Gamal, 2014 ³⁶	Ferrans, 1985 ¹⁰⁶	66 items 6-point scale	0-30 Subscales: Health and functioning (0-30) Social and economic (0-30)	-----	Approximately 10 min	Complex	Free	Internal consistency, hypothesis testing

World Health Organization Quality of Life Questionnaire-Bref (WHOQOL-bref)	Meier, 2011 ⁴¹	World Health Organization ¹⁰⁷	26 items 5-point scale	Psychological/spiritual (0-30) Family (0-30) 0-100 Domains: Physical health (0-100) Psychological health (0-100) Social relationships (0-100) Environment (0-100)	Last 2 weeks	10-20 min	Complex	Free	Internal consistency
<i>Other domains</i>									
Caregiver Reaction Assessment (CRA)	Burton, 2012 ⁴⁷ Hsiao, 2014 ⁶¹ Sautter, 2014 ²⁵ Wang, 2012 ⁶²	Given, 1992 ¹⁰⁸	24 items 5-point scale	Negative subscales: Impact on Schedule (1-5) Lack of family support (1-5) Impact on finances (1-5) Impact on health (1-5) Positive subscale: Caregiver's esteem (1-5)	-----	5-10 min	Moderate	NA	Content validity, internal consistency
COPD Disability Index (CDI)	Kühl, 2008 ⁵⁰	Pollard, 1984 ¹⁰⁹ Kuhl, 2009 ¹¹⁰	7 items 11-point scale	0-70	-----	Approximately 5 min	Easy	Free	Internal consistency
Family Appraisal of Caregiving Questionnaire for Palliative Care (FACQ-PC)	Janssen, 2012 ⁶³ Nakken, 2015 ²³	Cooper, 2006 ¹¹¹	25 items 5-point scale	Subscales: Caregiver strain (1-5) Positive caregiving appraisals (1-5) Caregiver distress (1-5) Family wellbeing (1-5)	-----	NA	Moderate	Free	No
Functional Assessment of Chronic Illness Therapy 12-item Spiritual Well-Being Scale (FACIT-Sp-12)	Burton, 2012 ⁴⁷	FACIT.org Copyright 1987, 1997	12 items 5-point scale	0-48 Subscales: Meaning (0-16) Peace (0-16) Faith (0-16)	Past week	NA	Complex	Free/ Not free	No
Health Perceptions	Ross, 1997 ⁴⁸	Ware, 1976 ¹¹²	9 items 5-point scale	9-45	-----	NA	Moderate	Free	Hypothesis testing

Questionnaire Form II Life Satisfaction Index-A (LSI-A)	(Current Health subscale) Sexton, 1985 ⁶⁵	Neugarten, 1961 ¹¹³	20 items Agree/disagree	0-20	-----	Approximately 10 min	Easy	Free	No
Nordic low back pain questionnaire (NLBPQ)	Synnot, 2002 ⁶⁰	Kuorinka, 1987 ¹¹⁴	7 questions Yes/No 2 questions with a 4-point or 5-point scale 1 body diagram	NA	Lifetime, last 12 months and last 7 days	Approximately 5 min	Easy	Free	No
Psychosocial Adjustment to Illness Scale – Self-Report (PAIS-SR – caregiver version)	Marques, 2015 ³² Marques, 2015 ³³	Derogatis, 1986 ¹¹⁵	46 items 4-point scale	0-138 Domains: Health-care orientation (0-24) Vocational environment (0-18) Domestic environment (0-24) Sexual relationships (0-18) Extended family relationships (0-15) Social environment (0-18) Psychologic distress (0-21)	Past 30 days including the present	20-25 min	Easy	Not free	Internal consistency
Revised UCLA Loneliness scale	Kara, 2004 ⁶⁴ Keele-Card, 1993 ⁴³	Russell, 1980 ¹¹⁶	20 items 4-point scale	20-80	-----	NA	Moderate	Free	Internal consistency, hypothesis testing

NA – Not available. *Easy of scoring was rated according to the following criteria: easy, when the items were simply summed; moderate, when a simple formula was used (e.g., the instrument has questions with reverse scores and the items are then summed; mean of the item scores); and difficult, when a complex formula was used.

Table 2. Summary of the sample characteristics in which the instruments were applied, the methodological quality of studies and the quality of the measurement properties of instruments.

Instrument	Study	Country	Caregivers' characteristics (n, mean age, gender, relationship)	Patients' specificities	Content validity	Construct validity		
						Hypothesis testing	Internal consistency	Test-retest reliability
<i>Psychological status and mood</i>								
Beck Depression Inventory (BDI)	Kara, 2004 ⁶⁴	Turkey	n=30 56.6 years All spouses	Outpatients of a hospital Duration of illness: 7.57 years (mean)		Fair/?		Poor/?
Center for Epidemiological Studies Depression Scale-10 item (CESD)	Keele-Card, 1993 ⁴³	USA	n=30 66.8 years Mostly women All spouses	Outpatients of a pulmonary clinic with FEV1<1.5 L				Fair/?
Geriatric Depression Scale (GDS)	Lee, 2010 ⁴⁰	China	n=81 63±12 years 89% female 86% spouses 8±9 years caring	Outpatients of a pulmonary clinic Duration of illness: 11±10 years		Poor/?		
Hospital Anxiety and Depression Scale (HADS)	Al-Gamal, 2014 ³⁶	Jordan	n=67 51.3±13.9 years 70% female All spouses	Inpatients or outpatients of a hospital		Fair/?		Poor/?
	Figueiredo, 2014 ³⁸	Portugal	n=167, 2 groups: caregivers of patients with early and advanced COPD 70-85% female 61-63% spouses 56-72% caring for >4 years	Patients with early (GOLD 1-2, n=113) or advanced (GOLD 3-4, n=54) COPD living in the community		Fair/?		
	Jácome, 2014 ³⁹	Portugal	n=203 58.2±14.8 years	Outpatients of primary care centers or hospital,				Fair/?

	Lee, 2010 ⁴⁰	China	75% female 60.6% spouses 80.3% caring for >2years n=81 63±12 years 89% female 86% spouses 8±9 years caring	at early (GOLD 1-2, n=137) or advanced (GOLD 3-4, n=66) COPD Outpatients of a pulmonary clinic Duration of illness: 11±10 years	Poor/?	
	Meier, 2011 ⁴¹	Switzerland	n=43 66.58±11.08 years 67.4% female All spouses	Patients receiving care from the Zurich Lung League FEV ₁ 39.42±11.58% predicted GOLD grades: 2 (n=6), 3 (n=21) and 4 (n=4) 74% receiving supplemental oxygen	Poor/?	
Patient Health Questionnaire (PHQ-9)	Badr, 2016 ⁵¹	USA	n=89 54.8±16.0 years 76.4% female 39.3% spouses, 28.1% son/daughter 5.10±1.6 years caring	Patients living in the community COPD Severity Index: 7±3.92 (mild COPD)	Fair/?	Poor/?
Profile of Mood States (POMS)	Ross, 1997 ⁴⁸	Canada	n=25 65±10.51 years All wives	Male patients with severe to very severe COPD (FEV ₁ <50% predicted) Duration of illness: 12±9 years 50% receiving supplemental oxygen	Poor/?	
Symptom Checklist-90 (SCL-90)	Cossette, 1993 ⁴⁹ (3 domains omitted)	Canada	n=89 65±7.81 years All wives	Male patients with moderate to very severe COPD	Poor/?	Fair/?

	Vaske, 2015 ²⁶	Germany	n=63 62.08±8.05 years 82.5 % female All spouses	FEV ₁ =36.18% (13–60%) predicted Duration of illness: 13±15 years Stable patients GOLD grades: 2 (n=34), 3 (n=23) and 4 (n=6)	Fair/?	Fair/?	
Burden/distress							
Caregiver Burden Scale (CBS)	Cedano, 2013 ⁵⁷	Brazil	n=80 48.7±15.6 years 81% female 41% daughters and 28% wives 60% cared for > 5years All living with patient	Patients using Long-Term Oxygen Therapy for ≥ 3 months GOLD grades: 1 (n=2), 2 (n=3), 3 (n=39) and 4 (n=36)	Fair/?		
	Lee, 2010 ⁴⁰	China	n=81 63±12 years 89% female 86% spouses Caregiving duration 8±9 years	Outpatients of a pulmonary clinic Duration of illness: 11±10 years	Poor/?		
Carers' Assessment of Difficulties Index (CADI)	Figueiredo, 2014 ³⁸	Portugal	n=167, divided in two groups: caregivers of patients with early (n=113) and advanced (n=54) COPD 70-85% female 61-63% spouses 56-72% caring for >4 years	Patients with early (GOLD 1-2, n=113) or advanced (GOLD 3-4, n=54) COPD living in the community	Fair/?	Poor/?	Poor/?
	Jácome, 2014 ³⁹	Portugal	n=203 58.2±14.8 years 75% female 60.6% spouses	Outpatients of primary care centers or hospital with early (GOLD 1-2,		Poor/?	

Relative Stress Scale (RSS)	Ross, 1997 ⁴⁸	Canada	80.3% caring for >2years n=25 65±10.51 years All wives	n=137) or advanced (GOLD 3-4, n=66) COPD Male patients with severe to very severe COPD (FEV ₁ <50% predicted) Duration of illness: 12±9 years 50% receiving supplemental oxygen	Poor/?	
Subjective Stress Scale	Cossette, 1993 ⁴⁹	Canada	n=89 65±7.81 years All wives	Male patients with moderate to very severe COPD FEV ₁ =36.18% (13–60%) predicted Duration of illness: 13±15 years	Poor/?	Poor/?
Zarit Burden Interview	Cain, 2000 ⁵²	USA	n=138 58.6±13.6 years 86% female 15% Black 70% spouses	Outpatients of pulmonary clinics		Poor/?
	Goris, 2016 ⁵⁴	Turkey	n=112 75% female 26.8% ≥60 years	Hospitalized patients with COPD Duration of illness: ≤1 year, 14.2%; 2-5 years, 25%; 6-9 years, 17%; 10-13 years, 17%; ≥14 years, 26.8% 53.6% receiving supplemental oxygen		Fair/?
	Wicks, 1997 ⁵⁶	USA	n=140 85% female 58.6 years	Outpatients of a hospital pulmonary		Poor/?

16% Black
 clinic and private
 practice
 Duration of illness: 11±9
 years

Health-related quality of life

European Quality of Life Questionnaire (EuroQol) visual analogue scale (0-100%)	Vaske, 2015 ²⁶	Germany	n=63 62.08±8.05 years 83% female All spouses	Stable patients GOLD grades: 2 (n=34), 3 (n=23) or 4 (n=6)	Fair/?	-----	Poor/?
Medical Outcomes Study Questionnaire 36-Item Short Form (SF-36)	Cedano, 2013 ⁵⁷	Brazil	n=80 48.7±15.6 years 81% female 41% daughters and 28% wives 60% cared for > 5years All living with patient	Patients using Long-Term Oxygen Therapy for ≥ 3 months GOLD grades: 1 (n=2), 2 (n=3), 3 (n=39) and 4 (n=36)	Fair/?		
	Lee, 2010 ⁴⁰	China	n=81 63±12 years 89% female 86% spouses Caregiving duration 8±9 years	Outpatients of a pulmonary clinic Duration of illness: 11±10 years	Poor/?		
Quality of Life Index – Generic version (QLI-G)	Al-Gamal, 2014 ³⁶	Jordan	n=67 51.3±13.9 years 70% female All spouses	Inpatients or outpatients of a hospital	Fair/?		Poor/?
World Health Organization Quality of Life Questionnaire-BREF (WHOQOL-bref)	Meier, 2011 ⁴¹	Switzerland	n=43 66.58±11.08 years 67.4% female All spouses	Patients receiving care from the Zurich Lung League FEV ₁ =39.42±11.58% predicted GOLD grades: 2 (n=6), 3 (n=21) and 4 (n=4)			Poor/?

74% receiving supplemental oxygen

Other domains						
Caregiver Reaction Assessment (CRA)	Hsiao, 2014 ⁶¹	China	n=406, divided in 2 groups: 79 elder caregivers (≥65 years) and 327 non-elder caregivers 60-79% female	Outpatients of medical centers and regional hospitals	Poor/-	Poor/?
COPD Disability Index (CDI)	Kühl, 2008 ⁵⁰	Germany	n=105 64.0±9.3 years 82% female All spouses	Patients with COPD GOLD grades: 2 (n=68), 3 (n=62) and 4 (n=13) Duration of illness: <1 year, 4.6%; 1–3 years, 12.8%; 3–10 years, 12.8%; >10 years, 50.5%		Fair/?
Health Perceptions Questionnaire - Form 11 (Current Health subscale)	Ross, 1997 ⁴⁸	Canada	n=25 65±10.51 years All wives	Male patients with severe to very severe COPD (FEV1<50% predicted) Duration of illness: 12±9 years 50% receiving supplemental oxygen		Poor/?
Psychosocial Adjustment to Illness Scale – Self-Report (PAIS-SR)	Marques, 2015 ³³	Portugal	n=42 mean 55.1-62.0 years 71.5% female 69.0% spouses, 26.2% sons/daughters	Patients with COPD from primary care centers GOLD grades: 1 (n=16), 2 (n=16) and 3-4 (n=10)		Poor/?
UCLA Loneliness scale	Kara, 2004 ⁶⁴	Turkey	n=30 56.6 years All spouses	Outpatients of a hospital Duration of illness: 7.57 years (mean)	Fair/?	Poor/?

Keele-Card, 1993 43	USA	n=30 66.8 years Mostly female All spouses	Outpatients of a pulmonary clinic with FEV ₁ <1.5 L	Poor/?
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Note: The possible scores for the assessment of the methodological quality of studies were the following: 'excellent', 'good', 'fair' or 'poor'¹⁷. The quality of the measurement properties of instruments was rated according to Terwee et al.¹² considering the possible scores: '+' (positive), '?' (indeterminate) or '-' (negative). COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; FEV₁, forced expiratory volume in 1 second.