



Understanding and addressing symptoms for those with kidney failure managed conservatively, without dialysis: considerations and models of care

Emma Murphy^{1,2^}, Fliss E. M. Murtagh^{3^}

¹Centre for Care Excellence, Coventry University and University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK; ²Institute for Cardio-Metabolic Medicine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK; ³Wolfson Palliative Care Research Centre, Hull Medical School, University of Hull, Hull, UK

Contributions: (I) Conception and design: Both authors; (II) Administrative support: Both authors; (III) Provision of study materials or patients: Both authors; (IV) Collection and assembly of data: Both authors; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

Correspondence to: Dr. Emma Murphy, RN, PhD. Associate Clinical Professor of Nephrology Nursing, Centre for Care Excellence, Coventry University and University Hospitals Coventry and Warwickshire NHS Trust, 20032, 2nd Floor, Clinical Sciences Building, Clifford Bridge Road, Coventry CV2 2DX, UK; Institute for Cardio-Metabolic Medicine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK. Email: emma.murphy@uhcw.nhs.uk; Professor Fliss E. M. Murtagh, PhD, FRCP, MRCP, MBBS. Professor of Palliative Care and Director of the Wolfson Palliative Care Research Centre, Hull Medical School, University of Hull, Third Floor, Allam Medical Building, Cottingham Rd., Hull HU6 7RX, UK. Email: fliss.murtagh@hums.ac.uk.

Abstract: For those who have kidney failure and are managed conservatively without dialysis, symptoms are often prevalent, multiple, and troublesome. They interfere with quality of life, reduce wellbeing, and can affect family carers too. Symptoms can sometimes be difficult to manage, and—for professionals—they are often hard to assess and not always amenable to management with medications appropriate for use in kidney failure. Fatigue is one of the most common symptoms; alongside a general overview of symptoms in this population, we include a more detailed discussion of this often-neglected symptom. The solutions to the main symptoms experienced by those with kidney failure managed conservatively without dialysis lie in detailed assessment and monitoring of symptoms, working as a multi-disciplinary team to the maximum to draw on the full range of skills and expertise, and use of non-pharmacological, as well as pharmacological, approaches. Both nephrology and palliative care skills and expertise are important to optimise the recognition, assessment, and management of symptoms. There are few published descriptions of models of conservative kidney management (CKM) or supportive kidney care and there is a lack of evidence to suggest which model is most effective. We therefore consider the evidence on optimal models of CKM and make suggestions for best practice.

Keywords: Conservative kidney management (CKM); renal supportive care (RSC); symptom prevalence

Submitted May 16, 2023. Accepted for publication Apr 12, 2024. Published online Jun 17, 2024.

doi: 10.21037/apm-23-422

View this article at: <https://dx.doi.org/10.21037/apm-23-422>

[^] ORCID: Emma Murphy, 0000-0001-7992-9709; Fliss E. M. Murtagh, 0000-0003-1289-3726.

Introduction

Within developed countries, the kidney replacement therapy (KRT) population continues to rise, with a disproportionately greater increase among older people (1,2). For many of these patients, KRT may offer little in the way of survival, symptom, and quality of life benefits (3-5), especially for those who are older (75 or 80 years plus) with multiple medical conditions (6,7). For patients with kidney failure who are unlikely to receive a survival and/or quality of life advantage with dialysis, conservative kidney management (CKM) is now widely accepted as an alternative to dialysis. CKM includes a combination of palliative nephrology interventions and expertise; defined as 'planned holistic person-centred care for patients with stage 5 chronic kidney disease (CKD) and including a full range of treatment and support but not dialysis', also known as 'Enhanced Supportive Kidney Care' in the UK (8).

There is limited evidence on the incidence and prevalence of CKM, and national registry data (which traditionally focused on KRT) are lacking internationally (9). There are a number of potential reasons why it is challenging to quantify patients treated with CKM, including the lack of international consensus on the classification of CKM and cause of death coding in renal disease. However, in high-income countries, ~15% of patients known to kidney clinics are estimated to be managed with CKM (10,11). Population-based studies from Australia and Canada suggest that for every new patient who received KRT, there was one who did not with the majority of patients not receiving KRT aged ≥ 75 years (12,13). However, there is an important distinction to be made between those who choose CKM through shared decision-making, where patients and healthcare teams carefully consider the benefits and burdens of KRT, and those who receive 'choice-restricted CKM', where there is limited or no access to KRT (8). In the UK, CKM has been provided for over 20 years (5,14), however, the reported rates and components of conservative care vary greatly depending on where patients are being looked after (15,16) with variation in the quality of CKM (17) which likely relates to the limited evidence to guide clinical practice in this group.

Identifying symptoms

If we are to deliver planned holistic person-centred CKM (8), we must consider what matters most to patients. There is good evidence that many patients with advanced illness

prioritise person-centred care, including, improved quality of life, good symptom control, and family support over prolonging life at any cost (18-21). Patients with kidney failure experience a high prevalence of symptoms such as fatigue, pain, itch, restless legs, and breathlessness (22-24). Therefore, proactive symptom assessment using valid and clinically relevant symptom measures should be incorporated into routine clinical practice for all patients with kidney failure.

The Palliative (or Patient) Outcome Scale (POS-S Renal) (23) developed in the UK, is a Patient Reported Outcome Measure (PROM) (www.pos-pal.org). The Integrated Palliative (or Patient) Outcome Scale (IPOS-Renal) (25) is a further development in this family of measures, which assesses the patient's physical and psychological symptoms. It also allows clinicians to capture the patient's illness concerns, such as information needs and existential distress and has been validated in patients with kidney failure (26,27). It has the advantage of both patient and proxy versions, allowing for staff report when patients are unable to complete IPOS independently (28,29). Both the shorter symptom-focused POS-Renal and the more comprehensive IPOS-Renal have been widely recommended and adopted.

The modified Edmonton Symptom Assessment Scale (ESAS) (30) is a tool for the assessment of physical and psychological symptoms, adapted from the original ESAS measure and validated for patients with kidney failure managed with haemodialysis (31). It too has been widely adopted, especially in Canada and the USA (32), but also in Europe (33).

Overall symptom prevalence in CKM

There is increasing evidence on person-centred outcomes in CKM, and studies have demonstrated the extent and severity of symptom burden in this population (23,34). For more than 10 years, several studies have reported on the symptom prevalence in CKM through cross-sectional study designs utilising clinically relevant and valid measures of symptoms (23,33-35). While there is clear evidence that, in general, patients managed conservatively without dialysis experience a high symptom burden when interpreting the findings of cross-sectional data, it is important to consider the methodological limitations. Unlike longitudinal studies, cross-sectional studies do not follow individuals retrospectively or prospectively over time. However, the studies of the symptom prevalence have

been useful for taking a “snapshot” of the symptom burden that patients managed conservatively without dialysis may experience. They raise important questions and highlight the importance of detailed symptom assessment and management in clinical practice, as well as informing future study designs.

In the systematic review by O'Connor and Kumar (36), 13 studies were included in the analysis; 5 of the included studies (23,33–35,37) reported symptom burden in CKM studies and revealed high symptom prevalence. The most common symptoms identified were pain, lack of energy, oedema, weakness, drowsiness, dyspnoea, difficulty sleeping and pruritus. In addition, the total number of symptoms is high, with patients experiencing symptoms averaging 6.8–17 per patient. Two studies included a comparison group. Saini and colleagues compared symptom burden in CKM patients versus patients with terminal malignancy (33), using Memorial Symptom Assessment Scale-Short Form (MSAS-SF), and reported a mean number of symptoms similar in both groups. Young *et al.* directly compared dialysis and CKM with similar symptoms reported between the two groups (35). Four studies were cross-sectional in design (23,33–35), with one longitudinal study that determined symptom prevalence and severity in the month before death (37). The results on symptom burden in CKM should be interpreted with caution. First, the cross-sectional studies do not necessarily reflect how patients experience symptoms over time; second, heterogeneity in patient-reported outcome measures used to assess symptom burden limits the comparability of findings across studies; and third, there are often small sample sizes in the studies. Nevertheless, the findings clarify that patients managed conservatively have considerable symptom burden, and clinical services need to prioritise proactive assessment and management of symptoms.

Longitudinal studies of symptoms in CKM

Longitudinal perspectives on symptoms and other concerns provide important insights into the pattern of illness for patients managed conservatively without dialysis and may better inform their choice of treatment. Questions frequently asked by patients include: ‘What will happen at the end?’ and ‘What symptoms should I expect?’ (38). To answer such questions, Murtagh and colleagues undertook a longitudinal study of symptoms across three UK renal units (37), using the MSAS-SF with 74 CKM patients [mean age: 81 years; standard deviation (SD): 6.8] to identify the

most common symptoms experienced over time. Symptom data in the month before death were reported for 43 (88%) of the 49 patients who died during study follow-up (mean age: 81 years; SD: 5.7). The findings demonstrated considerable symptom burden in the last month of life, with a range of prevalent symptoms, including, lack of energy [86%; 95% confidence interval (CI): 73–94%], itch (84%; 70–93%), drowsiness (82%; 68–91%), dyspnoea (80%; 66–90%), poor concentration (76%; 61–87%), pain (73%; 59–85%), poor appetite (71%; 57–83%), swelling arms/legs (71%; 57–83%), dry mouth (69%; 55–82%), constipation (65%; 50–78%), and nausea (59%; 44–73%) (37). Physical and psychological symptom prevalence and the number of symptoms reported in the month before death were higher than in patients with advanced malignancy. In addition, it became clear that the longer-term persistence of symptoms, as well as the unpredictability of symptoms over time, added to the psychological burden of dealing with the advanced illness.

In a recent systematic review, Wong *et al.* reported the long-term outcomes among patients with kidney failure managed without dialysis across studies (39), revealing 41 cohort studies relating to 5,102 patients (study size range, 11–812 patients; mean age range, 60–87 years). Only four of these studies measured symptom burden (40–43). In one study (40) older patients managed with CKM reported an improvement in symptom burden over the 12-month study duration. In the longitudinal study by Murtagh and colleagues, symptom scores were generally stable until the last 3 months of life, when the symptom burden increased towards death (43).

These findings have important clinical implications for CKM patients. The importance of assessment and monitoring of symptoms as part of the model of care for those on CKM pathways becomes evident. Addressing, reviewing, and monitoring symptoms carefully and well is paramount. Knowledge of what symptoms a patient is likely to expect throughout their illness trajectory and towards death is also important for anticipatory care and planning ahead.

Evidence on comparative symptom prevalence between dialysis and CKM

Several systematic reviews have compared outcomes for patients on maintenance dialysis versus CKM (7,36,39,44–47). Whilst there is good evidence that in general, patients who opt for dialysis have a lower mortality risk compared with patients managed conservatively (6,47), this survival

advantage associated with dialysis decreases in the presence of severe comorbidities and older age. Few comparative studies have included person-centred outcomes such as quality of life and symptom burden. Considering the evidence on person-centred priorities in advanced illness, the decision whether to pursue a KRT plan or CKM will be informed by detailed communication of the evidence on symptoms and quality of life rather than survival alone. A key question (alongside questions about survival), therefore, is whether there are symptom advantages associated with CKM versus KRT.

The systematic review by Buur and colleagues (7), whilst ostensibly focusing on survival and quality of life, included secondary outcomes of hospitalisation, symptom burden and place of death, in CKM versus dialysis. Five out of the 25 primary studies reported comparative symptom prevalence data (35,40,48-50) and concluded that, regarding symptom burden, CKM may have advantages. However, the included studies were all observational in design and of varying quality, and findings were limited by heterogeneity. It is therefore important to consider the risks of generalisability and bias when interpreting the results. The results regarding symptom burden were conflicting; however, in general, the findings suggest that for person-centred outcomes such as symptoms and quality of life, CKM offers an advantage compared to dialysis.

A systematic review of symptom prevalence and health-related quality of life (HRQoL) in patients with kidney failure managed conservatively versus dialysis (44) identified 11 observational studies, comprising 1,718 older people with kidney failure (with no randomised controlled trials). Nine of the included studies (35,40,41,48,50-54) compared symptoms of pain, anxiety, cognitive function, sleep, and depression by overall symptom scores. In contrast to the findings of Buur and colleagues, they concluded that no advantage was found concerning symptom burden in CKM versus dialysis. The findings suggest that symptom burden is high in patients managed conservatively and those on dialysis, emphasising the need for detailed symptom assessment and management across both treatments.

It is therefore hard to draw clear conclusions about symptom burden with CKM versus dialysis, except to say that there is no clear evidence—despite a range of studies—that symptoms are worse with CKM; they may be similar, or they may be better—it is uncertain. High-quality data regarding person-centred outcomes is lacking. One large randomised controlled trial—The Prepare for Kidney Care Study, examining this area is currently undergoing in the

UK (55).

Prevalence of fatigue or tiredness

Fatigue or tiredness is highly prevalent in patients with kidney failure (24,56) and can adversely influence quality of life (57). The pathogenesis of fatigue in kidney failure is multifactorial. One of the principal causes is anaemia, which is associated with fatigue, impaired quality of life, an increase in hospitalisations, and mortality (58-61). Erythropoiesis-stimulating agents (ESAs), acting to replace endogenous erythropoietin, have been demonstrated to improve quality of life (62-64). In current practice, the use of ESAs and iron therapies are the mainstays of treatment in patients with anaemia in advanced kidney disease and are not limited to patients on KRT but have extended to those on CKM (8,65). In a previous national survey of UK practice patterns in CKM, all renal units reported that they provided erythropoietin and iron therapy for patients with anaemia managed conservatively without dialysis (15,16). Despite anaemia management being a key component of CKM, the benefit and the best target level for this group are not clear.

As patients approach kidney failure, deciding between CKM and KRT can be complex, clinicians therefore, need to understand and communicate the evidence on a range of outcomes, including symptoms to facilitate shared decision-making. The recent systematic review of HRQoL and symptom burden in dialysis versus CKM revealed nine observational studies reporting evidence on symptoms (44). In two studies, a higher prevalence of dyspnoea in patients managed with CKM than in patients on KRT was observed, potentially caused by increasing oedema and/or anaemia (35,48). In patients managed conservatively, it is not known if there is a relationship between haemoglobin levels and various quality-of-life domains, including symptoms. However, in the dialysis population, the impact of anaemia has been well described (66,67) and is associated with a lower HRQoL (66,68-71). Most studies on ESAs involve patients in the pre-dialysis (non-dialysis) phase or receiving dialysis, therefore, there is limited evidence to guide anaemia management in CKM to help alleviate fatigue or when to discontinue ESA treatment as end-of-life approaches.

In contrast to the situation for patients on dialysis, there are only limited data available regarding the effects of anaemia treatment on Hb level and symptom burden in patients managed conservatively. A small retrospective study recruited patients with glomerular filtration rate (GFR) <15 mL/min/1.73 m² managed conservatively without

dialysis; 39 patients received ESAs while 31 controls did not. In the study, most patients were older, and about half of them had diabetes mellitus. Patients in both the ESA and control groups had low baseline haemoglobin levels (7.6 and 7.8 g/dL respectively). In the ESA group, there was a significant rise in haemoglobin and fatigue score from baseline as well as a reduction in all-cause hospitalisation (72). However, more substantive and robust evidence is needed to guide anaemia practice in patients managed conservatively without dialysis.

Current evidence on the use of ESAs in CKM is mostly derived from studies in pre-dialysis or dialysis patients. However, this trial evidence relates to people who tend to be younger than people managed conservatively, with lower comorbidity. Many older people with poorer function and additional comorbidities opt for CKM instead of dialysis (6). They will usually be treated with an ESA per guidelines for anaemia management in KRT, although there is little evidence on the best target haemoglobin levels for this relatively older group of people with higher comorbidity and poorer functional status. In addition, the goal of anaemia management in CKM is to improve symptoms (8), as opposed to focusing on haemoglobin levels and reducing cardiac mortality or morbidity as in the dialysis population. It is, therefore, important to consider quality of life, symptoms, and burden of treatment, as well as the benefits and risks, when deciding on an anaemia treatment plan in CKM. It is also important to consider the frequency of monitoring, as blood and iron management may be more problematic in CKM given their infrequent outpatient visits compared to patients receiving KRT. Whilst anaemia management is a key component of conservative kidney care (8,15), the lack of evidence-based guidelines leaves room for practice variation in anaemia treatment and haemoglobin targets of ESA therapy.

Little is known about the prevalence of anaemia in patients managed conservatively. A retrospective single-centre observational cohort study compared patients with kidney failure managed in a renal supportive care (RSC) programme and patients receiving standard conservative therapy (73). There was a significantly lower haemoglobin level in the RSC group *vs.* the non-RSC group Hb (102 *vs.* 111 g/L). One potential reason for the referral of patients to RSC is the presence of complex symptoms this is suggested by the lower haemoglobin in the RSC group, which is associated with a higher symptom burden. In addition, the prevalence of anaemia increases as renal function (estimated GFR) falls (74), therefore, patients managed conservatively without dialysis may experience significant symptom burden

associated with anaemia over time. Published longitudinal descriptions on the prevalence and practice patterns of anaemia management in CKM are scarce, and further research is needed. Therefore, in the absence of robust evidence, anaemia management in CKM will vary, based on clinical consensus, and evidence from studies in pre-dialysis or patients receiving KRT.

Qualitative studies of CKM

Quantifying symptom prevalence and associated demographic and medical factors in CKM does not address the question of how patients experience symptoms and their impact. Qualitative studies provide a lens through which to understand and interpret how patients experience symptoms. While cross-sectional survey-based studies capture the severity and frequency of symptoms, they cannot explain the experience or meaning of these symptoms from patient and/or family perspectives. Qualitative research has potential value in the advancement of CKM and in helping to inform optimal models of care by focusing on the behaviours, understandings, and lived experiences of those in receipt of CKM.

The qualitative study by Bristowe and colleagues explored symptom-related experiences, examining the impact of kidney failure over time in patients managed with CKM, and their understanding of the illness (75) using in-depth interviews with 20 people living with renal disease (mean age 82 years, range, 69–95 years). Participants described the challenges of living with kidney disease, reporting the illness as ‘invisible’ and ‘intangible’, as well as the considerable challenges of the unpredictable course of symptoms over time. This invisibility and intangibility impacted heavily on their daily lives, and they struggled with attributing symptoms, and, therefore, seeking professional help. Not knowing if the symptoms were caused by aging or by co-morbid illness contributed to their sense of disconnectedness from their diagnosis of kidney failure. A further useful qualitative study of the symptom experience in patients with stage 4–5 CKD (non-dialysis) (76), found that patients experienced a very wide range of symptoms. Symptoms were classified into physical symptoms, e.g., fatigue and sleep disturbance, and psychological symptoms, especially forgetfulness or a sensation of gradually slowing down. Similar to the study by Bristowe *et al.*, patients indicated that they frequently found it hard to report their symptoms to renal clinicians.

These qualitative studies illuminate the quantitative

findings on symptom prevalence in CKM and emphasise the need for routine and proactive symptom assessment in clinical practice. If we are to manage symptoms effectively, we must understand the emotional impact and meaning of symptoms and illness for the individual and their family. Emphasising psychological, social, and spiritual or existential domains alongside physical symptoms is critical. Dame Cicely Saunders, the founder of the modern hospice movement, coined the term ‘total pain’ encompassing the whole experience of pain as a symptom in patients with cancer, including physical, social, and spiritual components. Similarly, patients with advanced CKD may experience various symptoms across all these dimensions, affecting all aspects of their lives. There is a need for improved communication and assessment of symptoms in CKM, to recognise the invisibility, intangibility, and the sense of disconnectedness from their kidney failure, and address this through targeted interventions focusing on physical, psychological, and spiritual symptoms and concerns.

CKM models of care

There are few published descriptions of models of CKM, or supportive kidney care, and details of operationalising a supportive kidney care programme and the efficacy across different models are lacking. Classification systems for the different types of supportive kidney care programmes have been proposed (77,78). Drawing on these classification systems, in the recently published textbook ‘Palliative Care in Nephrology’, Lupu and Murphy (79) outline six innovative types of supportive kidney care programmes that have emerged internationally. These include:

- ❖ Embedded programmes with the provision of integrated supportive kidney care within nephrology services, usually led by a nephrologist or nephrology nurse with training in palliative care;
- ❖ Visiting palliative care teams, where specialist palliative care teams provide services to nephrology. They are integrated but two functionally separate teams;
- ❖ CKD case management programmes with an emphasis on case management of patients upstream in the illness trajectory;
- ❖ Medical management without dialysis programmes or CKM programmes which focus on shared decision-making, symptom assessment and management, advance care planning, spiritual, social, and psychological support;
- ❖ Concurrent hospice and dialysis programmes (relevant

to the United States) which aim to promote timely hospice and palliative care services for dialysis patients;

- ❖ Comprehensive regional or system-wide programmes integrated into kidney care. An example of this is the comprehensive supportive care programme in Alberta, Canada (80).

There is, however, a lack of evidence to suggest which of these programmes is most effective, and to our knowledge, there are no systematic comparisons on the efficacy of supportive kidney care models in the literature.

The development of supportive kidney care programmes requires careful consideration of local staffing and resources. In the UK, most renal units provide CKM, and closely resembles the embedded programme, nevertheless, the provision, organisation, and funding of CKM vary widely. In a national survey of practice patterns in UK renal units in the use of dialysis and conservative management—CKMAPPS (15,16), only 10 of 65 renal units had funding for CKM provision. The availability of funding was significantly related to higher numbers of CKM patients ($P=0.009$), and renal units without CKM funding were significantly less likely to have clinicians with dedicated time in their roles for CKM ($P=0.002$). However, 68% of units that had dedicated staff did not have any CKM funding, suggesting that a high proportion of renal units are providing CKM as part of their existing advanced kidney care clinical services. Two-thirds [43 of 65 (66%)] of renal units had a single-person or small team primarily responsible for CKM all were consultant nephrologists and/or renal nurses. This study demonstrated the widespread use of CKM in nephrology services in the UK; however, practice patterns varied across units. The authors therefore made recommendations to facilitate the development and assessment of CKM services, including, but not limited to, an agreed definition of CKM, training and education for renal clinicians in supportive and palliative care and provision of funding for CKM.

A white paper from the Coalition for Supportive Care for Kidney Patients described the experience of 16 supportive kidney care programmes globally. Programme leaders identified facilitators of success as: providing palliative care training to nephrology staff; collaborative working between nephrology and palliative care teams; identifying local supportive kidney care champions to lead change; national clinical practice guidelines; and conducting research to improve evidence-based care. Barriers to success ranged from resource and staff issues to cultural attitudes in nephrology. The participants identified that

the technological and disease focus in nephrology can be challenging to change as the end of life nears (81).

Individual CKM models have demonstrated improved person-centred outcomes (82,83), however, there are no comparative studies of the impact and outcomes of different programmes. Supportive kidney care interventions can significantly decrease the number and length of hospitalisations (73), establish and meet the preferred place of care at the end of life (82) and reduce symptom burden (40). Until recently, end-of-life care for patients with kidney failure has largely been in acute hospital settings; this has the potential to change as conservative management programmes expand and home deaths increase (83).

There remains a lack of evidence favouring any of these models of supportive kidney care over another, or which model is most effective or cost-effective. However, whichever model is adopted, proactive and detailed assessment and monitoring of symptoms by a palliative nephrology multi-professional team is the best option based on current evidence and clinical experience.

Future research should focus on:

- ❖ Longitudinal studies on symptoms and quality of life have the potential to provide important insights into the pattern of illness for CKM patients and may better inform their choice of treatment.
- ❖ High-quality data regarding person-centred outcomes in CKM versus dialysis is lacking, although one large randomised controlled trial—The Prepare for Kidney Care Study—examining this area is underway in the UK (55).
- ❖ Descriptions of models of CKM with details of operationalising a supportive kidney care programme and the efficacy of different models is needed.
- ❖ More substantive and robust evidence is needed to guide anaemia practice (including use of ESAs) in patients managed conservatively without dialysis.

Conclusions

There is increasing recognition among health services and clinicians of the complexity and challenges of delivering effective CKM. The palliative and supportive care needs of this population have become more prominent as the age and comorbid burden increase, and more patients may choose or be advised not to initiate dialysis therapy. Specialist palliative care services alone will not meet this growing demand and nephrology communities need to develop strategies for integrating palliative care components alongside nephrology

care, building palliative care collaborations, capacity, and capability within nephrology teams to deliver high-quality person-centred kidney care. This paper outlines the current evidence on the identification of symptoms, symptom prevalence (in particular, the sometimes-neglected symptom of fatigue and the management of anaemia), and evidence regarding models of supportive kidney care, including the gaps in that evidence, in order to deliver high-quality palliative and supportive care for those with advanced CKD.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editors (Kwok Ying Chan and Desmond Y. H. Yap) for the series “Kidney Palliative Care: Accessibility and Clinical Outcomes” published in *Annals of Palliative Medicine*. The article has undergone external peer review.

Peer Review File: Available at <https://apm.amegroups.com/article/view/10.21037/apm-23-422/prf>

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-23-422/coif>). The series “Kidney Palliative Care: Accessibility and Clinical Outcomes” was commissioned by the editorial office without any funding or sponsorship. F.E.M.M. is co-lead of the UK Kidney Association research workgroup of the Supportive Care Special Interest Group. F.E.M.M. is also a National Institute for Health and Care Research (NIHR) Senior Investigator. The views expressed in this article are those of the author(s) and not necessarily those of the NIHR, or the UK Department of Health and Social Care. E.M. is an Executive Committee Member of the Association of Nephrology Nurses UK. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons

Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Gilg J, Caskey F, Fogarty D. UK Renal Registry 18th Annual Report: Chapter 1 UK Renal Replacement Therapy Incidence in 2014: National and Centre-specific Analyses. *Nephron* 2016;132 Suppl 1:9-40.
2. Pippias M, Jager KJ, Kramer A, et al. The changing trends and outcomes in renal replacement therapy: data from the ERA-EDTA Registry. *Nephrol Dial Transplant* 2016;31:831-41.
3. Jassal SV, Watson D. Dialysis in late life: benefit or burden. *Clin J Am Soc Nephrol* 2009;4:2008-12.
4. Jassal SV, Chiu E, Hladunewich M. Loss of independence in patients starting dialysis at 80 years of age or older. *N Engl J Med* 2009;361:1612-3.
5. Chandna SM, Da Silva-Gane M, Marshall C, et al. Survival of elderly patients with stage 5 CKD: comparison of conservative management and renal replacement therapy. *Nephrol Dial Transplant* 2011;26:1608-14.
6. Foote C, Kotwal S, Gallagher M, et al. Survival outcomes of supportive care versus dialysis therapies for elderly patients with end-stage kidney disease: A systematic review and meta-analysis. *Nephrology (Carlton)* 2016;21:241-53.
7. Buur LE, Madsen JK, Eidemak I, et al. Does conservative kidney management offer a quantity or quality of life benefit compared to dialysis? A systematic review. *BMC Nephrol* 2021;22:307.
8. Davison SN, Levin A, Moss AH, et al. Executive summary of the KDIGO Controversies Conference on Supportive Care in Chronic Kidney Disease: developing a roadmap to improving quality care. *Kidney Int* 2015;88:447-59.
9. Bello AK, Levin A, Lunney M et al. Global Kidney Health Atlas: A report by the International Society of Nephrology on the Global Burden of End-stage Kidney Disease and Capacity for Kidney Replacement Therapy and Conservative Care across World Countries and Regions. Brussels, Belgium: International Society of Nephrology, 2019.
10. Morton RL, Howard K, Webster AC, et al. Patient Information about Options for Treatment (PINOT): a prospective national study of information given to incident CKD Stage 5 patients. *Nephrol Dial Transplant* 2011;26:1266-74.
11. van de Luijngaarden MW, Noordzij M, van Biesen W, et al. Conservative care in Europe--nephrologists' experience with the decision not to start renal replacement therapy. *Nephrol Dial Transplant* 2013;28:2604-12.
12. Sparke C, Moon L, Green F, et al. Estimating the total incidence of kidney failure in Australia including individuals who are not treated by dialysis or transplantation. *Am J Kidney Dis* 2013;61:413-9.
13. Hemmelgarn BR, James MT, Manns BJ, et al. Rates of treated and untreated kidney failure in older vs younger adults. *JAMA* 2012;307:2507-15.
14. Murtagh FE, Murphy E, Shepherd KA, et al. End-of-life care in end-stage renal disease: renal and palliative care. *Br J Nurs* 2006;15:8-11.
15. Roderick P, Rayner H, Tonkin-Crine S, et al. A national study of practice patterns in UK renal units in the use of dialysis and conservative kidney management to treat people aged 75 years and over with chronic kidney failure. Southampton (UK): NIHR Journals Library; April 2015.
16. Okamoto I, Tonkin-Crine S, Rayner H, et al. Conservative care for ESRD in the United Kingdom: a national survey. *Clin J Am Soc Nephrol* 2015;10:120-6.
17. Lunney M, Bello AK, Levin A, et al. Availability, Accessibility, and Quality of Conservative Kidney Management Worldwide. *Clin J Am Soc Nephrol* 2020;16:79-87.
18. Higginson IJ, Gomes B, Calanzani N, et al. Priorities for treatment, care and information if faced with serious illness: a comparative population-based survey in seven European countries. *Palliat Med* 2014;28:101-10.
19. Steinhauser KE, Christakis NA, Clipp EC, et al. Preparing for the end of life: preferences of patients, families, physicians, and other care providers. *J Pain Symptom Manage* 2001;22:727-37.
20. Parker SM, Clayton JM, Hancock K, et al. A systematic review of prognostic/end-of-life communication with adults in the advanced stages of a life-limiting illness: patient/caregiver preferences for the content, style, and timing of information. *J Pain Symptom Manage* 2007;34:81-93.
21. Morton RL, Snelling P, Webster AC, et al. Factors influencing patient choice of dialysis versus conservative care to treat end-stage kidney disease. *CMAJ* 2012;184:E277-83.
22. Davison SN. Pain in hemodialysis patients: prevalence,

- cause, severity, and management. *Am J Kidney Dis* 2003;42:1239-47.
23. Murphy EL, Murtagh FE, Carey I, et al. Understanding symptoms in patients with advanced chronic kidney disease managed without dialysis: use of a short patient-completed assessment tool. *Nephron Clin Pract* 2009;111:c74-80.
 24. Murtagh FE, Addington-Hall J, Higginson IJ. The prevalence of symptoms in end-stage renal disease: a systematic review. *Adv Chronic Kidney Dis* 2007;14:82-99.
 25. Murtagh FE, Ramsenthaler C, Firth A, et al. A brief, patient- and proxy-reported outcome measure in advanced illness: Validity, reliability and responsiveness of the Integrated Palliative care Outcome Scale (IPOS). *Palliat Med* 2019;33:1045-57.
 26. Raj R, Ahuja K, Frandsen M, et al. Validation of the IPOS-Renal Symptom Survey in Advanced Kidney Disease: A Cross-sectional Study. *J Pain Symptom Manage* 2018;56:281-7.
 27. Moskovitch JT, Mount PF, Davies MRP. Changes in Symptom Burden in Dialysis Patients Assessed Using a Symptom-Reporting Questionnaire in Clinic. *J Palliat Care* 2020;35:59-65.
 28. Breckenridge K, Bekker HL, Gibbons E, et al. How to routinely collect data on patient-reported outcome and experience measures in renal registries in Europe: an expert consensus meeting. *Nephrol Dial Transplant* 2015;30:1605-14.
 29. Morton RL, Lioufas N, Dansie K, et al. Use of patient-reported outcome measures and patient-reported experience measures in renal units in Australia and New Zealand: A cross-sectional survey study. *Nephrology (Carlton)* 2020;25:14-21.
 30. Davison SN, Jhangri GS, Johnson JA. Cross-sectional validity of a modified Edmonton symptom assessment system in dialysis patients: a simple assessment of symptom burden. *Kidney Int* 2006;69:1621-5.
 31. Davison SN, Jhangri GS, Johnson JA. Longitudinal validation of a modified Edmonton symptom assessment system (ESAS) in haemodialysis patients. *Nephrol Dial Transplant* 2006;21:3189-95.
 32. Davison SN, Klarenbach S, Manns B, et al. Patient-reported outcome measures in the care of in-centre hemodialysis patients. *J Patient Rep Outcomes* 2021;5:93.
 33. Saini T, Murtagh FE, Dupont PJ, et al. Comparative pilot study of symptoms and quality of life in cancer patients and patients with end stage renal disease. *Palliat Med* 2006;20:631-6.
 34. Murtagh FE, Addington-Hall JM, Edmonds PM, et al. Symptoms in advanced renal disease: a cross-sectional survey of symptom prevalence in stage 5 chronic kidney disease managed without dialysis. *J Palliat Med* 2007;10:1266-76.
 35. Yong DS, Kwok AO, Wong DM, et al. Symptom burden and quality of life in end-stage renal disease: a study of 179 patients on dialysis and palliative care. *Palliat Med* 2009;23:111-9.
 36. O'Connor NR, Kumar P. Conservative management of end-stage renal disease without dialysis: a systematic review. *J Palliat Med* 2012;15:228-35.
 37. Murtagh FE, Addington-Hall J, Edmonds P, et al. Symptoms in the month before death for stage 5 chronic kidney disease patients managed without dialysis. *J Pain Symptom Manage* 2010;40:342-52.
 38. Murtagh FE, Murphy E, Sheerin NS. Illness trajectories: an important concept in the management of kidney failure. *Nephrol Dial Transplant* 2008;23:3746-8.
 39. Wong SPY, Rubenzik T, Zelnick L, et al. Long-term Outcomes Among Patients With Advanced Kidney Disease Who Forgo Maintenance Dialysis: A Systematic Review. *JAMA Netw Open* 2022;5:e222255.
 40. Brown MA, Collett GK, Josland EA, et al. CKD in elderly patients managed without dialysis: survival, symptoms, and quality of life. *Clin J Am Soc Nephrol* 2015;10:260-8.
 41. Da Silva-Gane M, Wellsted D, Greenshields H, et al. Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. *Clin J Am Soc Nephrol* 2012;7:2002-9.
 42. Kilshaw L, Sammut H, Asher R, et al. A study to describe the health trajectory of patients with advanced renal disease who choose not to receive dialysis. *Clin Kidney J* 2016;9:470-5.
 43. Murtagh FE, Sheerin NS, Addington-Hall J, et al. Trajectories of illness in stage 5 chronic kidney disease: a longitudinal study of patient symptoms and concerns in the last year of life. *Clin J Am Soc Nephrol* 2011;6:1580-90.
 44. Verberne WR, van den Wittenboer ID, Voorend CGN, et al. Health-related quality of life and symptoms of conservative care versus dialysis in patients with end-stage kidney disease: a systematic review. *Nephrol Dial Transplant* 2021;36:1418-33.
 45. Fu R, Sekercioglu N, Mathur MB, et al. Dialysis Initiation and All-Cause Mortality Among Incident Adult Patients With Advanced CKD: A Meta-analysis With Bias Analysis. *Kidney Med* 2020;3:64-75.e1.
 46. Wongrakpanich S, Susantitaphong P, Isaranuwachai S,

- et al. Dialysis Therapy and Conservative Management of Advanced Chronic Kidney Disease in the Elderly: A Systematic Review. *Nephron* 2017;137:178-89.
47. Voorend CGN, van Oevelen M, Verberne WR, et al. Survival of patients who opt for dialysis versus conservative care: a systematic review and meta-analysis. *Nephrol Dial Transplant* 2022;37:1529-44.
 48. Tan T, Brennan F, Brown MA. Impact of dialysis on symptom burden and functional state in the elderly. *Renal Society of Australasia Journal* 2017;13:22-30.
 49. Almutary H, Bonner A, Douglas C. Which patients with chronic kidney disease have the greatest symptom burden? A comparative study of advanced ckd stage and dialysis modality. *J Ren Care* 2016;42:73-82.
 50. Shah KK, Murtagh FEM, McGeechan K, et al. Health-related quality of life and well-being in people over 75 years of age with end-stage kidney disease managed with dialysis or comprehensive conservative care: a cross-sectional study in the UK and Australia. *BMJ Open* 2019;9:e027776.
 51. Seow YY, Cheung YB, Qu LM, et al. Trajectory of quality of life for poor prognosis stage 5D chronic kidney disease with and without dialysis. *Am J Nephrol* 2013;37:231-8.
 52. Verberne WR, Dijkers J, Kelder JC, et al. Value-based evaluation of dialysis versus conservative care in older patients with advanced chronic kidney disease: a cohort study. *BMC Nephrol* 2018;19:205.
 53. De Biase V, Tobaldini O, Boaretti C, et al. Prolonged conservative treatment for frail elderly patients with end-stage renal disease: the Verona experience. *Nephrol Dial Transplant* 2008;23:1313-7.
 54. Iyasere O, Brown EA, Johansson L, et al. Quality of life with conservative care compared with assisted peritoneal dialysis and haemodialysis. *Clin Kidney J* 2018;12:262-8.
 55. Murphy E, Burns A, Murtagh FEM, et al. The Prepare for Kidney Care Study: prepare for renal dialysis versus responsive management in advanced chronic kidney disease. *Nephrol Dial Transplant* 2021;36:975-82.
 56. Karakan S, Sezer S, Ozdemir FN. Factors related to fatigue and subgroups of fatigue in patients with end-stage renal disease. *Clin Nephrol* 2011;76:358-64.
 57. Lowney AC, Myles HT, Bristowe K, et al. Understanding What Influences the Health-Related Quality of Life of Hemodialysis Patients: A Collaborative Study in England and Ireland. *J Pain Symptom Manage* 2015;50:778-85.
 58. Stevens LA, Levin A. Anaemia, cardiovascular disease and kidney disease: integrating new knowledge in 2002. *Curr Opin Nephrol Hypertens* 2003;12:133-8.
 59. Drozd M, Weigert A, Silva F, et al. Achievement of renal anemia KDIGO targets by two different clinical strategies - a European hemodialysis multicenter analysis. *BMC Nephrol* 2019;20:5.
 60. Macdougall IC, White C, Anker SD, et al. Intravenous Iron in Patients Undergoing Maintenance Hemodialysis. *N Engl J Med* 2019;380:447-58.
 61. Wetmore JB, Li S, Yan H, et al. Predialysis anemia management and outcomes following dialysis initiation: A retrospective cohort analysis. *PLoS One* 2018;13:e0203767.
 62. Bárány P, Pettersson E, Konarski-Svensson JK. Long-term effects on quality of life in haemodialysis patients of correction of anaemia with erythropoietin. *Nephrol Dial Transplant* 1993;8:426-32.
 63. McMurray J, Parfrey P, Adamson J, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl* 2012;2:279-335.
 64. Revicki DA, Brown RE, Feeny DH, et al. Health-related quality of life associated with recombinant human erythropoietin therapy for predialysis chronic renal disease patients. *Am J Kidney Dis* 1995;25:548-54.
 65. Cheng HW, Chan KY, Lau HT, et al. Use of Erythropoietin-Stimulating Agents (ESA) in Patients With End-Stage Renal Failure Decided to Forego Dialysis: Palliative Perspective. *Am J Hosp Palliat Care* 2017;34:380-4.
 66. Finkelstein FO, Story K, Firaneck C, et al. Health-related quality of life and hemoglobin levels in chronic kidney disease patients. *Clin J Am Soc Nephrol* 2009;4:33-8.
 67. Kimel M, Leidy NK, Mannix S, et al. Does epoetin alfa improve health-related quality of life in chronically ill patients with anemia? Summary of trials of cancer, HIV/AIDS, and chronic kidney disease. *Value Health* 2008;11:57-75.
 68. Lefebvre P, Vekeman F, Sarokhan B, et al. Relationship between hemoglobin level and quality of life in anemic patients with chronic kidney disease receiving epoetin alfa. *Curr Med Res Opin* 2006;22:1929-37.
 69. Alexander M, Kewalramani R, Agodoa I, et al. Association of anemia correction with health related quality of life in patients not on dialysis. *Curr Med Res Opin* 2007;23:2997-3008.
 70. Hansen RA, Chin H, Blalock S, et al. Predialysis chronic kidney disease: evaluation of quality of life in clinic patients receiving comprehensive anemia care. *Res Social Adm Pharm* 2009;5:143-53.

71. Leaf DE, Goldfarb DS. Interpretation and review of health-related quality of life data in CKD patients receiving treatment for anemia. *Kidney Int* 2009;75:15-24.
72. Chan KY, Li CW, Wong H, et al. Effect of erythropoiesis-stimulating agents on hemoglobin level, fatigue and hospitalization rate in renal palliative care patients. *Int Urol Nephrol* 2014;46:653-7.
73. Chia XX, Johnston R, Aggarwal R, et al. Renal supportive care programs: An observational study assessing impact on hospitalization and survival outcomes. *Nephrology (Carlton)* 2021;26:522-9.
74. Astor BC, Muntner P, Levin A, et al. Association of kidney function with anemia: the Third National Health and Nutrition Examination Survey (1988-1994). *Arch Intern Med* 2002;162:1401-8.
75. Bristowe K, Selman LE, Higginson IJ, et al. Invisible and intangible illness: a qualitative interview study of patients' experiences and understandings of conservatively managed end-stage kidney disease. *Ann Palliat Med* 2019;8:121-9.
76. Pugh-Clarke K, Read SC, Sim J. Symptom experience in non-dialysis-dependent chronic kidney disease: A qualitative descriptive study. *J Ren Care* 2017;43:197-208.
77. Purtell L, Sowa PM, Berquier I, et al. The Kidney Supportive Care programme: characteristics of patients referred to a new model of care. *BMJ Support Palliat Care* 2018;bmjspcare-2018-001630.
78. Lam DY, Scherer JS, Brown M, et al. A Conceptual Framework of Palliative Care across the Continuum of Advanced Kidney Disease. *Clin J Am Soc Nephrol* 2019;14:635-41.
79. Lupu DE, Murphy E. Models for operationalizing supportive care in kidney care. In: Moss AH, Lupu DE, Armistead NC, et al., editors. *Palliative Care in Nephrology*. First Edition. Oxford University Press; 2020:36-45.
80. Davison SN, Tupala B, Wasylynuk BA, et al. Recommendations for the Care of Patients Receiving Conservative Kidney Management: Focus on Management of CKD and Symptoms. *Clin J Am Soc Nephrol* 2019;14:626-34.
81. Lupu D, Nyirenda J. Creating supportive nephrology programs: lessons learned around the world. Coalition of Supportive Cre of Kidney Patients, 2018. Available online: <https://go.gwu.edu/creatingkidneysupportivecareprograms>. Accessed 16 May 2023.
82. Harrison JK, Clipsham LE, Cooke CM, et al. Establishing a supportive care register improves end-of-life care for patients with advanced chronic kidney disease. *Nephron* 2015;129:209-13.
83. Lovell N, Jones C, Baynes D, et al. Understanding patterns and factors associated with place of death in patients with end-stage kidney disease: A retrospective cohort study. *Palliat Med* 2017;31:283-8.

Cite this article as: Murphy E, Murtagh FEM. Understanding and addressing symptoms for those with kidney failure managed conservatively, without dialysis: considerations and models of care. *Ann Palliat Med* 2024;13(4):991-1001. doi: 10.21037/apm-23-422