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Managing the symptom burden associated with maintenance dialysis: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

Rajnish Mehrotra¹, Sara N. Davison², Ken Farrington³, Jennifer E. Flythe^{4,5}, Marjorie Foo⁶, Magdalena Madero⁷, Rachael L. Morton⁸, Yusuke Tsukamoto⁹, Mark L. Unruh¹⁰, Michael Cheung¹¹, Michel Jadoul¹², Wolfgang C. Winkelmayer¹³ and Edwina A. Brown¹⁴; for Conference Participants¹⁵

¹Division of Nephrology, Department of Medicine, University of Washington School of Medicine, Seattle, Washington, USA; ²Division of Nephrology and Immunology, Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; ³Renal Department, Lister Hospital, Stevenage, UK; ⁴University of North Carolina Kidney Center, Division of Nephrology and Hypertension, Department of Medicine, UNC School of Medicine, Chapel Hill, North Carolina, USA; ⁵Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, North Carolina, USA; ⁶Department of Renal Medicine, Singapore General Hospital, Singapore, Singapore; ⁷Department of Medicine, Division of Nephrology, Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico; ⁸National Health and Medical Research Council (NHMRC) Clinical Trials Centre, The University of Sydney, Camperdown, New South Wales, Australia; ⁹Department of Nephrology, Itabashi Medical System (IMS) Itabashi Chuo Medical Center, Tokyo, Japan; ¹⁰Department of Internal Medicine, University of New Mexico School of Medicine, Albuquerque, New Mexico, USA; ¹¹Kidney Disease: Improving Global Outcomes (KDIGO), Brussels, Belgium; ¹²Cliniques Universitaires Saint Luc, Université Catholique de Louvain, Brussels, Belgium; ¹³Selzman Institute for Kidney Health, Section of Nephrology, Department of Medicine, Baylor College of Medicine, Houston, Texas, USA; and ¹⁴Imperial College Renal and Transplant Centre, Hammersmith Hospital, London, UK

Individuals with kidney failure undergoing maintenance dialysis frequently report a high symptom burden that can interfere with functioning and diminish life satisfaction. Until recently, the focus of nephrology care for dialysis patients has been related primarily to numerical targets for laboratory measures, and outcomes such as cardiovascular disease and mortality. Routine symptom assessment is not universal or standardized in dialysis care. Even when symptoms are identified, treatment options are limited and are initiated infrequently, in part because of a paucity of evidence in the dialysis population and the complexities of medication interactions in kidney failure. In May of 2022, Kidney Disease: Improving Global Outcomes (KDIGO) held a Controversies Conference—Symptom-Based Complications in Dialysis—to identify the optimal means for diagnosing and managing symptom-based complications in patients undergoing maintenance dialysis. Participants included patients, physicians, behavioral therapists, nurses, pharmacists, and clinical researchers. They outlined foundational principles and consensus points related to identifying and addressing symptoms experienced by patients undergoing dialysis and described gaps in the

knowledge base and priorities for research. Healthcare delivery and education systems have a responsibility to provide individualized symptom assessment and management. Nephrology teams should take the lead in symptom management, although this does not necessarily mean taking ownership of all aspects of care. Even when options for clinical response are limited, clinicians should focus on acknowledging, prioritizing, and managing symptoms that are most important to individual patients. A recognized factor in the initiation and implementation of improvements in symptom assessment and management is that they will be based on locally existing needs and resources.

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KEYWORDS: health-related quality of life; hemodialysis; kidney failure; patient-reported outcome measures; peritoneal dialysis; symptoms

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Recognition is growing of the frequency and burden of symptoms experienced by individuals undergoing either hemodialysis or peritoneal dialysis. A multitude of symptoms are reported (Figures 1 and 2), such as fatigue, pain, poor mood, dry skin, poor sleep, and muscle cramps, with fatigue being the most common, and pain the most severe.^{1–6} The exact incidence and prevalence of individual symptoms vary depending on patient population studied (age, comorbidities, sex and gender, frailty, psychosocial concerns, etc.) or development of dialysis-related complications (e.g.,

Correspondence: Rajnish Mehrotra, University of Washington School of Medicine, 1959 NE Pacific Street, Box 356521, Seattle, Washington 98195, USA. E-mail: RMehrotra@nephrology.washington.edu; or Edwina A. Brown, Imperial College Renal and Transplant Centre, Hammersmith Hospital, London W12 0HS, UK. E-mail: e.a.brown@imperial.ac.uk

¹⁵Other Conference Participants are listed in the [Appendix](#).

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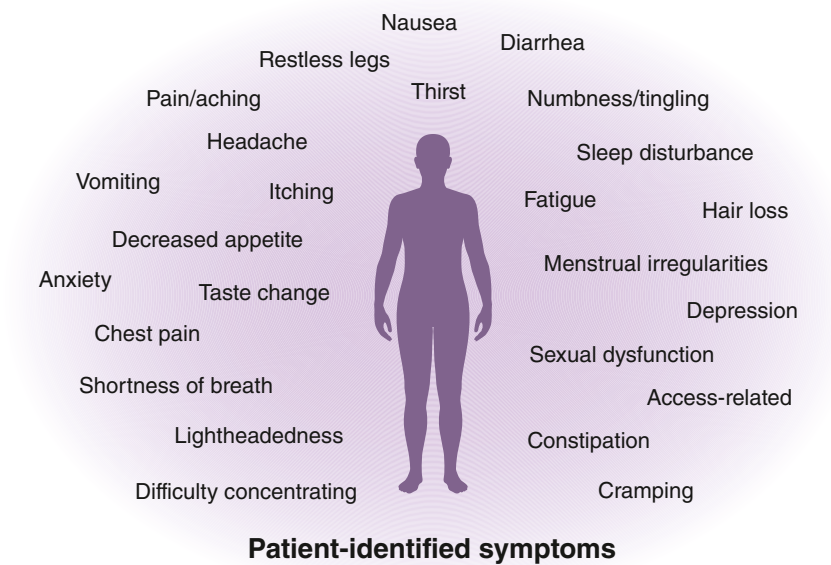


Figure 1 | Symptoms that kidney care teams should address. Some symptoms to consider when identifying those most important to the patient.

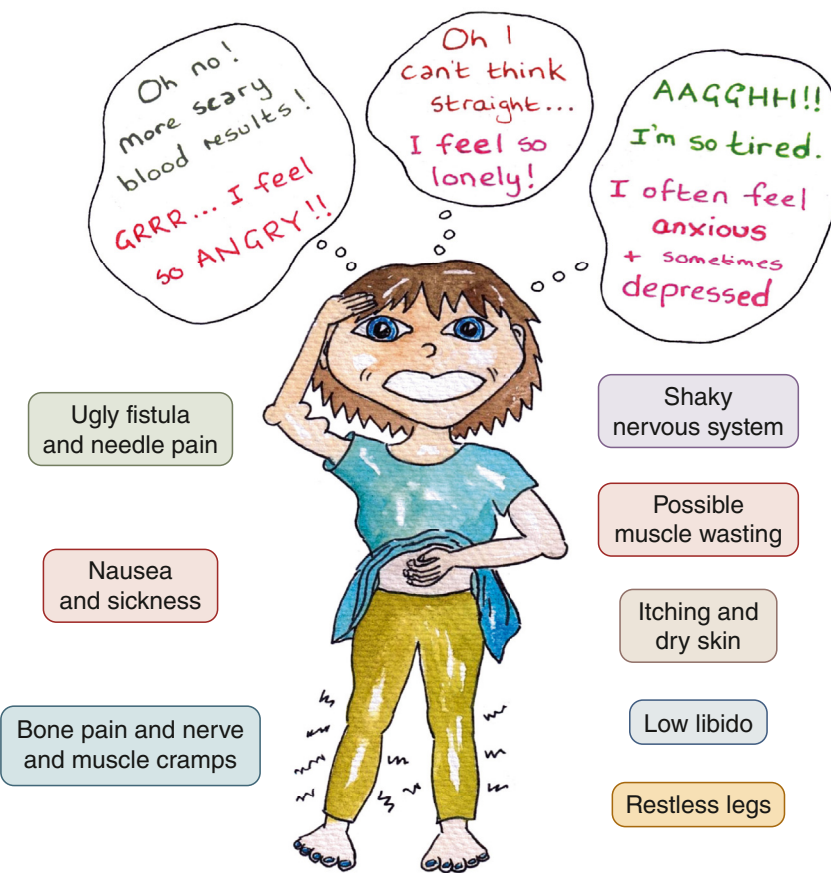


Figure 2 | Illustration of concerns arising from symptom perception among people undergoing dialysis, as drawn by a patient participant. Courtesy of Jayne Pigford.

vascular access related "steal" syndrome, dialysis-associated amyloid, or encapsulating peritoneal sclerosis). In addition to physical symptoms, approximately 40% of people receiving dialysis have symptoms of anxiety.⁷ Rates of depression vary by method of assessment,^{8–10} but when present, depressive symptoms are associated with nonadherence to diet, medication, and dialysis; poorer health-related quality of life¹¹; and more frequent hospitalizations and a higher mortality incidence.^{12,13} Symptom burden for people undergoing dialysis can limit participation in work, family, and social activities, and ultimately decrease life satisfaction.

Symptom identification and management in maintenance dialysis involve multiple individuals and levels of care, each having overlapping roles (Figure 3). Routine symptom assessment is not universal or standardized and is complicated by several factors.¹⁴ A point that is often unclear is whether the primary responsibility for managing symptoms lies with nephrologists or primary care teams. Individual symptoms may result from any of several, or multiple, potentially interacting and compounding chronic medical conditions and dialysis treatment-related factors. The pathophysiology of most symptoms is not well elucidated, and the occurrence and severity of symptoms can vary from hour to hour. Even when symptoms are identified, treatment is initiated infrequently.^{15,16} Treatment options may be limited, the evidence base is sparse,^{17,18} and constraints and complexities are present related to both medication use and behavioral interventions in the dialysis setting. With an already high pill burden and the possibility of additional drugs adding to symptom burden, people are often reluctant to take additional medications.¹⁹ Depending on the country

and the healthcare system, the wait may be long for appointments for alternative nonpharmacologic treatments, such as cognitive behavioral therapy for depression, and such appointments must be added to an already high number of treatment visits and the substantial time devoted to undergoing dialysis.

The level of discordance between symptoms experienced by people on dialysis and those identified or prioritized by their nephrology care providers is high.²⁰ For example, 1 study has shown that only half of hemodialysis patients with bone pain receive analgesia, and less than a quarter with sleep disturbance receive sleeping aids.¹⁵ This finding is not surprising given that, until recently, nephrology care has focused largely on numerical targets for laboratory measures, and outcomes such as mortality, rather than patient-reported outcomes, such as symptoms. People on dialysis may therefore perceive that communicating symptoms and personal challenges to their dialysis team is of limited usefulness or appropriateness.

In 2018, KDIGO (Kidney Disease: Improving Global Outcomes) initiated a series of Controversies Conferences focused on dialysis. The first 3 of these conferences (Dialysis Initiation, Modality Choice, Access, and Prescription²¹; Blood Pressure and Volume Management in Dialysis²²; and Home Dialysis²³) underscored the importance of patient preferences and life goals in decision-making surrounding kidney replacement therapy. A fourth conference, on symptom-based complications in dialysis, was convened in May of 2022 to identify the optimal means for diagnosing, managing, and treating symptom-based complications in people undergoing dialysis. (Videos of plenary presentations and preconference

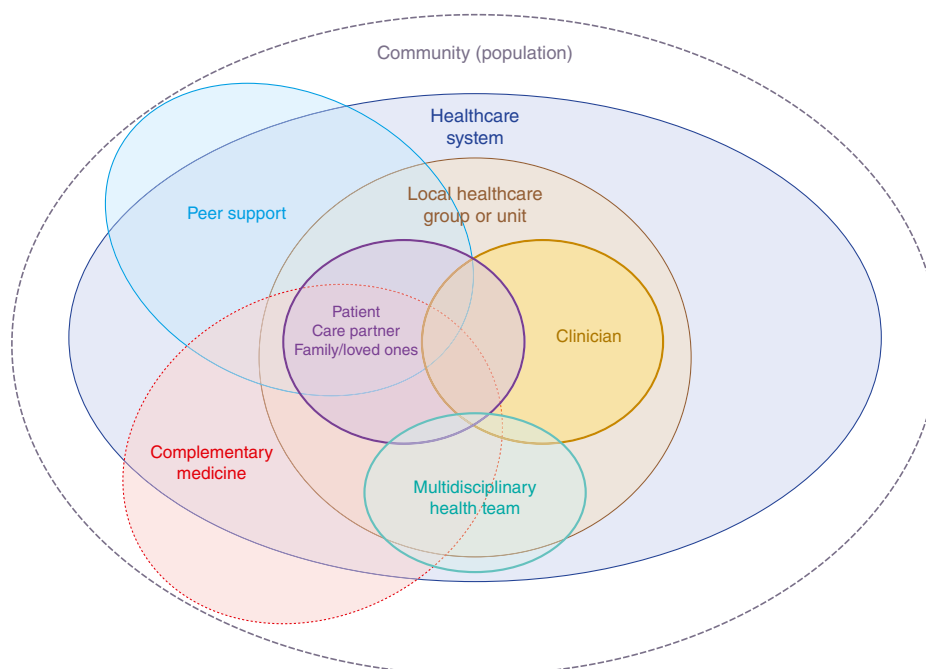


Figure 3 | The complex overlap of responsibilities in symptom recognition and management for patients undergoing dialysis. Among these groups, the kidney care team will take the lead.

webinars can be viewed at <https://kdigo.org/conferences/symptom-based-complications-in-dialysis/>.) Participants reflected the multidisciplinary nature of the dialysis team (physicians, behavioral therapists, nurses, pharmacists, and clinical researchers) and included people on dialysis. The core outcomes considered included patient-centered issues, and their perspectives, values, and preferences.

Meeting participants who had experience undergoing dialysis articulated 2 key areas of need related to identifying and addressing symptoms. First, clinicians often do not ask people on dialysis about their well-being, symptoms, or daily functioning. Second, providers need to recognize that symptom impact on functioning can be more important to patients than symptom frequency or even severity. For

Table 1 | Consensus points regarding symptom-based complications in dialysis

Statement	Additional comments
Clinicians should assess and focus on symptoms most important to individual patients	
Prioritization in symptom management should be based on patient perceptions of which symptoms are most negatively impacting their ability to live the life they want to live	
Nephrology multidisciplinary teams should take the lead in symptom management, with holistic care as the goal	- Initiating symptom screening is the responsibility of the kidney care team - Patients should share in this responsibility, but they need to be empowered to participate meaningfully in conversations - Many symptoms will require the expertise of other healthcare providers
The approach to routine symptom screening should remain consistent regardless of dialysis modality	
Regular global symptom screening should be incorporated into routine clinical practice. This ideally should involve using (i) an open-ended question approach that explores patient priorities for symptom management AND (ii) standardized PROMs	- Resource availability and workforce burden are key considerations for implementation - Opportunity costs need to be weighed: Should any current practices be dropped, or should more resources be devoted to symptom assessment?
PROMs play an important role in identifying patient-prioritized symptoms but should not be used in isolation	- Most current PROMs are not specific for dialysis care - Limitations of many current PROMs are as follows: (i) they insufficiently determine impact on the patients' lives (severity ≠ impact or patient priority); (ii) they do not necessarily identify all priority concerns—for example, cognitive and sexual dysfunction are frequently overlooked; and (iii) they may be burdensome to administer
PROMs for guiding clinical care should be: - relevant to patients with kidney diseases, with evidence for validity; - short and simple, requiring limited burden/resources for completion; - adaptable for language and vulnerable patients, such as those who are frail or have cognitive impairment and/or low health literacy; and - reliable and sensitive to change if being used to monitor treatment	The best format for administering PROMs in the dialysis unit remains unclear and will require customization based on available resources
The frequency of routine symptom screening should be individualized	The ideal frequency of routine symptom assessment to optimize patient outcomes but prevent patient, healthcare professional, and resource burden is not known. Intervals of once a year to every 1–3 months were discussed.^{14,24–28} Every 1–3 months was deemed reasonable and feasible by some patients and healthcare professionals, but at the risk of questionnaire fatigue
Symptom assessments should be incorporated into patient medical records to facilitate integration into overall clinical assessment AND they should be accessible to the interdisciplinary team within and beyond nephrology and the patient	- Optimal ways to incorporate symptom assessments into the patient medical record and most importantly into the patient's care plan also remain unclear and will require customization based on available resources - The communication of these assessments to patients should include formats such as simple, easy-to-understand visuals - Assessments ideally would be co-designed with patient representatives - Symptom scores can be reviewed routinely, alongside monthly blood-work results
Healthcare use and cost-effectiveness studies for symptom assessment and management programs are needed	

PROM, patient-reported outcome measure.

Table 2 | Key questions related to symptom-based complications in dialysis

1. How do we measure potential benefits of symptom assessment in improving health outcomes and meeting patient priorities?
2. How do we differentiate side effects of medicines versus symptoms related to chronic kidney disease?
3. What are patient attitudes about discussing symptoms, particularly anxiety-inducing symptoms such as cognitive and sexual dysfunction and mood disorders?
4. How do we improve understanding about the interplay between symptom burden and culture or psychological factors (e.g., depression and anxiety can result in more pain)?
5. To what extent does the treatment of symptoms improve health-related quality of life, function, adherence, hospitalization, or mortality?
6. How does staffing (physicians, psychologists, and other) influence the occurrence and severity of symptoms?
7. Should there be clearly defined roles and responsibilities for multidisciplinary team members or for specific types of clinicians?
8. How do we implement equitable symptom assessment and management in dialysis globally?
 - (a) What is needed to implement patient-centered care as standard care in different healthcare systems?
 - (b) Which system measures or key performance indicators should be used (reduced symptom burden, health-related quality of life, reduced hospitalizations)?
 - (c) Can mobile health applications improve the measuring, monitoring, and treating of symptoms of patients undergoing dialysis?
 - (d) Which model of symptom assessment and management is most cost-effective from a health-system perspective?
9. Does patient involvement in care (through patient-centered teaching tools/materials, patient-led teaching, peer mentors, peer support) result in improved patient experience? Could this include the transition from pediatric to adult care?
10. Would financial incentives impact attention to symptoms?
11. Can effective algorithmic management/treatment pathways be implemented for identifying and treating common symptoms such as depression, pain, itch, fatigue, and cramping (e.g., through pragmatic randomized research with patient-centered outcomes)?
12. How do dialysis systems reorganize to facilitate flexible, individualized, and patient-centered delivery?
13. Could standardized assessment widen health inequities (i.e., excluding the disadvantaged)?
14. How do we best adapt existing effective PROM implementation strategies to integrate PROMs and symptom assessment into dialysis units across diverse healthcare systems globally?
15. What are the optimal methods for facilitating clinician training in symptom assessment and management?
16. Does management of symptom-based complications in dialysis need explicit core requirements in training?
17. What is the optimal construct to assess the mental health component of quality of life in dialysis?
18. What is the best way to implement screening for depression? How soon after initiation of dialysis is it appropriate to begin screening for depression?
19. What is the role of nonpharmacologic treatment in de-escalating pharmacologic treatment in depression?
20. What is the impact of anxiety disorder in patients receiving dialysis?
21. What is the role of nonpharmacologic and pharmacologic therapy for management of anxiety?
22. Considering its overlap with depression, should anxiety be screened for as an independent entity?
23. What is the acceptability of cognitive screening among patients and clinicians?
24. What are the benefits and drawbacks of universal screening for cognitive functioning?

example, persistent or frequent symptoms may be more easily tolerated than less-frequent symptoms that impair participation in activities that hold value and meaning. Recognizing these issues, participants outlined foundational principles and consensus points related to identifying and addressing dialysis symptom-based complications (Table 1^{14,24–28}) and described gaps in the knowledge base (Table 2) and priorities for research (Table 3).

Foundational principles for dialysis care

- (i) The core of symptom management is individualization of approach, with elicitation of patient symptoms.
- (ii) Irrespective of availability of treatment options, the multidisciplinary care team, led by the nephrologist, should focus on acknowledging and managing symptoms that are most important to patients.
- (iii) Strategies for symptom assessment and management should take into consideration the biological, psychological, and social factors surrounding the patient, as well as the local resources available in the existing healthcare system.
- (iv) Healthcare delivery and education systems have a role in addressing symptom assessment and management for people undergoing maintenance dialysis, including incorporating changes to improve existing clinical pathways over time.

Identifying symptoms and establishing importance

Regular symptom screening should be incorporated into clinical practice.²⁹ Although the primary purpose of screening is to identify and manage symptoms, even when treatment options are limited, acknowledging and discussing symptoms is important because feeling heard and understood matters to people with life-limiting illness and can be therapeutic.³⁰ Symptom screening involves a dialogue between the patient and the clinician, with a focus on symptoms that are most important or bothersome to the patient. Recognition of symptoms takes time, and the short physician–patient interaction that typically occurs within dialysis units may not provide sufficient time to capture all symptoms of importance. Acknowledgment and recognition of symptoms can be accomplished by any member of the multidisciplinary team and may be facilitated by home visits or dedicated discussion time when patients attend in-center dialysis. A recognized issue is that individual communication styles and strategies vary greatly and are influenced by multiple personal and cultural factors. In the absence of a single approach to eliciting symptoms, to facilitate dialogue and education, clinicians can ask open-ended questions, such as the following: How are you feeling? Is there anything interfering with your life goals? Has anything changed? What do you need? What is bothering you most? Providing patients with a list of symptoms that are common to or previously reported by those

Table 3 | Research strategies to address symptom-based complications in dialysis

1. Elucidate the pathophysiology of symptoms and symptom clusters to drive the development of targeted therapies
 - (a) Emphasize fatigue and cramping, which have a poorly understood pathophysiology and are highly prioritized by patients
 - (b) Emphasize basic science and biomarker identification. Use science from other disciplines, e.g., oncology, as a foundation
2. Perform well-conducted studies on symptom-management strategies specifically in people undergoing maintenance dialysis
 - (a) Emphasize nonmedication strategies, as these have been under-investigated historically and are prioritized by patients
 - (b) Conduct well-designed trials powered to evaluate nonpharmacologic, pharmacologic, and combined interventions for treating depression in patients on dialysis
3. Design studies to investigate the efficacy of different management strategies for physical symptoms in subgroups (e.g., specify and power for *a priori* subgroup analyses; use adaptive designs to identify responders), with a goal of yielding evidence useful for providing evidence-based individualized management
4. Capitalize on routinely collected data (biomedical and patient-reported, even when the latter is imperfect) by integrating data and using artificial intelligence to identify clinical phenotypes or biomarkers that predict symptoms or symptom clusters. This would be a near-term, actionable strategy for proactively preventing symptoms
5. Develop an outcome measure for symptom interference/intrusiveness that could be used across symptoms
 - (a) Include cultural adaptation in the development process
 - (b) Create a measure useful in research and potentially in clinical care
6. Develop methodologic strategies for comparative effectiveness research that incorporate patient preferences for treatment into the research. This could be done by incorporating results of discrete-choice experiments or threshold-technique studies or by conducting randomized trials with a participant choice arm
7. Develop a population health-level intervention testing whether patient-reported outcome screening and treatment impacts emergency department visits, hospitalization, patient experience, and costs

undergoing dialysis can serve to normalize reporting of symptoms and help overcome the perception that discomfort (such as itch, for example) is to be expected. A list may also indicate that asking about symptoms considered taboo, such as pain, sexual symptoms, and depressive symptoms, is in fact appropriate and acceptable.

Symptoms associated with dialysis. Patients on dialysis can experience a large number of symptoms. The Dialysis Symptom Index has 30 key patient-identified symptoms,³¹ and using this tool, individuals on hemodialysis report a median of 9 symptoms.³² Fatigue affects at least half of people undergoing long-term dialysis.^{32,33} The symptom burden extends beyond the patient to their caregivers and family members. Identifying clusters of symptoms that tend to coexist has several potential benefits for clinical care. These include helping direct clinicians to other symptoms about which to inquire, supporting proactive symptom prevention rather than reactive symptom management, guiding research on pathophysiology or treatments (some treatments may address more than 1 symptom), validating symptom experiences, and serving as a reminder that symptoms are not isolated and can have cascading effects. For example, major depressive disorder can lead to changes in sleep and appetite, and insomnia can lead to increased pain perception, anxiety, and depression. Additionally, major depressive disorder and anxiety often coexist.³⁴ Consideration of clusters in the clinical setting does have potential drawbacks, as this could constrain patient reporting of symptoms if presented too rigidly and could lead to dismissal of symptoms that do not cluster.

The scope of the conference did not include consideration of screening methods for each symptom. For depression, evidence about use of validated screening tools is better developed than that for other symptoms and therefore was considered in more depth (Figure 4).

Depression and anxiety, separately or together,^{35,36} influence patient outlook, perception, and decision-making and are believed to be underrecognized. Given the benefits of recognizing depression, including any potential benefits of pharmacologic and nonpharmacologic treatments, an offer to screen for depression is recommended for all dialysis patients, using a validated tool with a defined cutoff point to indicate potential depression in this population, such as Patient Health Questionnaire-9.^{37–39} Screening should be coupled with clinical evaluation and interpretation. For anxiety, formal screening is not indicated at this time; a clinical approach of asking open-ended questions is most appropriate. Conference participants did not have consensus regarding whether universal screening for cognitive impairment should be conducted, as many felt that the data supporting such an approach are limited. Although validated assessment tools are available,⁴⁰ concerns regarding universal screening for cognitive impairment include the potential for screening-associated anxiety, an unclear correlation between test scores and function, and a lack of potential interventions.

The optimal frequency of routine symptom assessment among patients on dialysis to improve clinical outcomes without overburdening the patients is not known. Using intervals of every 1–3 months^{14,24–28} was discussed. The frequency of routine symptom screening likely would depend upon several factors, including purpose (routine screening vs. assessing a treatment or intervention), illness status and trajectory, availability of resources, patient choice and/or ability, and the specific assessment tools being used.

Important steps in assessing symptoms are incorporating any assessment into the patient's medical records, facilitating integration into the overall clinical assessment, and making the assessment accessible to both the multidisciplinary team, within and beyond nephrology, and the patient.

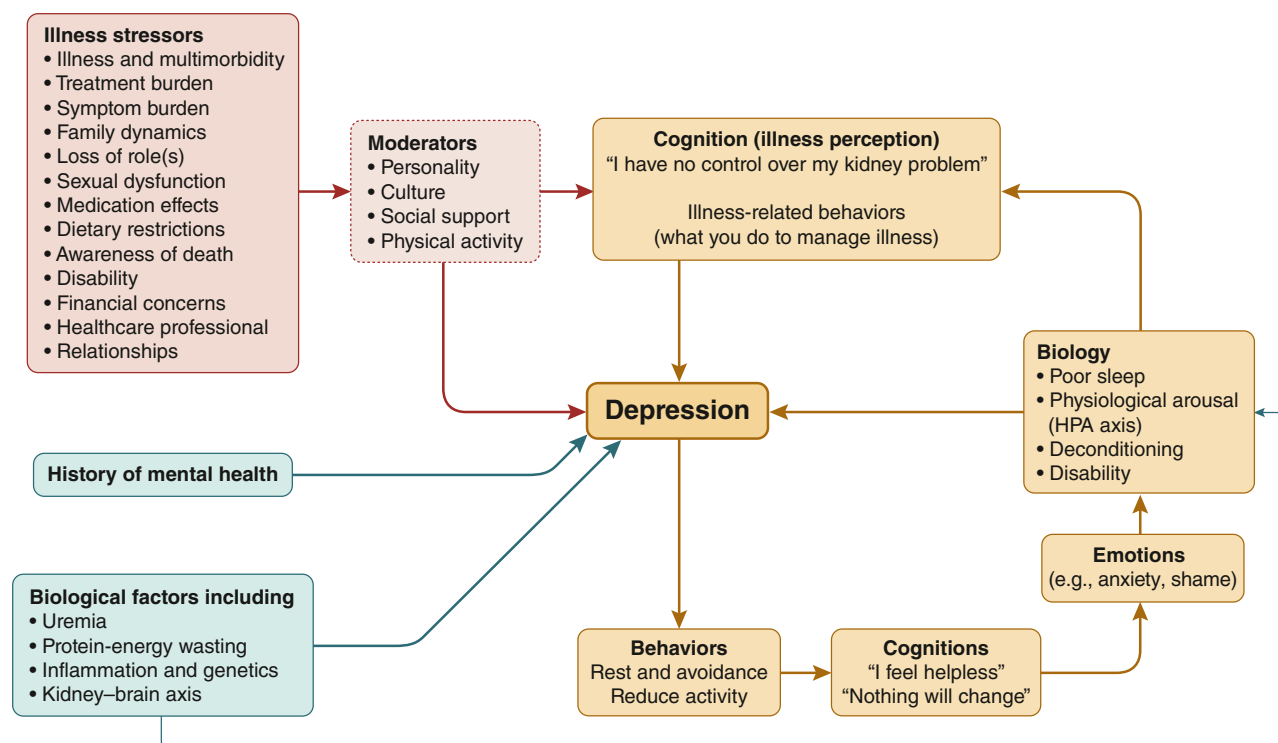


Figure 4 | Proposed biopsychosocial model using depression in advanced kidney disease as an example. HPA, hypothalamus–pituitary–adrenal axis.

Patient-reported outcome measures. Patient-reported outcome measures (PROMs) have been used widely in clinical effectiveness research. Some, such as screening for depression or assessment of health-related quality of life, are used routinely in some parts of the world, and they may enhance the patient–provider relationship, improve communication, and support shared decision-making.⁴¹ Some evidence in the cancer literature supports PROM use for specific decision points.^{42–44} Current PROMs are insufficient for determining symptom impact on the patient’s life, and they do not necessarily identify all priority concerns. In addition, in the absence of data indicating that detecting symptoms with PROMs leads to meaningful improvements in health and well-being with dialysis, the cost-effectiveness of PROMs cannot be calculated. Reassuring to note is that randomized trials are underway to investigate this issue.

To optimize the use of PROMs in clinical settings, gaps between practice and evidence must be closed, and the value of their use, given the resources required from both clinicians and patients, must be determined (Table 4^{45–52}). To have utility in dialysis, PROMs must be supported by evidence of validity relevant to kidney failure (Table 5^{29,31,53–58}), must be short and simple with limited resource burden, and must be adaptable for vulnerable patients (such as those with limited dexterity, visual impairment, frailty, cognitive impairment, low health literacy, or who speak a different language than their clinicians). If they are being used to monitor treatment, PROMs should be reliable and sensitive to change in symptoms. PROMs should include at least 1 free response or fill-in

option to support elicitation of symptoms not included on the PROM. Important in using this approach is to frame the delivery of PROMs as a part of clinical assessment and not as a survey. This framing will remove some patient barriers in reporting symptoms and reinforce the clinical necessity of reporting. The provision of a feedback mechanism to the patient is essential to close the loop, consolidating trust, and for accurate future reporting. If PROM data are used, their collection should be followed by patient–clinician discussion about the responses.

Considerations for managing and monitoring symptoms

Strategies for treating symptom-based complications in dialysis care are inextricably linked to resource availability and contextual circumstances. Access to dialysis-related treatments and services varies regionally, sometimes even within a single country, and having access to dialysis does not necessarily equate to having access to supportive therapies. Factors related to or determined by resources that affect symptom management include dialysis modality, dialysis prescription, cost, payer(s), water quality, treatment access prior to kidney failure, available medications or ancillary services, providers of care, how care is provided, patient education, and support from support groups, peer workers, and family members.

Recognition of factors such as culture, religion, age, and sex or gender should arise from an understanding of the patient as an individual. Getting to know patients well can be challenging due to patient–clinician differences (age, background), potential lack of continuity of care, and other

Table 4 | Strategies for Implementation of PROMs into clinical practice

Step	Considerations	Suggested strategy
Determination of goal ⁴⁵	- Screening or monitoring of treatment - Setting a goal for team to focus on and target - Providing basis for improvement	- Identify and understand key attitudes of staff and patients to PROMs within units. Care teams and patients must see the overall clinical utility.⁴⁶ - Align patient and clinician expectations of PROMs as part of shared decision-making.⁴⁷ - Frame delivery of PROMs as part of the clinical assessment and not as a survey.
Identification of appropriate PROMs	- Should address the desired goal and be relevant to people undergoing dialysis - Short and simple to use - Appropriate for high-risk patients such as those who are frail with cognitive impairment - Reliable and sensitive to change - Actionable	Some suggested tools can be found in Table 5.
Identification of barriers and available resources	- Patient perception or acceptance of symptoms leading to symptoms not reported - Clinician and care team perception - Fragmentation of patient data	- Set up of infrastructure needed to consider embedding PROMs into overall clinical notes and workflow - Data need to be accessible to all members of the care team. - With multiple points of data entry and exit, data security is of utmost importance. - Establishment of a clear and unambiguous line of communication among staff members with regard to responsibility and accountability of PROMs implementation steps, such as when, how, and where to document - Pen-and-paper questionnaires can be adapted to digital administration, although this can be labor-intensive. - Technology (e.g., smartphone, tablet) can be used to enter, collect, and collate data. Passive data entry (i.e., needs no active involvement of clinician or patient) could aid in the interpretation of symptoms. - Remote monitoring systems built into modern HHD and PD machines could allow patient input of symptoms/HRQOL assessments for transmittal to care teams⁴⁸: - Accelerometers could be used to detect scratching as evidence of itching.⁴⁹ - Sleep trackers may be able to inform on insomnia in hemodialysis patients.⁵⁰ - Multi-sensor systems can monitor ECG, respiratory activity, and activity/accelerometers, and can be embedded in clothing.⁵¹ - Multimedia format PROMs (mPROMs)⁵² could be adapted for low literacy.
Closing the loop with feedback and support management	Determine action steps to respond to issues identified through PROMs.	- Link PROMs with clinical tools to manage symptoms identified by assessments. - Individualize management, tailoring treatment in all aspects of care, from medical to psychosocial. - Acknowledge the power of acknowledgment, even if treatment is not available or cannot be rendered. - Offer coping strategies when symptoms cannot be relieved.

ECG, electrocardiogram; HHD, home hemodialysis; HRQOL, health-related quality of life; PD, peritoneal dialysis; PROM, patient-reported outcome measure.

factors, but having a diverse care team may help meaningfully bridge any gaps in perspective.

Symptoms can be managed with changes in dialysis prescription, nonpharmacologic strategies, medications, or a combination of these. Management may require a stepwise approach²⁹ whereby nonpharmacologic interventions precede complex or pharmacologic therapy. When initiating

pharmacologic therapies, consideration should be given to use of low-dose medications that may have efficacy across several symptoms. Choice of management should be based on shared decision-making and should be individualized according to comorbid health conditions, existing medications, patient preferences, availability and accessibility, and other relevant factors.

Table 5 | PROMs with evidence of validity for comprehensive symptom assessment in chronic kidney disease

For kidney failure²⁹	
Assessment tool	Description
Edmonton Symptom Assessment System: revised—Renal (ESAS-r) ⁵³	13 symptoms; visual analogue scale with a superimposed 0–10 numerical rating scale for severity
Integrated Palliative Care Outcome Scale—Renal (iPOS-renal; https://pos-pal.org/maix/ipos-renal-in-english.php)	17 symptoms; rated in terms of their impact on the patient over the last week from 0 (not at all) to 4 (overwhelmingly) Additional questions covering carer anxiety, practical issues, and optional items for any other concerns
Dialysis Symptom Index ³¹	30 symptoms; rated from 1 (not at all bothered) to 5 (very much bothered)
Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Health Experience Questionnaire ⁵⁴	83-item health-related quality-of-life tool; designed to complement the generic SF-36 (similar to the KDQOL) Incorporates symptom assessment as 1 of 13 dimensions: (i) freedom; (ii) travel restrictions; (iii) cognitive functioning; (iv) financial; (v) restrictions on diet and fluids; (vi) recreation; (vii) work; (viii) body image; (ix) symptoms; (x) sleep; (xi) sexual functioning; (xii) access-related problems; and (xiii) health-related quality of life
Symptom Monitoring on Renal Replacement Therapy-Hemodialysis (SMaRRT-HD) ⁵⁵	14-item PROM intended for use in chronic hemodialysis patients. Uses a single treatment recall period and a 5-point Likert scale to assess symptom severity
For chronic kidney disease	
Assessment tool	Description
Physical Symptom Distress Scale ⁵⁶	16 symptoms; rated from 0 (not bothered at all) to 4 (extremely bothered); some redundancy in items pertaining to pain
The CKD Symptom Burden Index ⁵⁷	32 symptoms (a modification of the Dialysis Symptom Index ³¹); assesses prevalence, distress, severity, and frequency of symptoms • Prevalence rated as yes/no • Other dimensions rated on a 0–10 numerical rating scale anchored by descriptors
Leicester Uraemic Symptom Score ⁵⁸	11 symptoms; assesses frequency and intrusiveness
KDQOL- SF-36 (https://www.rand.org/health-care/surveys_tools/kdqol.html)	36-item health-related quality-of-life tool (less burdensome version of the longer KDQOL) • 3 dimensions: (i) symptoms and problems; (ii) burden of CKD; (iii) effects of kidney disease • Incorporates the generic health-related quality-of-life tool—the SF-12

CKD, chronic kidney disease; KDQOL, Kidney Dialysis Quality of Life; PROM, patient-reported outcome measure; SF-, Short-Form Health Survey (12-item or 36-item).

Targeting some symptoms may address other symptoms (for example, treating depression may improve insomnia, pain, and anorexia). However, the reverse may be true—that is, treating one symptom may worsen another, creating the need for more medication to manage adverse effects. The risk of polypharmacy should be addressed through deprescription as appropriate, involvement of pharmacists in the multidisciplinary team, and frequent surveillance and reconciliation of medications as appropriate. The nephrology team will not necessarily have ownership of all prescriptions; prescribing and deprescribing should be within the domain of all care providers.

Preparing people for the realities of living while undergoing long-term dialysis and thereby setting realistic expectations may reduce psychological distress, although whether predialysis preparation improves psychological adjustment to dialysis is not clear currently, based on existing evidence.^{59–63}

Dialysis prescription. Tailoring the dialysis prescription to align with individual patient goals is important, although which variables have a clinically relevant effect is unclear. Apart from some improvement in physical symptoms with frequent hemodialysis in a selected patient population,^{64,65} knowledge gaps remain as to whether mode of dialysis delivery (hemodialysis or peritoneal dialysis) has any significant clinical impact on physical or psychological symptom burden.^{66–70} Evidence indicates statistical but uncertain clinical benefit of extended hemodialysis hours on the mental health component of quality of life.^{71,72}

Nonpharmacologic approaches. Nonpharmacologic interventions include cognitive behavioral therapy or other forms of psychotherapy; social or peer support; exercise; addressing of socioeconomic factors, such as food and housing insecurity; mindfulness; and meditation. Nonpharmacologic approaches have several favorable features. These include the lack of adverse

effects and of potential for interactions with medications, flexibility in delivery mode and accessibility (even during intradialytic intervals), and a lower burden of polypharmacy. Many of these interventions are supported by evidence in the general population,^{73,74} but evidence for efficacy, accessibility, and acceptability for most nonpharmacologic interventions in dialysis patients is limited.

Existing evidence demonstrates that psychological interventions, such as cognitive behavioral therapy, have efficacy in reducing depression.^{75–78} Logistical and resource issues are recognized potential limits to access to behavioral therapy. Results from small-scale studies suggest that mindfulness, music, and spiritual interventions may reduce the prevalence of depressive symptoms.⁷⁹ Limited evidence has indicated that manual acupressure has short-term benefits as an adjuvant intervention for fatigue and depression.⁸⁰

In patients with chronic kidney disease, data from small clinical trials indicate that physical activity can reduce fatigue.^{81–83} Moderate-quality evidence from meta-analyses indicates that aerobic exercise decreases depressive symptom burden in hemodialysis,^{84,85} supporting its use among people with dialysis according to their ability. Evidence from systematic reviews of small-scale studies is mixed, but it suggests that aerobic exercise may also improve anxiety symptoms in people undergoing hemodialysis.^{74,84} Evidence also indicates that music can reduce pain perception during cannulation of an arteriovenous fistula.⁸⁶

Pharmacologic approaches. For many therapies, the evidence base in this population is not robust, and description of all available medications for managing symptoms in dialysis was beyond the scope of this meeting. New drugs may become available. For example, the highly selective kappa opioid

receptor agonist difelikefalin has shown significant improvement in pruritis in some patients undergoing hemodialysis⁸⁷ and is now approved in several regions, including the US and Europe. Although meeting deliberations did not describe all available treatments comprehensively, the evidence base for using psychotropic medication for depression and anxiety was discussed. Although selective serotonin reuptake inhibitors (SSRIs) play an important role in managing depression in the general population, for people on hemodialysis, existing small, randomized, placebo-controlled trials using SSRIs have not shown that they have a consistent benefit over placebo and have documented increased adverse effects, particularly gastrointestinal.^{78,88–91} No existing randomized controlled clinical trials address SSRI use in peritoneal dialysis, and none addresses pharmacologic management of anxiety in kidney failure populations.⁹²

More evidence is needed regarding the use of SSRIs in the population of patients with kidney failure. Caution is warranted when prescribing SSRIs, owing to their adverse-effect profile. The principles of psychotropic medication prescription in medically fragile patients apply in kidney failure, including up titration of subtherapeutic doses with care, keeping efficacy and safety as a top priority. Adverse effects, such as QT prolongation and altered pharmacokinetics, in the setting of kidney failure should be considered.⁹³

System approaches and organization

Healthcare systems should provide equitable symptom assessment, management strategies, and resources for patients. From a health system perspective, activities for symptom assessment and management fall within the

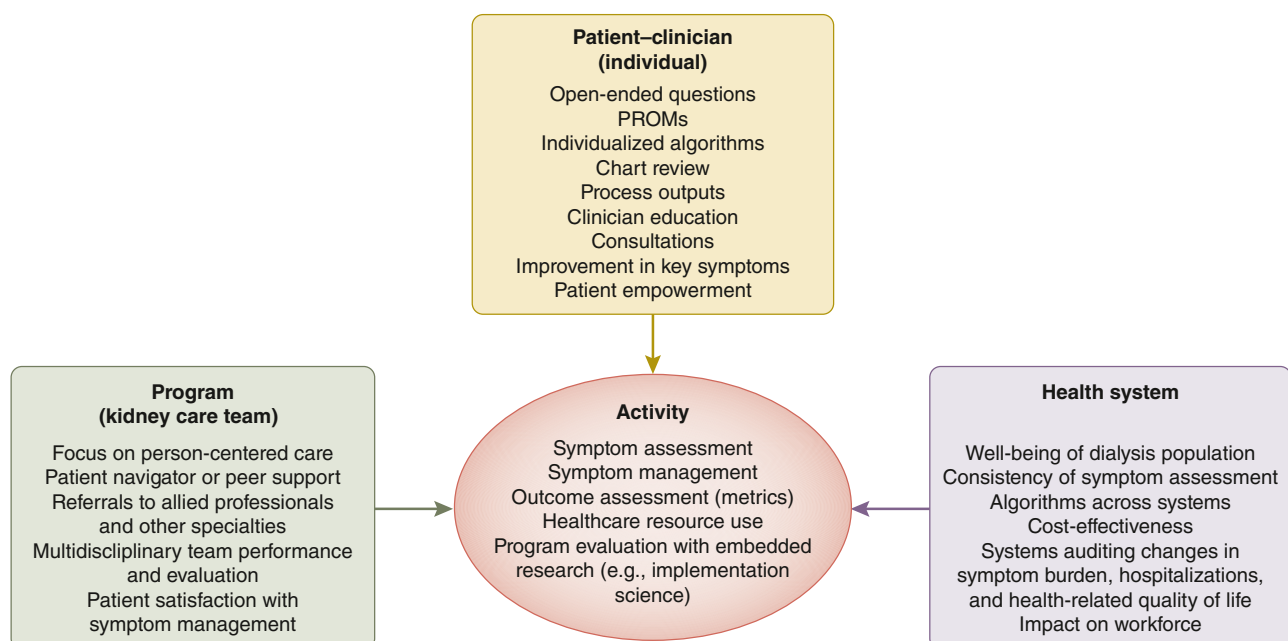


Figure 5 | Multilevel approaches to enable symptom assessment and management. PROM, patient-reported outcome measure.

categories of patient–clinician interactions, program improvement, and population health (Figure 5). Core processes for implementation include symptom elicitation, evaluation, management, and clinician follow-up, which have been described previously, as well as process and outcome metrics. Process metrics should measure whether a symptom assessment and management program occurred as intended and will evaluate, for example, the percentage of patients approached for program entry or who completed a program. Outcome metrics should apply to both the short-term and the longer-term and should focus on patient outcomes as well as workforce impact. Health-related quality of life is a possible outcome measure for effectiveness of symptom management programs. Important to any approach is that processes involved in delivery and quality control of symptom assessment not take time away from patient–clinician interactions. Models of care need to be flexible and adaptable to each country's health system.

Future directions

Symptom management is a research priority in kidney failure. Research should engage stakeholders in all stages, from design to conduct and dissemination, with particular focus on design and development. Stakeholders include but are not limited to patients, care partners, families, dialysis clinic personnel, nephrology care team members, trainees, dialysis providers, pharmaceutical companies, and payers. Ongoing trials using symptom assessment include the Symptom Monitoring with Feedback Trial (SWIFT),⁹⁴ Symptom Monitoring on Renal Replacement Therapy-Hemodialysis (SMaRRT-HD),⁹⁵ Evaluation of Routinely Measured Patient-Reported Outcomes in Hemodialysis Care (EMPATHY),⁹⁵ the HOPE Consortium Trial to Reduce Pain and Opioid Use in Hemodialysis (ClinicalTrials.gov NCT04571619), Short and Long-Term Effectiveness of Existing Insomnia Therapies for Patients Undergoing Hemodialysis (SLEEP-HD),⁹⁶ and the Technology-Assisted stepped Collaborative Care trial (TACcare).⁹⁷ Also ongoing are genotype and biomarker analyses to characterize symptoms reported by patients.⁹⁸

Fortunately, dialysis care is an optimal setting for evaluating the efficacy of new therapies—in both research and clinical care—given the frequency and amount of interaction individuals undergoing dialysis have with healthcare providers and systems. Randomized controlled trials are recognized as the gold standard in clinical research, yet using real-world data and evidence to support decision-making on effectiveness of interventions could also be leveraged. Particular attention is required regarding the relative effectiveness of management strategies, including the impact on outcomes most relevant to patients, such as overall symptom burden, physical function, and health-related quality of life.

APPENDIX

Other conference participants

Peace Bagasha, Uganda; Joanne M. Bargman, Canada; Sunita Bavanandan, Malaysia; Hannah Beckwith, United Kingdom; Paul N. Bennett, Australia; Clara

Bohm, Canada; Frank Brennan, Australia; James O. Burton, United Kingdom; Kerri L. Cavanaugh, USA; Joseph Chilcot, United Kingdom; Peter Choi, Australia; Daniel Cukor, USA; Laura M. Dember, USA; Jie Dong, China; Dawn Edwards, USA; Kevin F. Erickson, USA; Ana Figueiredo, Brazil; Fredric O. Finkelstein, USA; Masafumi Fukagawa, Japan; Michael J. Germain, USA; Franklin B. Guilliano, Philippines; Helen Hurst, United Kingdom; Kunitoshi Iseki, Japan; Meg J. Jardine, Australia; Allison Jauré, Australia; Vivekanand Jha, India; Manisha Jhamb, USA; Talermsak Kanjanabuch, Thailand; Edgar V. Lerma, USA; Philip Kam-Tao Li, Hong Kong; Adrian Liew, Singapore; Jolanta Malyszko, Poland; Thyago Proença de Moraes, Brazil; Olivier Moranne, France; Marques Shek Nam Ng, Hong Kong; Marlies Ostermann, United Kingdom; Jeffrey Perl, Canada; Jayne Pigford, United Kingdom; Wolfgang Pommer, Germany; Michelle M. Richardson, USA; Matthew B. Rivara, USA; Glenda V. Roberts, USA; Pantelis A. Sarafidis, Greece; Rukshana Shroff, United Kingdom; Maria Fernanda Slon Roblero, Spain; Brendan Smyth, Australia; Henning Søndergaard, Denmark; Sabine N. Van Der Veer, United Kingdom; Joseph A. Vassalotti, USA; Marc G. Vervloet, Netherlands; Lloyd Vincent, Kenya; Rachael C. Walker, New Zealand; Madeleine Warren, United Kingdom; Betty Ann Waslynyuk, Canada; Melissa West, USA; and Caroline Wilkie, USA.

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