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Conservative vs. preservative management of chronic kidney disease: similarities and distinctions

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Purpose of review
Dialysis has been the prevailing treatment paradigm in advanced chronic kidney disease (CKD) for patients ineligible for or unlikely to receive kidney transplantation. As dialysis may neither offer survival benefit nor improved quality of life in certain groups, there has been increasing interest in conservative management as an alternative approach.

Recent findings
Experts and workgroups suggest the main goals of conservative management are to optimize quality of life, treat symptoms of end-stage renal disease without dialysis or transplant, and improve survival and cardiovascular health. Given the implications of preserved kidney function on clinical outcomes, preservative management has been proposed as an integral component of conservative management. Growing evidence suggests the survival benefit of dialysis vs. conservative management without dialysis is marginal or even reversed in certain subpopulations (elderly, multimorbid, cardiovascular disease). Limited data suggest that conservative and preservative management is associated with equivalent to more favorable trajectories of health-related quality of life and symptom burden over time as opposed to dialysis.

Summary
Whereas existing data suggest conservative management is a viable patient-centered treatment strategy, further research is needed to determine the comparative effectiveness of preservative kidney management vs. dialysis or palliative management, as well as which patient subgroups will most benefit from these treatment strategies.

Keywords
comorbid, conservative management, dialysis-free, elderly, end-stage renal disease, nondialysis

INTRODUCTION

Since 1972, the Medicare End-Stage Renal Disease (ESRD) Program has led to near-universal access to dialysis as a means to extend the survival of non-dialysis-dependent chronic kidney disease (NDD-CKD) patients progressing to ESRD [1,2]. Each year, over 120 000 advanced NDD-CKD patients in the United States (US) transition to dialysis as the dominant treatment paradigm for uremic, biochemical, and volume derangements [3–5]. Many of these patients are in fact ineligible for kidney transplantation because of older age and/or comorbidity burden (less than 3% of incident ESRD patients undergo kidney transplantation) [3]. As dialysis may have marginal to no survival benefit or even survival disadvantage in certain subpopulations (elderly, multimorbid) [6–9], there has been growing interest in the conservative management of advanced CKD, defined as 'treat[ment] of kidney failure without dialysis or transplant', and which encompasses management of ESRD complications, preservation of residual kidney function, and optimization of health-related quality of life, as a viable treatment strategy [10]. In this review, we will discuss trends in the incident ESRD population, outcomes data in patients transitioning to dialysis, conservative and

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KEY POINTS

- As dialysis may have marginal survival benefit in certain subpopulations (i.e. elderly, multimorbid), there has been growing interest in the conservative management of advanced CKD.
- Conservative management focuses upon nondialytic management of ESRD complications, preservation of remaining kidney function, and optimization of health-related quality of life, patient longevity, and cardiovascular health.
- Given the clinical implications of preserved kidney function upon patients' solute clearance, fluid balance, uremia control, health-related quality of life, nutritional status, and survival, preservative management of remaining kidney function in advanced CKD patients is an integral component of the conservative nondialytic treatment of this population.

preservative management without dialysis as an alternative treatment strategy for advanced CKD and which is distinct from traditional palliative and supportive care, and existing data on the comparative effectiveness of conservative management vs. dialysis in this population.

AN AGING AND AILING END-STAGE RENAL DISEASE POPULATION

In the United States, approximately 11% of the population (30 million adults) has CKD [3], with prevalence estimates as high as 30% in elderly patients [11,12]. Epidemiologic data show that the most rapid rates of ESRD growth are occurring in patients at least 75 years of age [13,14], which parallels trends observed in the broader non-CKD population. These upward trends in age have been met with an increasing prevalence of chronic diseases (cardiovascular disease, malignancy, cognitive impairment) in incident ESRD patients, which may preclude kidney transplantation [14,15]. Additional barriers to transplantation in the elderly may include long wait times depending on geographic area, lack of potential living donors, and presence of high levels of broadly reactive antibodies. Furthermore, dialysis as an alternative renal replacement therapy option may not per se improve survival in the elderly population.

These observations have also been corroborated in the 'Transitions of Care in CKD' (TC-CKD) United States Renal Data System (USRDS) Special Study that has been centered on investigating the characteristics, trajectories, and outcomes of US Veterans with advanced NDD-CKD patients transitioning to ESRD. Among approximately 13 000 Veterans with NDD-CKD who annually progress to ESRD (~11% of the US incident ESRD population) [16], there was a consistent rise in the proportion of elderly (60–80 years of age) patients transitioning to dialysis over 2007 to 2015 [7]. In a subcohort of 90 676 TC-CKD patients, 88% had at least one or more serious comorbidities in the prelude (pre-ESRD) period, with diabetes and congestive heart failure (CHF) observed in 74% and 59% of patients, respectively. Although the proportion of patients with diabetes and CHF largely remained stable over time, there were more marked rises in prevalence of mental health disorders (depression, posttraumatic stress disorder) from 2007 to 2015.

DIALYSIS AS THE DEFAULT TREATMENT OPTION FOR ADVANCED CHRONIC KIDNEY DISEASE?

In advanced CKD patients with progressive uremia, dialysis has been the prevailing treatment paradigm, particularly in those ineligible for kidney transplantation because of advanced age or multimorbid status. With inception of outpatient dialysis programs in the 1960s, 'death panels' initially applied strict criteria in order to deliver scarce resources to patients who were most likely to benefit from this treatment strategy. Implementation of the 1972 Medicare ESRD Program and growth of the dialysis industry have since led to relaxation of acceptance criteria and near-universal access to dialysis [1,2,17]. Although intended as a form of life support for advanced CKD patients who develop uremic symptoms, biochemical emergency (hyperkalemia), or decompensated volume status, there is growing data to suggest that dialysis may neither exert the intended effect of extending life nor restoring health in certain subpopulations (older age, high comorbidity burden) [6–9].

Early dialysis mortality

A number of studies have shown that incident ESRD patients experience very high mortality rates during the early dialysis transition period. In a study of 18 707 incident hemodialysis patients from a large US dialysis organization, standardized mortality ratios were highest in the first 6 months of treatment, with 80% higher death risk in the first 2 months [18]. In a subsequent study of 86 886 in-center hemodialysis patients across 11 countries from the Dialysis Outcomes and Practice Patterns Study (DOPPS), mortality rates in the early period (first 120 days of treatment) were nearly two-fold higher than that of the intermediate (121–365 days

of treatment) and late (>365 days of treatment) periods (26.7, 16.9, and 13.7 deaths per 100 patient-years, respectively) [19]. In another study of 498 577 patients initiating dialysis from the USRDS database, mortality rates peaked at week six and declined steadily by week 51 of treatment (37.0 and 14.8 deaths per 100 patient-years, respectively) [20]. Notably, recent USRDS data have shown that this early dialysis mortality peak is observed in hemodialysis patients but not in those receiving peritoneal dialysis, which may be because the latter patients are a selected group (younger, lower comorbidity burden, greater pre-ESRD preparation, higher residual kidney function) [3]. Data from the TC-CKD USRDS Special Study have also shown that, in 89 527 Veterans transitioning to dialysis from 2007 to 2015, the highest rates of mortality were observed during the first several months of treatment [7]. This peak in early dialysis mortality may be particularly heightened in patients of elderly age. In the above-mentioned international DOPPS study, the ratio of elevated mortality rates in the early-to-intermediate hemodialysis periods were progressively higher with increasing age [19]. Several smaller cohorts have shown that the 1-year and 2-year mortality rates of incident dialysis patients at least 75 years of age is 47% [21] and greater than 50% [22▪,23], respectively. In this context it should be highlighted that, in elderly NDD-CKD patients, death may overshadow the likelihood of transitioning to dialysis. For example, in a study of 209 622 Veterans with stages 3–5 NDD-CKD, the risk of mortality exceeded the risk of progression to ESRD across all levels of kidney function [24].

Hospitalizations

Even when dialysis can be expected to prolong survival, patients transitioning to ESRD experience high rates of healthcare utilization, including hospitalizations, ICU admissions, intensive procedures, and institutionalization, particularly in those of older age. On average, dialysis patients are hospitalized twice per year [25], and over one-third of discharges result in a 30-day readmission [26]. In a recent study of 142 210 hospitalizations among prevalent Medicare-eligible dialysis patients, one in six cardiovascular hospitalizations resulted in a 10-day readmission and one in 20 cardiovascular hospitalizations resulted in a 30-day death [27▪▪]. Data from the 'Palliative and End-of-Life' USRDS Special Study have also revealed that nearly two-thirds, one-third, and one-third of Medicare beneficiaries with ESRD are admitted to an ICU/coronary care unit, receive an intensive procedure, or are admitted to a skilled nursing facility during their last 90 days of life, respectively [28]. USRDS data have also shown that proportion of Medicare beneficiaries who die in the hospital has decreased over time (49% to 40% from 2000 to 2014, respectively) [28]. However, observational studies have shown that, among elderly ESRD patients whose lives are prolonged by dialysis, a large proportion of their survival is in fact spent in the inpatient setting (20% of time [21]).

Physical function

In the elderly ESRD population, transition to dialysis has been associated with a marked decline in physical function [29–32]. In a study of 3702 nursing home residents transitioning to dialysis identified from the USRDS database and Minimum Dataset, only 39% of patients maintained their pre-ESRD functional status after 3 months of treatment; furthermore, after 12 months of dialysis treatment, only 13% of patients maintained their pre-ESRD functional status and 58% of patients experienced death [32]. In a longitudinal study of 90 patients at least 80 years of age who transitioned to dialysis, within 6 months of treatment, over 30% experienced loss of functional status, defined as a permanent transfer to an assisted-living setting or nursing home and/or requirement of caregiver support [29].

Health-related quality of life, mental health, and symptom burden

Even if dialysis prolongs survival, it is important to recognize that ensuing functional disability [32], loss of independence [29], and restructuring of lives around dialysis [14] may have downstream consequences upon patients' health-related quality of life. Indeed, multiple studies have shown that dialysis patients suffer from worse levels of health-related quality of life ascertained by Short Form 36 and Kidney Disease Quality of Life Instruments across a broad range of case-mix characteristics [33,34]. In several prospective and retrospective dialysis cohorts, high rates of anxiety and depression have been reported in those transitioning to dialysis. In a cross-sectional analysis of 72 maintenance hemodialysis patients, anxiety (ascertained by the Beck Anxiety Inventory) and depression (ascertained by the Beck Depression Index-II) were identified in 43% and 33% of the cohort, respectively [31]. A corollary study of 246 ESRD patients found that anxiety and emotional distress were directly associated with hemodialysis treatments. When asked the question if 'coming to dialysis makes me anxious', 7%, 11%, and 12% of the cohort reported responses of 'extremely', 'quite a bit', and 'moderately', respectively, whereas 20% and 50%

reported responses of 'a little bit' and 'not at all', respectively [35]. Data from the TC-CKD cohort has also exposed a high prevalence of depression (23%) among 45 076 Veterans transitioning to ESRD, which was linked with higher post-ESRD mortality risk [36].

Although renal replacement therapy is oftentimes initiated in order to alleviate uremic symptoms (nausea, pruritis, etc.), observational data have also found that symptom burden may not per se improve with dialysis treatment. In a study of 90 ESRD and 87 NDD-CKD patients who underwent a Dialysis Symptom Index survey, the overall number of symptoms and total Dialysis Symptom Index symptom-severity score did not differ among ESRD vs. NDD-CKD patients [37].

Withdrawal from dialysis

Worse health-related quality of life and mental health engendered by dialysis may also contribute to the high rates of withdrawal from dialysis. In parallel with the rise in elderly ESRD patients, there has been an increase in the rates of dialysis withdrawal (3 vs. 49 per 1000 person-years in 1966 vs. 2010, respectively [38]). These trends may be amplified in the elderly population. Among 113 162 incident hemodialysis patients from a large US dialysis organization, those at least 80 years old had a 10-fold higher likelihood of withdrawal compared with patients less than 50 years of age [39▪▪]. Withdrawal was also found to be the second and third most common cause of death among patients at least 80 and less than 80 years of age, respectively, consistent with USRDS registry data [3].

CONCEPTS OF CONSERVATIVE DIALYSIS-FREE AND PRESERVATIVE KIDNEY MANAGEMENT

Given that dialysis may not offer improved survival nor patient-centered outcomes in certain subpopulations (elderly, high comorbidity burden, poor functional status), there has been increasing interest in conservative nondialytic management and preservative management as potentially viable treatments option for advanced CKD (Fig. 1).

Definition of conservative management

Although several definitions have been proposed, an expert working group who convened for the Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference in Supportive Care in CKD have defined 'comprehensive conservative care' as 'planned holistic patient-centered

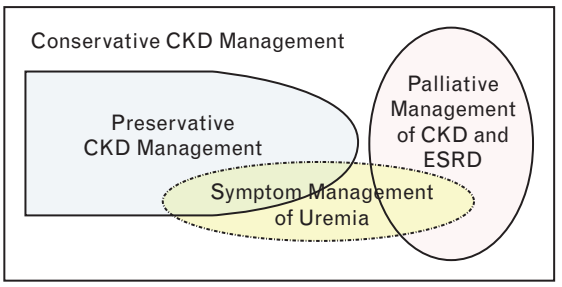

FIGURE 1. Conceptual model of conservative management.

care for patients with glomerular filtration rate (GFR) category (G) 5 CKD that includes interventions to delay progression of kidney disease and minimize risk of adverse events or complications, shared decision-making, active symptom management, detailed communication including advance care planning, psychological support, social and family support, and cultural and spiritual domains of care' [40]. Although conservative dialytic-free management may appear to include several aspects of palliative and supportive care, it bears mention that the KDIGO definition might leave the misguided perception that conservative care is equated with end-of-life care and a palliative medicine approach. Moreover, conservative management should not be conflated with 'no care' or 'rationing of care', which would be more consistent with palliative and supportive care. In fact, as a form of 'active medical management' and 'comprehensive' care, conservative dialysis-free management may warrant more attentive and frequent treatment of uremic, biochemical, and volume derangements as compared with dialysis and kidney transplantation. To this end, conservative nondialytic management requires a multidisciplinary team who can provide medical treatment to preserve kidney function longer, uremia management without dialysis, proactive symptom management, nutritional care including a low protein diet [41▪], and psychological support [40].

Concept of preservative management

The primary objectives of conservative nondialytic management include optimization of patients' health-related quality of life, treating symptoms of ESRD without dialysis or transplant, and preserving the remaining kidney function as long as possible [14,20,40]. In regards to the latter goal, kidney function preservation has important clinical implications in patients with advanced NDD-CKD progressing to ESRD, as well as ESRD patients receiving dialysis [17,42–44,45▪]. Even at very low levels of GFR, given its continuous nature, remaining kidney

function has substantial impact on *solute clearance,* and may in fact provide greater clearance of middle-molecular weight and large-molecular weight solutes as compared with dialysis [46]. Prolonging preservation of kidney function also promotes *better fluid balance* [47], and mitigates the risk of large inter-dialytic weight gains and high ultrafiltration rates that may lead to left ventricular hypertrophy, intra-dialytic hypotension, myocardial stunning, and sudden cardiac death. Preserving kidney function and urine output has also been associated with *greater survival* in both the peritoneal dialysis and hemodialysis populations [43,48,49]. With respect to patient-centered outcomes, residual urine output has been associated with i*mproved health-related quality of life* in hemodialysis patients [49], and may allow for *dietary liberalization*, with downstream benefits on patients' nutritional parameters [50,51] and satisfaction/quality of life.

Given the paramount importance of preserving kidney function over longer time, we have, therefore, proposed the concept of preservative management as an integral component of the conservative nondialytic treatment of advanced NDD-CKD (Fig. 1). In advanced NDD-CKD, preservative management may involve a multifaceted approach, including frequent monitoring of kidney function, dietary interventions (low protein diet, dietary potassium and phosphate restriction), cautious blood pressure management (averting hypertension and relative hypotension), and avoidance of nephrotoxins as a means to preserve the remaining kidney function. Preservative management of kidney function in advanced CKD may also have a role in the treatment of incident and prevalent dialysis patients, although specific aspects of management may differ among advanced NDD-CKD vs. dialysis patients [42].

CURRENT EVIDENCE OF CONSERVATIVE DIALYSIS-FREE MANAGEMENT

Trends in utilization

In parts of North America, Australia, Europe, and Asia, conservative nondialytic management has been increasingly recognized as a 'patient-centered' alternative treatment option for advanced CKD. Although there is heterogeneity in the definitions, provisions of care, and patient case-mix across international studies of conservative management, existing data suggest that there is growing implementation of nondialytic treatment of CKD in parts of the world. This has catalyzed a number of studies examining the comparative effectiveness of conservative management vs. dialysis across the outcomes of survival, hospitalization, and patient-centered endpoints (Table 1) [6–9,22▪,52–59].

Survival

In general, survival is expected to be longer for advanced CKD patients undergoing treatment with renal replacement therapy in the form of dialysis or kidney transplantation vs. conservative management. However, growing evidence suggests that the survival benefit of dialysis vs. conservative management is marginal or even reversed in certain subpopulations, such as those of elderly age, multimorbid conditions, and with underlying cardiovascular disease (Table 1). In an observational study of 129 elderly (>75 years old) patients with stage 5 CKD who underwent conservative management vs. dialysis, 1-year and 2-year survival were greater for dialysis in the overall cohort; however, among patients with higher comorbidity scores (defined as a Davies score = 2) or ischemic heart disease, the survival of those undergoing conservative management vs. dialysis were equivalent [8]. In a subsequent study of 844 stage 5 CKD patients by Chandna *et al.* [6], the survival advantage of dialysis vs. conservative management was also mitigated in those greater than 75 years old, after accounting for age and comorbidity status. Among 311 patients with advanced CKD by Verberne *et al.* [9], the survival advantage of dialysis was reduced in patients at least 70 years of age, with high comorbidity scores (Davis score $\geq$3), or with cardiovascular disease, and mitigated in patients at least 80 years of age. In a study of 73 349 Veterans with eGFRs less than 30 ml/min/1.73 m^2 by Kurella Tamura *et al.* [22▪], the association of time-varying nondialytic vs. dialytic management with survival were modified by age and eGFR by dialysis initiation, such that in patients initiating dialysis at eGFRs 9 to less than 12 ml/min/1.73 m^2, the difference in median life expectancy was less than 1 year.

Hospitalization

There have been a limited number of studies comparing hospitalization and other healthcare utilization rates among patients treated with conservative management vs. dialysis, which have shown mixed findings (Table 1). Data by Carson *et al.* [54] has shown that, among 202 ESRD patients more than 70 years old, hospitalization rates were higher for dialysis vs. conservative management. However, in a study of 199 patients at least 65 years old with stage 5 CKD by Shum *et al.* [58], ED-hospitalization rates and number of days spent in the hospital were greater among patients undergoing conservative

Table 1. Selected studies of conservative management vs. dialysis (study sample size >100 patients)

Author (year)	Study population (*N*)	Country (era)	Main outcomes	Results
Joly *et al.* (2003) [56]	At least 80 years with CrCl <10 ml/min (*N*=146)	France, single center (1989–2000)	Survival	Median survival of conservative management vs. dialysis: 8.9 vs. 28.9 months 12-month survival of conservative management vs. dialysis: 29% vs. 74% 24-month survival of conservative management vs. dialysis: 15% vs. 60%
Murtagh *et al.* (2007) [8]	More than 75 years with stage 5 CKD (*N*=129)	UK, multicenter (2003–2004)	Survival	1-year survival of conservative management vs. dialysis: 68% vs. 85% 2-year survival of conservative management vs. dialysis: 47% vs. 76% Survival equivalent in patients with high comorbidity scores (Davies score = 2) or ischemic heart disease
Carson *et al.* (2009) [54]	More than 70 years with ESRD (*N*=202)	UK, single center (1997–2003)	Survival and hospitalization	Median survival of conservative management vs. dialysis: 13.9 vs. 37.8 months Hospitalization rates higher for dialysis vs. conservative management: 0.069 vs. 0.043 hospitalization days/patient-days survived
Chandna *et al.* (2011) [6]	Stage 5 CKD (*N*=844)	UK, single center (1990–2008)	Survival	Median survival of conservative management vs. dialysis: 21.2 vs. 67.1 months In patients >75 years of age, after accounting for age and comorbidity status, survival advantage of dialysis mitigated to ~4 months (not statistically significant)
Da Silva-Gane *et al.* (2012) [55]	Late stage 4 and 5 CKD from 'Low Clearance Clinics' (*N*=170)	UK, single center (2005–2007)	HRQOL and mental health Short Form 36 Hospital Anxiety and Depression Scale Satisfaction with Life Scale	Adjusted median survival of conservative management vs. dialysis: 913 vs. 1317 days Conservative management associated with higher anxiety, but similar mental health, depression, and life satisfaction scores vs. dialysis HRQOL scores stable over time with conservative management, but declined with dialysis
Seow *et al.* (2012) [57]	At least 75 years or age-adjusted Charlson Comorbidity Index at least 8 and eGFR 8–12 (*N*=101)	Singapore, single center (2007–2009)	HRQOL Kidney Disease Quality of Life Short Form	Conservative management and dialysis both showed stable Physical and Mental Component scores Dialysis showed improvement in cognitive function scale score, but worse Effect of Kidney Disease and Burden of Kidney Disease Scale scores
Hussain *et al.* (2013) [7]	More than 70 years with stage 5 CKD (*N*=441)	UK, single center (2006–2010)	Survival and hospitalization	Overall cohort: dialysis associated with better survival at all time points vs. conservative management Patients more than 80 years, WHO performance score at least 3, and higher Charlson Comorbidity Index score: no survival difference between dialysis vs. conservative management Hospitalization risk 60% higher with dialysis vs. conservative management
Shum *et al.* (2014) [58]	At least 65 years with stage 5 CKD (*N*=199)	China, single center (2003–2010)	Survival, ED visits, hospitalization, institutionalization, palliative and end-of-life care	Survival of conservative management vs. PD: 2.35 vs. 3.75 years ED-hospitalization rate of conservative management vs. PD: 3.51 vs. 1.63 events per person-years Hospitalization days of conservative management vs. PD: 38.0 vs. 16.2 days per person-years No difference in institutionalization between conservative management vs. PD Receipt of palliative care with conservative management vs. PD: 15.4% vs. 0%

Table 1 (*Continued*)

Author (year)	Study population (*N*)	Country (era)	Main outcomes	Results
Brown *et al.* (2015) [53]	Stage 4–5 CKD with renal supportive care without dialysis vs. planning or commencing dialysis ($N=567$)	Australia, single center (2009–2013)	Symptoms, HRQOL, and survival Memorial Symptom Assessment Scale Palliative Care Outcomes Scale – Symptoms Inventory Short Form 36	Survival in renal supportive care patients: Median survival 12 months After eGFR declined below 10ml/min/1.73 m^2, 32% survived >12 months Symptoms: Baseline symptom score higher (worse) in renal supportive care patients No difference in symptom trajectory in renal supportive care or predialysis patients HRQOL Baseline Physical Component Scores worse in renal supportive group, but baseline Mental Component Scores similar No difference in trajectory of Physical or Mental Component Scores in renal supportive care or predialysis patients
Teruel *et al.* (2015) [59]	Stage 5 CKD ($N=232$)	Spain, single-center (2013–2014)	Survival	Median survival of conservative management vs. dialysis: 4.9 ± 3.2 vs. 7.2 ± 3.7 months Mortality rate of conservative management vs. dialysis: 8.2 vs. 0.6 per 100 patient-months
Verberne *et al.* (2016) [9]	At least 70 years with advanced CKD ($N=311$)	Netherlands, single center (2004–2014)	Survival	Median survival of conservative management vs. dialysis: 1.5 vs. 3.1 years Survival advantage of dialysis reduced in patients with high comorbidity scores (Davies score ≥ 3) or cardiovascular disease Survival advantage equivalent in patients at least 80 years
Wong *et al.* (2018) [60]	Veteran decedents with eGFR <15 ($N=14071$)	US, multicenter (2000–2009)	Hospitalization, intensive procedure in last month of life, inpatient death, palliative care/ hospice before death	Median survival of conservative management vs. dialysis: 5.7 vs. 32.0 months Conservative management with decreased hospitalization, intensive procedures, inpatient deaths Conservative management with greater palliative care/hospice
Kurella Tamura *et al.* (2018) [22▪]	Veterans with eGFR <30ml/min/1.73 m^2 ($N=73349$)	US, multicenter (2005–2010)	Survival	Effect modification of association of conservative management vs. dialysis with survival by age and eGFR Among patients initiating dialysis at eGFR 9-<12ml/min/1.73 m^2, difference in median life expectancy less than 1 year

CKD, chronic kidney disease; CrCl, creatinine clearance; ED, emergency department; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HRQOL, health-related quality of life; PD, peritoneal dialysis; UK, United Kingdom; US, United States.

management vs. peritoneal dialysis. Yet in a study of 14 071 US Veteran decedents with eGFRs less than 15 ml/min/1.73 m^2 by Wong *et al.* [60], conservative management was associated with fewer hospitalizations, intensive procedures in the last month of life, and inpatient deaths.

Patient-centered outcomes

A sparse number of studies have also compared patient-centered endpoints, including health-related quality of life, mental health, and symptoms, among patients receiving conservative vs. dialytic management. In a study of 170 stage 4 to 5 CKD patients by Da Silva-Gane *et al.* [55] who underwent repeated Short Form 36, Hospital Anxiety and Depression Scale, and Satisfaction with Life Scale surveys over time, at baseline, conservative management was associated with higher anxiety but similar mental health, depression, and life satisfaction scores compared with dialysis. However, over time, health-related quality of life scores remained stable in the conservative management group but declined in those receiving dialysis. Seow *et al.* [57] found that, among 101 patients of elder age (≥75 years old) or higher comorbidity status (Charlson Comorbidity Index ≥8) who underwent Kidney Disease Quality of Life Short Form assessments, conservative management and dialysis both showed stable Physical and Mental Component Scores; however, in dialysis patients Effect of Kidney Disease and Burden of Kidney Disease Scale scores declined over time. In a study of 567 stage 4 to 5 CKD patients who underwent renal supportive care without dialysis vs. planning or commencement of dialysis by Brown *et al.* [53], Memorial Symptom Assessment Scale, Palliative Care Outcomes Scale-Symptoms Inventory, and Short Form 36 surveys were compared over time. Although baseline symptom scores were higher (worse) in patients receiving renal supportive care, there was no difference in symptom trajectory across the two groups over time.

CHALLENGES IN THE IMPLEMENTATION OF CONSERVATIVE MANAGEMENT

Conservative management expands potential treatment options for advanced CKD patients in whom there has previously been a perception that dialysis is the default treatment option with few to no alternatives. However, there remains under-utilization of this 'patient-centric' treatment strategy. Qualitative research studies have provided insight into the challenges that may operate at provider, patient, and institutional levels with respect to the broader implementation of conservative management (Table 2) [60–65,66▪]. In a study conducted among clinical directors of renal units by Okamoto *et al.* [62], lack of a uniform definition of conservative management, as well as need for better evidence comparing conservative management vs. dialysis were cited as potential obstacles. In another of study of nephrologists' perceptions by Ladin *et al.* [61▪▪], challenges in defining the nephrologists' role (treatment decisions, managing symptoms), navigating end-of-life discussions (uncertain prognosis, insufficient training, lack of confidence), and institutional barriers (time constraints, difficulties in care coordination) were also cited as barriers.

Surveys of primary care providers providing conservative care to advanced CKD patients have also highlighted limited access to renal expertise and resources as potential impediments, as shown in two studies by Tam-Tham *et al.* [64,65]. Finally, there is greater need for an expanded role of personalized medicine in the management of CKD. Although the traditional paradigm has been to initiate renal replacement therapy in advanced CKD patients with progressive disease, there is increasing recognition that alternative strategies, such as conservative management may be more aligned with certain patients' preferences [45▪].

CONCLUSION

On the basis of existing observational data, conservative management to preserve remaining kidney function and to manage uremia and other CKD comorbidities without dialysis appears to be associated with equivalent survival [6–9] and similar to improved health-related quality of life and symptom burden [52,54,56] in certain advanced CKD subpopulations as compared with dialysis. However, further comparative effectiveness studies with rigorous examination of a broader range of hard outcomes and patient-centered endpoints with conservative management vs. dialysis are needed to better inform treatment decisions among advanced CKD patients, caregivers, and providers. Although limited data suggest that patients of elderly age, with higher comorbidity scores, and underlying cardiovascular disease may have marginally improved to worse outcomes with dialytic vs. nondialytic management, further investigation is needed to more precisely determine, which patients will most benefit from conservative management vs. renal replacement therapy strategies. Finally, as ESRD poses major financial burden to the US healthcare system (annual Medicare spending $30 billion [3,4]), further study of the impact of conservative management vs. dialysis upon healthcare utilization and costs are needed. As dialysis has been the prevailing

Table 2. Qualitative studies identifying challenges in the implementation of conservative management

Author (year)	Study population (*N*)	Country (era)	Challenges
Okamoto *et al.* (2015) [62]	Clinical directors of renal units (N = 67 facilities)	UK (2013)	Lack of agreed upon definition for conservative management Providing more conservative management training to renal staff and GPs Increasing communication and involvement with GPs, community, and palliative care teams Need for better evidence comparing conservative management vs. dialysis
Tam-Tham *et al.* (2016) [64]	Primary care providers caring for patients ≥75 years with stage 5 CKD not planning dialysis (*N* = 409)	Canada (2015)	Inability to access support to maintain patients in the home setting and avoid transitions of care Extent to which able to select medications and adjust their dosages Knowing when to discontinue preventive measures Helping patients/their family understand the risks/benefits of treatment options Working with healthcare providers with limited renal expertise Limited ability to access resources from the conservative management clinic
Tam-Tham *et al.* (2016) [65]	Primary care providers (*N* = 27)	Canada (2015)	Managing patient and family expectations of CKD Uncertainty of prognosis Fostering acceptance of kidney disease severity Misperceptions of dialysis Complexity of medical management of patients requiring conservative care Ability to provide the best practices in renal care Integrating multidisciplinary health professionals Challenges associated with managing patients jointly with specialists Negotiating healthcare provider roles and responsibilities
Ladin *et al.* (2018) [61▪▪]	Nephrologists (*N* = 35 at 18 centers)	US (2016–2017)	Struggling to define nephrologists' role Determining treatment (nephrologist role vs. patient autonomy) Instilling hope Improving symptoms Circumventing end-of-life conversations Uncertain prognosis Fearing emotional backlash Concern over jeopardizing therapeutic relationship Insufficient training and lack of confidence in discussing conservative management and end of life Institutional barriers Time constraints Attempting care coordination Financial incentives for dialysis Discomfort with varied conservative management approaches Perceptions of conservative care as no care
Susanto *et al.* (2018) [63]	Medical managers of nephrology departments (*N* = 60)	Netherlands (2016)	No written guideline for how to management patients with conservative care Lack of staff who specialize in conservative care Lack of time Unclear need for formal training in conservative care Lack of funding specifically for conservative care Nephrologists' lack of interest in conservative management training
Wong *et al.* (2019) [66▪]	Veterans who chose not to start dialysis (*N* = 851)	US (2010–2011)	When patients expressed desire to forgo dialysis, unusual for clinicians to readily accept patients' decisions Clinicians determined noncandidacy for dialysis based on patients' characteristics and prognosis as opposed to patients' goals and values If patients did not pursue dialysis, clinicians believed they had little to offer and signed off from their care

CKD, chronic kidney disease; GP, general practitioner; UK, United Kingdom.

treatment paradigm among advanced CKD patients ineligible for or unlikely to receive kidney transplantation, there is compelling need for further investigation of conservative management as an alternative patient-centered treatment strategy in this population.

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Conflicts of interest

There are no conflicts of interest.

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