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Patient-Reported Outcome Instruments for Physical Symptoms Among Patients Receiving Maintenance Dialysis: A Systematic Review

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Abstract

Background—Patients with end-stage renal disease (ESRD) receiving dialysis have poor health-related quality of life (HRQoL). Physical symptoms are highly prevalent among dialysis-dependent patients and play important roles in HRQoL. A range of symptom assessment tools have been used in dialysis-dependent patients, but there has been no previous systematic assessment of the existing symptom measures' content, validity, and reliability.

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Supplementary Material

Table S1: Search strategies.
Table S2: Instrument validity and reliability testing.
Table S3: Instrument intended population, recall periods, and symptom attributes assessed.
Table S4: Summary of validity and reliability testing in instruments assessing physical symptoms.
Note: The supplementary material accompanying this article (doi:_____) is available at www.ajkd.org

Study Design—systematic review of the literature

Settings & Population—ESRD patients on maintenance dialysis

Selection Criteria for Studies—instruments with ≥3 physical symptoms previously used in dialysis-dependent patients and evidence of validity or reliability testing

Intervention—patient-reported physical symptom assessment instrument

Outcomes—instrument symptom-related content, validity, and reliability

Results—From 3,148 screened abstracts, 89 full-text articles were eligible for review. After article exclusion and further article identification via reference reviews, 58 articles on 23 symptom assessment instruments with documented reliability or validity testing were identified. Of the assessment instruments, 43.5% were generic and 56.5% were ESRD-specific. Symptoms most frequently assessed were fatigue, shortness of breath, insomnia, nausea and vomiting, and appetite. The instruments varied widely in respondent time burden, recall period, and symptom attributes. Few instruments considered recall periods less than 2 weeks and few assessed a range of symptom attributes. Psychometric testing was completed for congruent validity (70%), known group validity (25%), responsiveness (30%), internal consistency (78%), and test-retest reliability (65%). Content validity was assessed in dialysis populations in 57% of the 23 instruments.

Limitations—Consideration of physical symptoms only and exclusion of single symptom-focused instruments

Conclusions—The number of available instruments focused exclusively on physical symptoms in dialysis patients is limited. Few symptom-containing instruments have short recall periods, assess diverse symptom attributes, and have undergone comprehensive psychometric testing. Improved symptom-focused assessment tools are needed to improve symptom evaluation and symptom responsiveness to intervention among dialysis-dependent patients.

INDEX WORDS

maintenance dialysis; end-stage renal disease (ESRD); health-related quality of life (HRQoL); physical symptoms; patient-reported symptom tool; patient-reported outcome instrument; patient-centered care; comorbidity burden; fatigue; shortness of breath; insomnia; poor appetite; nausea; systematic review

Patients with end-stage renal disease (ESRD) on dialysis have poor health-related quality of life (HRQOL) compared to members of the general population.[1–4] A high burden of co-morbid illness, impaired physical function, and other factors contribute to this suboptimal HRQOL, and existing data suggest that physical symptoms also play important roles.[5, 6]

Dialysis-dependent patients have numerous physical symptoms with more than half of patients reporting fatigue, pain, cramps, sleep disturbance, and sexual dysfunction.[7–9] Despite the relevance of symptoms to HRQOL, healthcare providers are not adept at recognizing them. One study found that providers frequently do not identify key symptoms, and when symptoms are recognized, providers underestimate their severity.[8] Additionally, evidence-based dialysis treatment interventions and symptom-targeted pharmaceutical therapies are lacking. Erythropoiesis-stimulating agent use is associated with improved

HRQOL and reduced fatigue,[10, 11] but few other dialysis prescription changes have been shown to modulate HRQOL or symptoms. To inform the development of new symptom interventions, an accurate understanding of symptom prevalence, patient prioritization of symptoms, and the pathophysiology underlying common symptoms is needed.

To assess symptoms, clinicians and investigators rely on a range of patient-reported symptom tools including instruments that measure HRQOL,[12–18] dialysis-specific symptom indices,[5, 19] and symptom questionnaires originally developed for non-dialysis patients.[20–23] As a result, the type and quality of data collected is widely varied, thus limiting precise conclusions about patient prioritization of symptoms and symptom responsiveness to mitigation strategies. Understanding symptoms related to dialysis procedures may inform symptom pathophysiology comprehension and may help identify therapeutic treatment modifications.

We undertook this systematic review to identify measures used to assess patient-reported physical symptoms in the dialysis-dependent population and to describe instrument development, symptom-related content, and psychometric properties of the identified measures. We limited our review to physical symptoms to capture symptoms most likely to fluctuate on a treatment-to-treatment basis. To establish a baseline quality threshold for considered instruments, we limited the review to measures with published validity and/ or reliability assessments.

Methods

Study Overview

We conducted a systematic literature review according to guidelines provided by the US Department of Health and Human Services Agency for Healthcare Research and Quality,[24, 25] and we used the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines to guide data collection and reporting of evidence.[26]

Selection Criteria for Articles and Instruments

Eligibility criteria were developed using modified PICOT (population of interest, intervention of interest, comparison, outcomes, time frame) criteria (Figure 1).[27] Full inclusion and exclusion criteria are reported in Table 1. We began by identifying relevant articles for review, but the unit of analysis was the patient-reported outcome instrument ascertained from the identified articles.

Article and Instrument Identification

Articles for review were identified from MEDLINE (via PubMed) and Embase (via Elsevier), which were searched from 1946 (MEDLINE) and 1966 (Embase) to December 31, 2014 with the assistance of an experienced reference librarian (L.H.). Key words and controlled vocabulary were used for each database, and searches were constructed using a combination of medical subheadings, keywords, and text words. As physical symptom assessments are often embedded in HRQOL assessments, we conducted searches for HRQOL or symptoms. Complete search strings are available in Table S1 (provided as online

supplementary material). Reference lists of selected studies were further searched for additional instruments and articles. Individual instruments were identified within each of the articles. Focused searches to identify psychometric analyses of the identified instruments were then performed.

Data Abstraction and Psychometric Assessment

A pre-determined methodology was followed to determine articles for inclusion. Two non-clinicians with training in literature reviews and patient-centered outcomes (J.D.P., C.J.P.) independently reviewed all article titles and abstracts in accordance with the selection criteria. If either reviewer deemed an article potentially eligible based on the title or abstract, a full-text review was completed. Articles marked for possible inclusion by either reviewer underwent independent, full-text review by two investigators (J.D.P., J.E.F.) to determine final inclusion or exclusion. In the full text review, investigators used a standardized spreadsheet to extract each article and determine eligibility. Reviewer disagreement was resolved by consensus.

Trained reviewers (J.D.P., K.D.W.) extracted relevant data from each included article into a standardized abstraction form. The structured abstraction tool included the following: instrument descriptive data (symptoms assessed, symptom attributes, recall period, response format, burden), instrument development data (year and country of development, intended use, target population, population involved in questionnaire development, and development process), and instrument psychometric assessment (content validity, construct validity, responsiveness to change, internal consistency reliability, and test-retest reliability). A third team member (J.E.F.) compared all extractions with original articles for completeness and accuracy.

Assessment of Instrument Reliability and Validity

An overview of the considered instrument psychometric properties, definitions, and common assessment methods is provided in Table 2. For this review, content validity was deemed present if the target population (dialysis patients) was involved in instrument item development, and a clear description of concepts being measured was provided.[28] Construct validity was considered as congruent validity or known-group validity as these were the two most commonly reported forms of construct validity in the evaluated instruments. Responsiveness to change was deemed present if score change statistics were assessed in an ESRD population.[29] With the exception of content validity and responsiveness, testing in an ESRD population was not required.[30] We elected to report on the presence or absence of selected psychometric testing rather than rendering a quality assessment of the reported psychometric measures. Lack of consensus regarding quality thresholds for many of the psychometric measures exists, and there are few accepted standards for rating subjective aspects of psychometric evaluations such as content and construct validity.[31, 32] To facilitate the interested reader's assessment of psychometric testing quality, we provided a summary of available psychometric results for each instrument in Table S2.

Data Analysis

Physical symptoms assessed by the included instruments were tabulated, descriptive statistics were reported, and instrument symptom assessment criteria were tabulated. To examine the frequency of validity and reliability testing, descriptive statistics for the percentage of instruments that underwent such assessment were compiled. We considered instruments overall and categorized as ESRD-specific and non-ESRD-specific. We considered psychometric assessments specific to the symptom domain and specific to non-symptom domains or to the overall instrument.

Results

Literature Search

Figure 2 is a flow diagram of article and instrument selection. The initial search identified 1,968 articles/abstracts from MEDLINE and 2,345 articles/abstracts from Embase. After duplicates were removed, 3,059 articles/abstracts were excluded based on selection criteria, leaving 89 for full-text review. Sixty-eight full text articles were excluded and 37 additional articles were identified from reference review and instrument-specific literature searches. A total of 58 full text articles and 23 instruments were included in the final analysis (Table S2).

While 23 instruments met selection criteria, there were several notable exclusions. We excluded the Merkus questionnaire, a symptom-based HRQOL instrument developed specifically for dialysis-dependent patients, because instrument validation was reported only in a Dutch language publication.[6, 33] Furthermore, symptom-specific instruments such as those focused exclusively on sleep, pain, and fatigue were excluded. Patients often experience multiple symptoms simultaneously, and symptoms can have important interactions, such as pruritus and insomnia.[34] Single symptom-focused instruments preclude the study of such interactions. To ensure inclusion of a range of symptoms and to limit the scope of this review, we excluded measures focused on <3 symptoms. This choice led to the exclusion of such commonly used instruments as the Pittsburgh Sleep Quality Index, McGill Pain Inventory, Fatigue Severity Scale, International Index of Erectile Function Index, Restless Leg Syndrome Questionnaire, and Dialysis Thirst Index.[35–43]

Instrument Symptom Assessment

Table 3 provides an overview of the included instruments. We identified 13 instruments assessing ≥3 physical symptoms developed specifically for use among dialysis-dependent patients and 10 instruments used in dialysis-dependent patients but developed in non-dialysis populations. Four of the 13 dialysis-specific instruments focused exclusively on symptoms, and the others included symptom assessment as a relevant HRQOL domain. Four of the 10 non-dialysis-specific instruments focused exclusively on symptoms, and 6 instruments included symptoms as one of multiple instrument domains.

Table 4 displays the physical symptoms included in the identified instruments. The symptoms most commonly assessed were: fatigue or low energy (17 instruments (81%)); cough or shortness of breath (15 (71%)); insomnia or trouble falling asleep, (14 (67%)), poor appetite (14 (67%)), and nausea or vomiting, (14 (67%)). The symptoms of feeling

sick, restless, experiencing muscle loss, easy bruising, and perceived hypotension appeared in only one instrument each (5%). Seven (33%) instruments had blank fields to allow for patient reporting of additional symptoms not listed elsewhere. Three instruments contained blank fields for patient-identified symptoms only and had no standardized symptom questions.

Table 5 summarizes symptom categories, instrument burdens (time for completion), and symptom attributes assessed across instruments. More detailed instrument symptom question descriptions are available in Table S3. The least time-intensive instruments were the Symptom Distress Scale and Physical Symptom Distress Scale, each requiring 5 minutes for completion.[14, 44] The most burdensome instruments were HRQOL-focused measures such as the CHOICE (Choices for Healthy Outcomes in Caring for ESRD) Health Experience Questionnaire (CHEQ), Kidney Disease Questionnaire (KDQ), and Kidney Disease Quality of Life (KDQoL), all requiring nearly 30 minutes for completion.[13, 45–47] Symptom recall periods ranged from 1 year (the Bowel disease questionnaire) to “present” (modified Edmonton Symptom Assessment System [ESAS]). Five instruments considered symptoms with respect to the dialysis procedure (e.g. inter-, intra-, or post-dialysis). The majority of dialysis patient-specific instruments considered symptoms over 2–4 weeks. The modified ESAS instrument was the only dialysis patient-specific instrument that assessed symptoms at “present.”

Overall, the instruments selectively addressed symptom attributes (severity, bother, frequency, timing, HRQOL impact). The Parfrey Symptom Assessment tool assessed the most symptom attributes including severity, frequency, necessity of drug treatment, sleep and daily activity interference, and quality of life impact. The non-dialysis specific Memorial Symptom Assessment Scale (MSAS) considered symptom bother, severity, and frequency and served as the basis for the Dialysis Symptom Index (DSI). However, when modified for a dialysis-dependent population, the DSI was simplified to include assessment of symptom bother only. Other instruments selectively addressed symptom attributes, often varying symptom attribute evaluation by discrete symptom. For example, the KDQOL, the most widely used HRQOL instrument among dialysis-dependent patients, assessed bother for all symptoms, but considered severity, life interference, and frequency for only select symptoms (pain, sexual dysfunction, sleep, and fatigue).

Instrument Validity and Reliability Assessment

Table 6 displays the validity and reliability testing of the symptom domains of the included instruments. Complete psychometric assessment results and an overall summary of psychometric testing are available in Tables S2 and S4. Overall, 13 (57%) instruments met criteria for content validity assessment. One of the 10 non-ESRD-specific instruments met such criteria, while 12 of the 13 ESRD-specific instruments displayed content validity evidence. For generic and ESRD-specific instruments, congruent construct validity was the most commonly tested form of construct validity. Fifteen (65%) instruments underwent congruent construct validity assessment and 8 (35%) underwent known groups construct validity assessment for symptom-related domains. Only 7 (30%) instruments were tested for responsiveness among patients with ESRD. Symptom-related domain internal consistency

was assessed in 16 (70%) instruments. Overall, 15 (65%) instruments underwent test-retest reliability testing with only 11 (48%) undergoing such testing for the symptom-specific domain.

A detailed list of validity and reliability testing for each instrument can be found in Table S3. The KDQOL showed evidence of content validity, known group validity, congruent validity, internal consistency reliability, and responsiveness for the symptom-specific domains. The DSI, the most commonly used dialysis-specific, symptom-focused instrument, demonstrated content validity and test-retest reliability but had no reported testing of construct validity, internal consistency reliability, or responsiveness. The modified ESAS demonstrated content validity, congruent validity, test-retest reliability, and responsiveness. We found no evidence of internal consistency reliability of the modified ESAS in dialysis patients, but did find such testing of the non-modified instrument in cancer patients.[48, 49]

Discussion

We identified 23 instruments with reported validity and/ or reliability testing that were used to assess a wide range of patient-reported physical symptoms in dialysis-dependent populations. Few measures considered short symptom recall periods (<1 week), and few assessed a range of symptom attributes. Additionally, the number of instruments focused exclusively on symptoms was limited, and psychometric testing of the available symptom-focused instruments was variable. A valid, symptom-focused instrument with short recall and assessment of multiple symptom attributes is needed to improve symptom assessment among maintenance dialysis patients.

Symptoms are a critical contributor to overall HRQOL, satisfaction with care, and medical decision-making among dialysis-dependent patients.[5, 6, 50, 51] In a survey of patients on or nearing dialysis, caregivers, and healthcare providers, 3 of the top research priorities were symptom-related. Patient-identified research priorities included improved treatments for itching, poor energy, sleep disorders, restless leg syndrome, and cramping.[52] Additionally, patient acceptance of different dialysis modalities, and dialysis treatment length or frequency, may be influenced by the treatment's perceived symptom impact. Ramkumar, *et al*. administered a utility measure questionnaire assessing patient preferences for 3 in-center, intensive HD schedules and found that anticipated improvement in energy and sleep increased patient acceptance of all 3 proposed schedules.[51] Despite the high importance of symptoms to dialysis-dependent patients, few symptom-targeted therapies exist, and we have limited understanding of the effect of treatment modifications on symptoms.

Improved symptom recognition and assessment may enhance provider-patient communication about therapy plans. In contrast to the findings of Ramkumar *et al*. that symptoms influence treatment acceptance, a study of patient preferences in fluid management found that patient-reported cramping, dyspnea, and swelling did not increase patient willingness to extend treatment times or try alternative HD schedules.[53] While longer treatment times might relieve intradialytic cramping and hypotension, and more frequent HD might mitigate dyspnea and swelling, symptom presence did not influence the acceptance of such treatment changes. A potential explanation for this seeming incongruity

is poor patient understanding of potential treatment and symptom associations. Improved evidence regarding symptom-treatment associations may allow providers to better educate patients about potential benefits of different modalities and treatment aspects.

To identify symptoms and to assess the efficacy of interventions, valid, reliable, and responsive symptom assessment tools are needed. In current practice, symptoms are typically assessed as part of broader HRQOL evaluations. The KDQOL, the most commonly administered HRQOL survey, contains a symptom domain, but the associated items cover a limited range of symptom attributes and have long recall periods (4 weeks). Additionally, the instrument requires up to 30 minutes for completion. These features make the KDQOL and other HRQOL instruments less suitable for frequent symptom assessment compared to more concise, symptom-focused measures with shorter recall periods and greater symptom attributes.

Of the dialysis-specific instruments four instruments focused exclusively on symptoms: Curtin *et al*., DSI, modified ESAS, and Physical Symptom Distress Scale. Curtin *et al*. and Physical Symptom Distress Scale have no reported use outside of their development. The modified ESAS has been used more extensively and underwent robust psychometric testing. As modified ESAS measures “present” symptoms, it is a potentially sensitive tool for assessing treatment-to-treatment symptom fluctuation. However, the modified ESAS examines symptom severity only and does not assess symptom frequency or impact on HRQOL. Similar to the modified ESAS, the DSI also had extensive patient and expert input during development, but psychometric testing outside of test-retest reliability was not reported.

While not focused exclusively on symptoms, the Parfrey Symptom Assessment is a HRQOL tool that considers a wide range of symptom attributes. The Parfrey tool addresses symptom severity and frequency and symptom impact on HRQOL, daily living, and sleep. With the inclusion of other aspects of HRQOL such as overall life satisfaction and general affect, the Parfrey tool is longer than symptom-limited tools and requires 15–20 minutes for completion.[17] This tool has many advantages over the other identified instruments, but its recall period of weeks limits its utility for assessment of short-term symptom fluctuation. Improved physical symptom assessment tools with short recall periods (<1 week), multi-attribute symptom assessment, and consideration of symptoms relevant to the timing of the dialysis procedure may enhance our understanding of symptom pathophysiology and response to intervention.

The ideal symptom assessment tool for dialysis patients must capture symptoms important to dialysis patients. Content validity measures the extent to which instruments capture concepts relevant to the targeted population. Two key elements of content validity are 1) incorporation of target population input into item generation and prioritization, and 2) evaluation of respondent comprehension of survey items.[54, 55] Engagement of the target population in instrument development is fairly routine: 12 of the 13 symptom-related instruments developed for dialysis patients reported dialysis patient involvement in item generation. Evaluation of patient comprehension of measure content is an equally important, but often neglected aspect of content validity. Cognitive interviewing, the process of probing

respondent thought processes to elucidate question understanding, is often performed to assess item understanding as it can identify problems with comprehension, recall, and decision processes. Furthermore, it can also detect structural defects in a questionnaire.[56, 57] We identified no instrument in which in-depth cognitive interviewing was described in measure development. The fluid management survey did undergo "comprehension testing" in which dialysis patients were interviewed following survey completion and asked to point out ambiguous questions or other points of confusion. However, these interviews were not standardized and were dependent on patient-identified survey ambiguities.[53] As new symptom instruments are developed for dialysis patients, greater attention to cognitive interviewing and other comprehension testing is warranted.

Finally, the selection of the optimal symptom evaluation measure depends on the purpose of the symptom assessment. For example, when testing new drugs, devices, or other therapeutic interventions directed at specific symptoms such as pruritus, restless legs, or sleep disorders, in-depth, symptom-specific instruments are appropriate. These measures need to be symptom-targeted, inclusive of a range of symptom attributes, and be responsive to change over time and to intervention. Measures assessing the broader concept of symptom burden and its contribution to HRQOL require different characteristics. Such symptom assessments should include a wide range of potential symptoms and may benefit from greater focus on life interference and burden rather than symptom timing and duration. Furthermore, whether the purpose of the symptom instrument is for detailed research purposes or broader clinical assessments, it is our recommendation that measures include blank, respondent-generated items to ensure that the full range of the patient symptom experience is captured.

While we approached this systematic review with methodological rigor, our review does have limitations. We included instruments with ≥3 physical symptoms, excluding those focused on single symptoms and those assessing only mood-related symptoms. This led to the exclusion of symptom measures focused exclusively on sleep, restless legs, sexual dysfunction, and depression, all important symptoms and co-morbid conditions among dialysis-dependent patients. Review of these symptom-specific instruments is warranted. Additionally, we excluded instruments that had no evidence of validity or reliability testing. This choice resulted in a higher percentage of included instruments with validity and reliability testing compared to prior reports.[58] Finally, we did not provide an assessment of the quality of instrument psychometric testing as standards, particularly for the subjective aspects of psychometric testing, are controversial, and gold standards do not exist. Instrument reliability and validity must ultimately be determined by individual providers and investigators with consideration given to the patient population, intervention, and desired outcome. We provided psychometric testing results to help inform these decisions in Table S2.

In summary, our review highlights the diversity of methods used for physical symptom assessment among dialysis-dependent patients and identifies the lack of a valid, symptom-focused instrument with short recall and assessment of multiple symptom attributes. Improved symptom assessment tools are needed to improve symptom evaluation and symptom responsiveness to intervention among dialysis-dependent patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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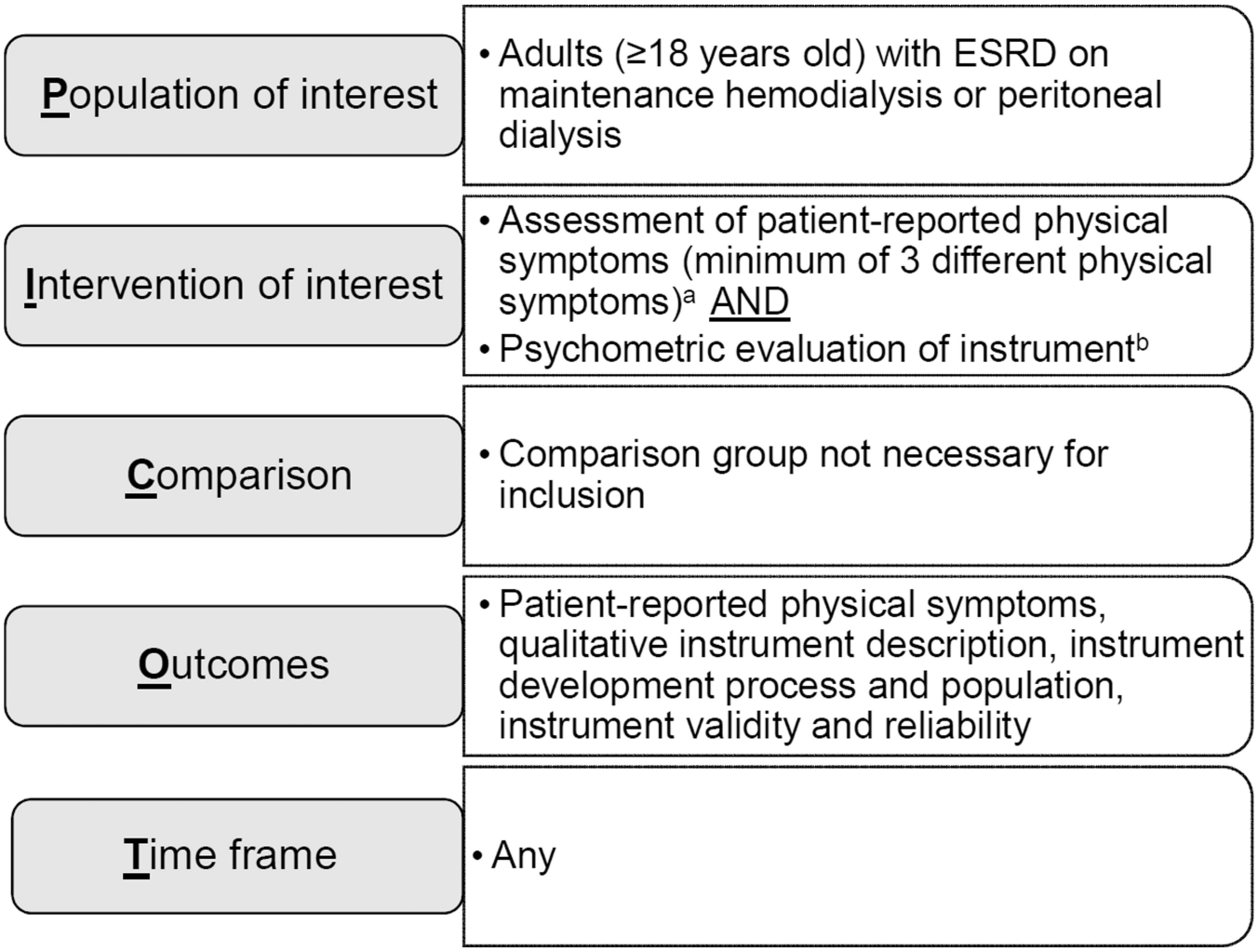

Figure 1.

PICOT criteria and search strategy.[27]

[a] Instruments focused on a single symptom such as pruritus, thirst, fatigue, sleep, or sexual dysfunction and instruments with mood symptoms only were excluded. Physical function and capacity were not considered symptoms. Instruments focused exclusively on physical function were excluded.

[b] Instrument psychometric assessment included content validity, construct validity, responsiveness, internal consistency reliability, and test-retest reliability. Instruments with no retrievable information on validity or reliability were excluded.

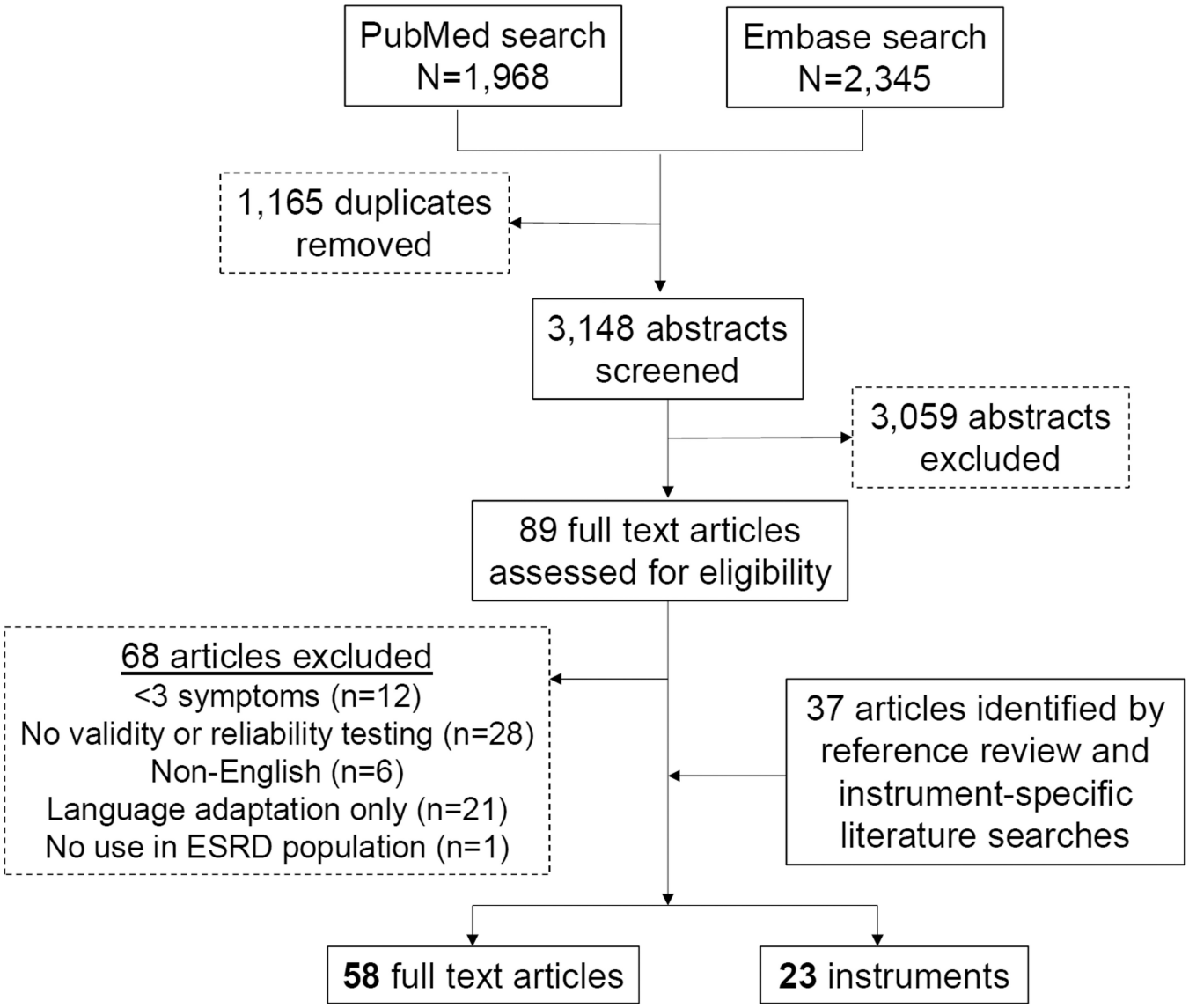

Figure 2.
Flow chart of article and instrument selection.
Abbreviations: ESRD, end stage renal disease.

Table 1

Article and instrument selection criteria.

	Inclusion criteria	Exclusion criteria
Article-level	• Studies of patients with end stage renal disease on dialysis who were ≥ 18 years old • Reported use of a patient-reported outcome instrument that included physical symptoms	• Studies of patients with acute kidney injury or those requiring short-term dialysis • Non-English articles • Letters and case reports
Instrument-level	• Instruments with ≥3 unique physical symptoms[a] • Instruments with psychometric evaluation that included reporting of validity and/or reliability testing results	• Instruments focused on a single symptom • Instruments with mood or mental health symptoms only • Instruments with no retrievable data on validity or reliability

[a] Physical function and capacity were not considered symptoms.

Table 2

Psychometric measures considered in patient-reported outcomes instrument evaluations.

Measure	Definition	Common methods of assessment	Interpretation[a]
Validity (degree to which an instrument measures the concept it is intended to measure)[28,30,31,59]			
Content validity	Extent to which the instrument includes the most relevant and important aspects of a concept[54]	Stakeholder focus groups, interviews, surveys	Qualitative evidence from development and pre-testing[60]
Construct validity[b]	Evidence that relationships among items, domains, and concepts conform to a priori hypotheses[28]	Correlation statistics	≥0.70 supports strong correlation
Congruent	Extent to which measure correlates with measure assessing the same construct		
Known group	Extent to which measure is sensitive to differences and similarities in groups with known attributes		
Responsiveness	Extent to which instrument can detect changes in the construct being measured over time[30]	Score change statistics	Statistically significant difference in scores pre- and post-clinically relevant events[29]
Reliability (degree to which an instrument is free from measurement error)[30, 31,59]			
Internal consistency reliability	Degree of the interrelatedness among the items in a multi-item measure[30,31]	Cronbach's α	≥0.70: adequate internal consistency[60]
Test-retest reliability	Measure of the ability to provide consistent scores over time in a stable population[30]	Intraclass correlation coefficient; Kappa statistic	≥0.70: supports test-retest reliability[29]

[a] Interpretation score thresholds are not well established and may differ across populations and sources.

[b] Construct validity was considered as congruent and known group validity as these were the construct validity sub-types most commonly assessed in identified instruments.

Table 3

Description of 23 included physical symptom instruments

Instrument [a]	Brief description
Developed for Dialysis Populations (n=13)	
100 Category Checklist; *Japan (2009)*	Developed to assess physical and psychosocial problems as well as functional and environmental factors affecting QoL in hemodialysis patients
CHOICE Health Experience Questionnaire (CHEQ); *US (2000)*	Developed to complement the generic 36-Item Short Form Health Survey (SF-36), be sensitive to the effectiveness of alternative dialysis modalities and dosing regimens, and be useful for longitudinal collection in routine practice
Curtin, *et al.*[63]; *US (2002)*	Developed to catalogue symptoms experienced by dialysis patients with the goal of improving functional status
Dialysis Symptom Index (DSI); *US (2003)*	Developed to assess the physical and emotional symptom burdens of hemodialysis patients
Fluid Management Survey; *US (2014)*	Developed to assess hemodialysis patient-stated preferences regarding fluid management
Hemodialysis Quality of Life Questionnaire (HQL); *Canada (1990)*	Developed to assess hemodialysis patient QoL and physical and emotional symptoms
Kidney Disease Quality of Life Instrument (KDQoL); *US (1994)*	Developed to assess disease-specific health-related QoL encompassing both generic and disease-specific elements
Kidney Disease Questionnaire (KDQ) *Canada (1990)*	Developed to assess disease-specific QoL for use in clinical trials of maintenance hemodialysis patients
Modified Edmonton Symptom Assessment System (ESAS); *Canada (2006)*	Modification of existing instrument specific to dialysis population developed to assess the physical and emotional symptom burdens of dialysis patients
National Kidney Dialysis and Kidney Transplantation Study (NKDKTS); *US (1980s)*	Developed as part of government-commissioned study to investigate QoL, quality of care, rehabilitation, and health status of US patients undergoing dialysis
Parfrey Symptom Assessment; *Canada (1987)*	Developed to measure QoL among ESRD patients
Physical Symptom Distress Scale; *Taiwan (1997)*	Developed to estimate the degree of symptom distress experienced by ESRD patients
Short-Version Checklist; *Japan (2013)*	Developed as a shortened version of the 100 Category Checklist to assess physical problems as well as functional and environmental factors affecting QoL in hemodialysis patients
Developed for Non-dialysis Populations (n=10)	
Bowel Disease Questionnaire; *US (1989)*	Developed to elicit gastrointestinal symptoms relevant to functional disorders.
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30); *Belgium (1987)*	Developed to assess health-related QoL of cancer patients in clinical trials
McGill Quality of Life Questionnaire (MQOL); *Canada (1995)*	Developed to assess general domains of QoL in patients at all stages of life-threatening illnesses from diagnosis to cure or death
Memorial Symptom Assessment Scale (MSAS); *US (1990)*	Developed to measure the prevalence and characteristics of physical and emotional symptoms experienced by diverse types of cancer patients
Nottingham Health Profile (NHP); *UK (1980)*	Developed to assess an individual's perception of his or her own health status
Palliative Care Outcome Symptom Scale (POS-S Renal); *UK (1998)*	Developed to improve outcome measurement by evaluating different outcomes in palliative care for patients with advanced disease; disease-specific modules were developed
Quality of Life at the End of Life (QUAL-E); *US (2001)*	Developed to assess QoL at the end of life in a range of diseases and degrees of illness across care settings
Quality of Well Being Self-Administered Scale (QWB-SA); *US (1970s)*	Developed to estimate QoL-adjusted years (cost utility analysis metric)
Rotterdam Symptom Checklist (RSCL); *Netherlands (1980s)*	Developed to measure the symptoms reported by cancer patients participating in clinical research

Instrument [a]	Brief description
Symptom Distress Scale (SDS); *US (1970s)*	Developed to measure the construct of symptom distress from the specific symptoms being experienced as reported by the patient

[a] Instrument; country of development (estimated year of development).

ESRD, end-stage renal disease; QoL, quality of life; US, United States

Table 4

Physical symptoms included in patient-reported outcome instruments used for patients on dialysis (N=21).[a,b]

Symptom	No. (%) of Instruments
General	
fatigue/ low energy	17 (81%)
dizziness/ faintness/ lightheadedness	12 (57%)
skin: dry/ itchy/ color change	11 (52%)
numbness/ tingling	8 (38%)
weakness	7 (33%)
restless legs	4 (19%)
sweats/ fever/ chills/ shivering	3 (14%)
weight loss or gain	3 (14%)
stiffness	2 (10%)
hair loss	2 (10%)
easy bruising	1 (5%)
feeling sick	1 (5%)
muscle loss	1 (5%)
restless	1 (5%)
Cardiovascular/Respiratory	
cough/ shortness of breath/ dyspnea	15 (71%)
chest pain/ angina	7 (33%)
swelling (legs/ arms/ nonspecific)	7 (33%)
asthma or wheeze	2 (10%)
heart palpitations	2 (10%)
perceived hypotension	1 (5%)
Sleep	
insomnia/ trouble falling asleep	14 (67%)
awaken during sleep	5 (24%)
drowsiness	5 (24%)
Gastrointestinal	
loss of appetite/ poor appetite	14 (67%)
nausea/ vomiting	14 (67%)
diarrhea/ constipation	10 (48%)
abdominal pain/ ulcer	5 (24%)
dry mouth	5 (24%)
stomach cramps/ gas pain	3 (14%)
fullness/ bloating	3 (14%)
thirst	3 (14%)
change in taste/ metallic taste	2 (10%)

Symptom	No. (%) of Instruments
difficulty swallowing/ mouth sore	2 (10%)
Pain	
Pain/aches	10 (48%)
Headache	9 (43%)
Muscle cramps/ cramps	8 (38%)
Backache	5 (24%)
Bone/joint pain	5 (24%)
Muscle soreness/muscle pain	4 (19%)
Spasm	2 (10%)
Other	
Confusion or memory difficulty	4 (19%)
Difficulty is sexual arousal	4 (19.%)
Dialysis access problem or pain	3 (14%)
Self-reported symptom*	8 (38%)

Note: Excludes mood-related symptoms such as depression, anxiety, irritability, and boredom. Excludes 100 Category Checklist[61] and Short-Version Checklist[62] as these instruments each contained 2 symptom domains referred to as “body function component” and “body structure component.” Each component contained multiple categories. Many of the categories were non-specific, and we were unable to re-categorize them as discrete symptoms comparable to the other instruments. These 2 instruments were developed in the Japanese language, likely contributing to such discrepancies in categorization. The “body function component” of the Short-Version Checklist contained the following 17 categories: sleep functions, seeing functions, sensations associated with hearing and vestibular function, sensation of pain, blood pressure functions, hematological system functions, general physical endurance, aerobic capacity, fatigability, defecation functions, urinary excretory functions, urination functions, mobility of joint functions, sensations related to muscles and movement functions, protective functions of the skin, sensation related to the skin, and functions of hair. The “body structure component” contained the following 5 categories: structure of eyeball, structure of urinary system, kidneys, structure of upper extremity, and structure of nails.[62] The 100 Category Checklist followed a similar pattern, and specific symptoms could not be tabulated.[61]

*Patient fill-in.

Table 5

Physical symptom evaluation in patient-reported outcome instruments used in patients on dialysis.

Instrument	Completion time	No. of symptoms	Symptom Categories[c]							Dialysis treatment specific	Recall	Symptom attributes**	Symptom frequency **	Symptom QoL impact**
			Gen.	*CV/ Pulm*	*Sleep*	*GI*	*Pain*	*Other*	*Self-report*					
Developed for Dialysis Populations														
100 Category Checklist[e, f]	NR	35	Y	Y	Y	Y	Y	Y	N	N	u/k	N	N	N
CHOICE Health Experience Questionnaire	25–30 min[13]	17	Y	Y	Y	Y	Y	Y	N	Y (intra-dialysis)	4 wk; 3 mo	bother (14) severity (2) problem (3)	Y(8)	N
Curtin, *et al.*[63]	NR	47*	Y	Y	Y	Y	Y	Y	N	N	4 wk	N	Y(47)	N
Dialysis Symptom Index	NR	30*	Y	Y	Y	Y	Y	Y	N	N	1 wk	bother (30)	N	N
Fluid management Survey	10–28 min[53]	10	Y	Y	N	Y	Y	N	N	Y (intra-dialysis)	2 wk	bother (8)	Y(2)	N
Hemodialysis QoL Questionnaire[e14,64]	NR	51	Y	Y	Y	Y	Y	N	N	Y (intra- and inter-dialysis)	NR	NR	NR	NR
Kidney Disease QoL Instrument	5–25 min[47]	30	Y	Y	Y	Y	Y	Y	N	N	4 wk	bother (13) severity (2) problem (2)	Y(13)	N
Kidney Disease Questionnaire[e 15,65,66]	10–38 min[45,46]	self-report only	N	N	N	N	N	N	Y	N	2 wk	NR	NR	NR
Modified Edmonton Symptom Assessment System	NR	10*	Y	Y	Y	Y	Y	N	Y	N	present	severity (10)	N	N
National Kidney Dialysis and Kidney Transplantation Study[e 16, 67]	NR	13	Y	Y	Y	Y	Y	Y	N	Y (post-dialysis)	4 wk last dialysis	N	Y(13)	N
Parfrey Symptom Assessment	15–20 min[17]	12 +	Y	Y	Y	Y	Y	N	Y	Y (intra- and post-dialysis)	previous few wk	severity (12)	Y(12)	Y(12)
Physical Symptom Distress Scale	5 min[68]	16*	Y	Y	Y	Y	Y	N	N	N	1 wk	bother (16)	N	N
Short-Version Checklist[e, f]	NR	22	Y	Y	Y	Y	Y	N	N	N	NR	N	N	N

Instrument	Completion time	No. of symptoms	Symptom Categories[c]							Dialysis treatment specific	Recall	Symptom attributes**	Symptom frequency **	Symptom QoL impact**
			Gen.	*CV/ Pulm*	*Sleep*	*GI*	*Pain*	*Other*	*Self-report*					
Developed for Nondialysis Populations														
Bowel disease questionnaire	NR	17[d]	Y	Y	Y	Y	Y	N	N	N	1 y	bother (17)	Y(17)	N
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire	12 ± 7.5 min[20]	18	Y	Y	Y	Y	Y	N	N	N	1 wk	burden (18)	N	N
McGill Quality of Life Questionnaire	15–20 min[18]	self-report only	N	N	N	N	N	N	Y	N	2 d	problem	N	N
Memorial Symptom	NR	32*	Y	Y	Y	Y	Y	Y	Y	N	1 wk	bother (32)	Y(24)	N
Assessment Scale												severity (32)		
Nottingham Health Profile	11 min[45]	33	Y	N	Y	N	Y	N	N	N	present	N	N	N
Palliative Care Outcome Symptom Scale	<10 min[69]	17*	Y	Y	Y	Y	Y	N	Y	N	1 wk	bother (17)	N	N
Quality of Life at the End of Life	NR	self-report only	N	N	N	N	N	N	Y	N	1 wk	bother severity	Y	Y
Quality of Well Being Self-Administered Scale	14 min[70]	58	Y	Y	Y	Y	Y	Y	Y	N	3 d	N	N	N
Rotterdam Symptom Checklist	8 min[71]	30*	Y	Y	Y	Y	Y	Y	N	N	2 wk	bother (30)	N	N
Symptom distress scale	5 min[44]	10*	Y	Y	Y	Y	Y	N	N	N	lately	severity (4)	Y(8)	N

** Numbers in parentheses denote numbers of symptoms for which each attribute (bother, severity, problem, burden) or parameter was evaluated when known. Bother and interference reported as bother.

CHOICE: Choices for Healthy Outcomes in Caring for ESRD; CV/Pulm, cardiovascular/pulmonary; Gen, general; GI, gastrointestinal; NR, not reported; QoL, quality of life; u/k, unknown

[c] General (fatigue, low energy, dizziness, faintness, lightheadedness, skin changes, numbness, tingling, weakness, restless legs, sweats, chills, weight loss or gain, stiffness, hair loss, easy bruising, feeling sick, muscle loss restless); CV/Pulm (cough, shortness of breath, dyspnea, chest pain, angina, swelling, asthma, wheeze, heart palpitations, perceived hypotension); Sleep (insomnia, trouble falling asleep, awaken during sleep, drowsiness, lack of sleep); GI (loss of appetite, poor appetite, nausea, vomiting, diarrhea, constipation, abdominal pain, ulcer, dry mouth, stomach cramps, gas pain, fullness, bloating, thirst, change in taste, metallic taste, difficulty in swallowing, mouth sore); Pain (pain, aches, headache, muscle cramps, cramps, backache, bone pain, joint pain, muscle soreness, muscle pain, spasm); Other (confusion, memory difficulty, difficulty in sexual arousal, lack of sexual interest, dialysis access problem or pain).

[d] Instrument contains a non-gastrointestinal symptom checklist which is the basis for this report.

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[e] Copy of instrument could not be obtained for investigator review (n=5). In these instances, symptom evaluation criteria were garnered from associated references noted in the table.

[f] The 100 Category Checklist[61] and Short-Version Checklist[62] contained 2 symptom domains referred to as "body function component" and "body structure component." Each component contained multiple categories. Many of the categories were broad and potentially inclusive of multiple symptoms. In this table, we report the total number of symptom-related categories.

[*] instrument evaluates symptoms only;

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Table 6

Presence of validity and reliability testing of the symptom domain in instruments assessing physical symptoms.

	Measures of Validity				Measures of Reliability	
Instrument	**Content**	**Congruent Construct**	**Known Group Construct**	**Responsiveness**	**Internal Consistency**	**Test-Retest**
Developed for Dialysis Populations						
100 Category Checklist	Y	Y	Y	N	Y	N
CHOICE Health Experience Questionnaire	Y	N	Y	N	Y	N
Curtin, *et al.*[63]	Y	Y	N	N	Y	N
Dialysis Symptom Index	Y	N	N	N	N	Y
Fluid management Survey	Y	N	N	N	Y	N
Hemodialysis Quality of Life Questionnaire	Y	N	N	Y	N	Y
Kidney Disease Quality of Life Instrument	Y	Y	Y	Y	Y	
Kidney Disease Questionnaire	Y	Y	N	Y	Y	Y
Modified Edmonton Symptom Assessment System	Y	Y	N	Y	Y	Y
National Kidney Dialysis and Kidney Transplantation Study	Y	N	Y	Y	Y	Y
Parfrey Symptom Assessment	Y	N	Y	Y	N	N
Physical Symptom Distress Scale	N	Y	N	N	Y	Y
Short-Version Checklist	Y	Y	Y	N	Y	N
Developed for Nondialysis Populations						
Bowel disease questionnaire	N	N	N	N	N	N
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire	N	Y	N	N	Y	N
McGill Quality of Life Questionnaire	N	Y	N	N	Y	Y
Memorial Symptom Assessment Scale	N	Y	Y	N	Y	N
Nottingham Health Profile	N	Y	N	Y	N	Y
Palliative Care Outcome Symptom Scale	N	Y	N	N	N	Y
Quality of Life at the End of Life	Y	Y	N	N	Y	Y
Quality of Well Being Self-Administered Scale	N	N	N	N	N	N

	Measures of Validity				Measures of Reliability	
Instrument	**Content**	**Congruent Construct**	**Known Group Construct**	**Responsiveness**	**Internal Consistency**	**Test-Retest**
Rotterdam Symptom Checklist	N	Y	N	N	Y	N
Symptom distress scale	N	Y	Y	N	Y	Y

Note: All psychometric measures except for content validity were deemed present if assessed quantitatively. Content validity was deemed present if a clear description of the measurement aim was provided and if dialysis patients were involved in instrument item development. Responsiveness was deemed present only if analyzed in an end-stage renal disease population.