The value of dialysis and conservative care for older patients with advanced chronic kidney disease

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Hospital utilization and costs in older patients with advanced chronic kidney disease choosing conservative care or dialysis: a retrospective cohort study

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ABSTRACT

Background

Non-dialytic conservative care has been recognized as a viable alternative to chronic dialysis in older patients with end-stage kidney disease, but little is known about its consequences on hospital utilization and costs.

Methods

We performed a retrospective cohort study to compare outpatient and inpatient hospital utilization, place of death, and hospital costs in patients aged ≥70 years old who chose conservative care (n = 100) or dialysis (n = 162) after shared decision-making in a non-academic teaching hospital between 2008 and 2016.

Results

Patients who chose conservative care were older than patients who chose dialysis (82.5 versus 76.3 years). Comorbidity did not differ between the two patient groups. The incidence rates of outpatient visits per year were 7.1 in patients who chose conservative care and 10.7 in patients who chose dialysis (incidence rate ratio: 0.67, 95% confidence interval: 0.55 to 0.81). The incidence rates of in-hospital days per year were, respectively, 6.0 and 9.8 (incidence rate ratio: 0.50, 95% confidence interval: 0.29 to 0.88). Also in the final month of life, patients on conservative care had less outpatient visits, were less frequently hospitalized, and died less frequently in hospital than the dialysis patient group. The cost rates per year, measured from original treatment decision, were €5,859 in conservative care patients and €28,354 in patients who chose dialysis comprising both the predialysis and dialysis period (cost rate ratio: 0.42, 95% confidence interval: 0.27 to 0.65). Patients who chose dialysis had higher costs on dialysis sessions, outpatient care, inpatient care, laboratory tests, and medical imaging.

Conclusions

Patients who decided to forego dialysis and chose conservative care had less outpatient and inpatient hospital utilization than patients who chose dialysis, including less intensive hospital utilization near the end of life. Both overall and non-dialysis-related costs were lower in patients on a conservative care pathway.

INTRODUCTION

The incidence and prevalence of patients with advanced chronic kidney disease are increasing worldwide [1, 2]. Older patients represent the fastest growing group. In older patients, dialysis has become the most common treatment for end-stage kidney disease, but some might consider dialysis as too burdensome outweighing its benefits [3, 4]. Non-dialytic conservative care has been recognized as a viable alternative, which aims to preserve quality of life by active medical treatment and multidisciplinary care including all interventions as needed although without dialysis [5-7].

Emerging observational studies showed that dialysis may not prolong life or improve health-related quality of life compared to conservative care in selected older patients, particularly in the oldest patients and patients with multiple comorbidities [8-13]. Treatment pathways as conservative care that have the potential to achieve reasonable health outcomes could also reduce the treatment burden and costs associated with resource-intensive care that may not be aligned with a patient's values and preferences [14]. To inform shared decision-making on conservative care and dialysis, data on treatment burden related to hospital utilization could be helpful for patients, their family, and clinicians [15-19]. Also, value-based evaluations of patient-relevant outcomes, including treatment burden, and costs may inform health-care planning [5, 14].

It makes sense to assume that hospital utilization and costs appear to be lower in patients who choose conservative care rather than dialysis because less interventions are being applied. However, patients on conservative care might have symptoms that are normally targeted by dialysis which could in turn result in a higher need of other hospital resources and associated costs to treat symptoms. Understanding which hospital resources are used in each treatment pathway is therefore needed to evaluate whether conservative care is a viable alternative to dialysis in terms of hospital utilization and costs. Few small studies have compared hospital utilization in older patients receiving either conservative care or dialysis but at a general level only [20-26]. Overall, they observed less intensive hospital utilization in patients on conservative care pathways than in dialysis patients. It is unknown whether hospital utilization differences between conservative care and dialysis were observed for both outpatient and inpatient utilization, at all hospital departments, and whether this changes near the end of life. Comparative data on costs are also lacking [5, 14, 27]. The aim of our study was to determine and compare outpatient and inpatient

hospital utilization and costs overall and per hospital department in older patients on a conservative care or dialysis pathway. We also determined hospital utilization and costs near the end of life.

PATIENTS AND METHODS

Study population

We identified a retrospective cohort of all patients aged ≥70 years old with stage 4/5 chronic kidney disease who received nephrology care in a non-academic teaching hospital between January 1, 2008 and May 1, 2016, based on a previous cohort [10, 11]. Patients were included if they had made a decision to be treated with conservative care or dialysis after a shared decision-making process (original treatment decision). Patients needing immediate start of dialysis at presentation, or who were lost to follow-up, were excluded. As part of standard care, shared decision-making on preferred treatment had been initiated by the nephrologist when the patient's estimated glomerular filtration rate (eGFR) dropped <20 mL/min/1.73 m^2. During the decision-making process, an experienced multidisciplinary team of nephrologists, nephrology nurses, social workers, and dieticians discussed the various treatment pathways for end-stage kidney disease with the patient and family. Oral and written information about treatment modalities, including practicalities, potential benefits, and risks, were given. Alongside standard outpatient visits, patients and their relatives were offered an one-hour counselling session by the nephrology nurse, a home visit by the social worker, and a visit to the dialysis unit. Each decision-making process was tailored to the individual patient's needs and preferences in decision-making. A treatment decision was finally made during consultation with the nephrologist and recorded in the medical record. This original treatment decision was evaluated regularly. Patients always had the opportunity to change their decision. In patients selecting conservative care, active medical treatment and multidisciplinary care were continued including all interventions needed except for dialysis. In patients selecting hemodialysis or peritoneal dialysis, dialysis treatment was prepared and initiated once needed. The dialysis group comprised all patients who chose dialysis irrespective whether or not dialysis was started during follow-up. Standard outpatient care for all patients involved a three-monthly visit including blood tests, which was intensified if necessary.

Baseline data

The following baseline data were collected from electronic medical records: age, sex, comorbidities, primary kidney disease according to the European Renal Association–Dialysis and Transplantation Association's codes, eGFR at treatment decision and dialysis initiation measured with the four-point Modification of Diet in Renal Disease formula [28], and dates when eGFR permanently dropped <20 and <15 mL/min/1.73 m^2. Comorbidity was scored using the Davies comorbidity score [29].

Study outcomes

Hospital utilization was determined as outpatient utilization (total number of outpatient visits) and inpatient utilization (total number of in-hospital days). Both outcomes were also assessed per hospital department (internal medicine, surgery, cardiology, pulmonology, gastro-enterology, neurology, gynaecology and urology, and other [psychiatry, rehabilitation medicine, dermatology, ophthalmology]). Hospital costs included total costs incurred at all departments and costs per subcategory (dialysis sessions, outpatient care, inpatient care, laboratory tests, medical interventions, medical imaging, and functional tests). Data were derived from electronic medical records and the hospital's financial administration by performing systematic searches. Place of death, defined as hospital death or non-hospital death (at home, hospice, nursery home), was collected from electronic medical records.

Statistical analysis

We compared baseline characteristics between both patient groups using descriptive statistics. Outcomes were assessed from date of recording note of original treatment decision until kidney transplantation, death, or end of study (May 1, 2016). We calculated the study outcomes as annual rates to adjust for differences in follow-up length, dividing the total number of events or costs with total follow-up time in years [30]. We primarily based the analyses on original treatment decision. We performed a sensitivity analysis on the main outcomes based on categorization of both patient groups according to the most recent documented treatment plan at the end of study or at the time of death.

To test group differences on hospital utilization, incidence rate ratios were estimated using generalised linear regression models with negative binomial distribution, because data were not normally distributed and overdispersed. Adjustment variables were age, sex, Davies comorbidity score, eGFR, and primary kidney disease.

We calculated mean cost rates, recommended as most informative measure [31], although data were not normally distributed. To assess group differences, negative binomial regression with adjustment for age, sex, Davies comorbidity score, eGFR, and primary kidney disease was performed to estimate the cost rate ratio. As recommended [32], sensitivity analyses using generalised linear regression models with log-gamma and Poisson distribution were performed to test best model fit.

We performed subgroup analyses in patients who died during follow-up to determine hospital utilization and costs near the end of life, using similar negative binomial regression models. Patients with a minimum follow-up time of four months were included to assess outcomes in the first month after original treatment decision and in the three months before death. The dialysis group was subdivided into a group of predialysis patients and a group of patients receiving dialysis in the corresponding time periods. We also assessed the hazard ratios of being hospitalized near the end of life, using Cox regression with adjustment for age, sex, Davies comorbidity score, and primary kidney disease. Furthermore, we determined the odds ratios of place of death, using logistic regression with adjustment for age, sex, and Davies comorbidity score. A P value < 0.05 was considered statistically significant. Analyses were performed using IBM SPSS 24.0.

RESULTS

We included 262 patients in our study (Figure 1): 100 patients who chose conservative care (total follow-up time of 153.2 person years), and 162 patients who chose dialysis (380.7 person years). Of 162 patients who chose dialysis, 84 (52%) started dialysis during follow-up. Three patients underwent kidney transplantation after dialysis initiation (censored at transplantation). Few patients changed their original treatment decision during follow-up: three from conservative care to dialysis, and ten from dialysis to conservative care. Analyses were primarily based on original treatment decision.

Baseline characteristics are shown in Table 1. Compared to patients who chose dialysis, conservative care patients were older, more often female, and had a higher eGFR at original treatment decision. There were no differences in comorbidity and primary kidney disease.

Table 1. Baseline characteristics of patients who chose either conservative care or dialysis

	Choice for conservative care *n* = 100	**Choice for dialysis** *n* = 162
Age (years), mean (SD)	82.5 (4.6)	76.3 (4.4)
Sex (female)	44 (44%)	51 (32%)
Davies comorbidity score[a]		
No comorbidity (score = 0)	8 (8%)	19 (12%)
Intermediate comorbidity (score = 1 or 2)	60 (60%)	97 (60%)
Severe comorbidity (score ≥ 3)	32 (32%)	46 (28%)
Ischemic heart disease	45 (45%)	70 (43%)
Left ventricular dysfunction	29 (29%)	46 (28%)
Peripheral vascular disease	51 (51%)	70 (43%)
Malignancy	12 (12%)	19 (12%)
Diabetes mellitus	45 (45%)	64 (40%)
Systemic collagen vascular disease	8 (8%)	4 (3%)
Other significant disorder	19 (19%)	32 (20%)
Primary kidney disease		
Renal vascular disease	49 (49%)	54 (33%)
Diabetes mellitus	15 (15%)	27 (17%)
Etiology uncertain	22 (22%)	53 (33%)
Other	14 (14%)	28 (17%)
eGFR at treatment decision (mL/min/1.73 m^2), mean (SD)	16.2 (5.1)	14.3 (4.0)
Time of eGFR decline from <20 to <15 mL/min/1.73 m^2 (days), median (IQR)	286 (74 – 676; *n* = 64)	225 (42 – 406; *n* = 115)
Time from original treatment decision to dialysis start (days), median (IQR)	316[b] (21 – 715; *n* = 3)	153 (54 – 443; *n* = 84)
eGFR at dialysis start (mL/min/1.73 m^2), mean (SD)	6.7[b] (2.1; *n* = 3)	8.4 (2.6; *n* = 84)

Values are numbers (percentages) unless stated otherwise; the total number of patients is indicated in case of missing data.

[a] Davies comorbidity score is based on the presence of seven comorbidities [28]: ischemic heart disease (defined as prior myocardial infarction, angina pectoris, or ischemic changes on electrocardiograph), left ventricular dysfunction (defined as clinical evidence of pulmonary edema not caused by errors in fluid balance), peripheral vascular disease (including distal aortic, lower extremity, and cerebrovascular diseases), malignancy, diabetes mellitus, systemic collagen vascular disease, and other significant disorder (*e.g.*, chronic obstructive pulmonary disease). The score assigns one point for each present condition and produces three groups: no comorbidity (Davies score = 0), intermediate comorbidity (Davies score = 1–2), and severe comorbidity (Davies score ≥3).

[b] Three patients changed their original treatment decision in favour of conservative care to dialysis; all three initiated dialysis during follow-up.

eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD, standard deviation.

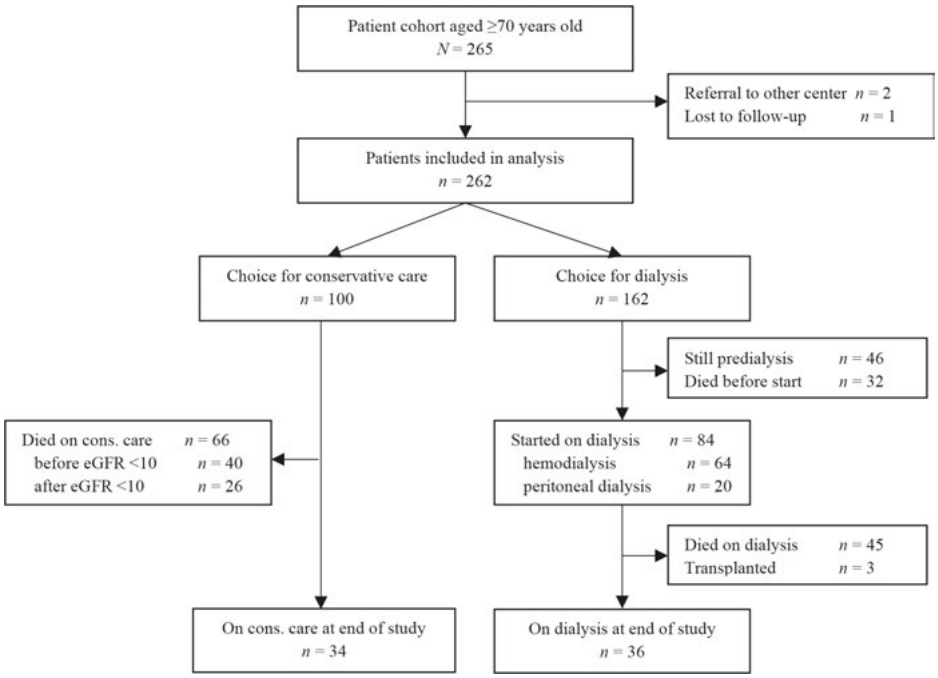

Figure 1. Overall flow of all patients aged ≥70 years old with stage 4/5 chronic kidney disease who had made a choice for either conservative care or dialysis after shared decision-making. Three patients changed their original treatment decision in favour of conservative care to dialysis (all three initiated dialysis), and ten patients changed their original decision from dialysis to conservative care (all were still predialysis). Analyses were based on original treatment decision. Cons. care, conservative care; eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2).

Hospital utilization

Table 2 shows the results on outpatient and inpatient utilization. Overall, 5,153 outpatient visits took place during follow-up: 1,081 in patients who chose conservative care and 4,072 in patients who chose dialysis. The overall incidence of outpatient visits in the conservative care group was 7.1 per person year compared with 10.7 per person year in the dialysis group. The incidence rate ratio, adjusted for age, sex, Davies comorbidity score, eGFR, and primary kidney disease, was 0.67 (95% confidence interval: 0.55 to 0.81). Patients who chose dialysis had more outpatient visits than patients who chose conservative care to the departments of internal medicine, surgery, and neurology.

Table 2. Annual rates of outpatient visits and in-hospital days in patients selecting either conservative care or dialysis, measured from original treatment decision until death or end of study

	Choice for conservative care *n* = 100 Crude incidence rate	**Choice for dialysis** *n* = 162 Crude incidence rate	**Incidence rate ratio**[a] (95% CI)	***P* value**[a]
Outpatient visits per person year	7.1	10.7	0.67 (0.55 to 0.81)	< 0.001
Internal medicine	3.8	6.0	0.65 (0.52 to 0.80)	< 0.001
Surgery	0.6	1.7	0.35 (0.22 to 0.54)	< 0.001
Cardiology	0.8	0.9	0.77 (0.44 to 1.32)	0.34
Pulmonology	0.2	0.3	0.97 (0.34 to 2.73)	0.95
Gastro-enterology	0.1	0.3	0.84 (0.32 to 2.22)	0.72
Neurology	0.1	0.3	0.36 (0.17 to 0.82)	0.02
Gynaecology and Urology	0.4	0.5	1.14 (0.50 to 2.60)	0.76
Other[b]	1.1	0.8	1.06 (0.54 to 2.04)	0.88
In-hospital days per person year[c]	6.0	9.8	0.50 (0.29 to 0.88)	0.015
Internal medicine	3.1	5.4	0.38 (0.18 to 0.82)	0.01
Surgery	0.5	1.7	0.40 (0.18 to 0.87)	0.02
Cardiology	0.7	1.2	0.51 (0.18 to 1.42)	0.19
Pulmonology	0.6	0.5	1.09 (0.05 to 23.00)	0.96
Gastro-enterology	0.8	0.3	10.51 (1.11 to 99.96)	0.04
Neurology	0.1	0.3	0.05 (0.003 to 0.82)	0.04
Gynaecology and Urology	0.2	0.3	0.69 (0.09 to 5.12)	0.72
Other[b]	0.1	0.1	0.23 (0.02 to 2.68)	0.24

[a] Negative binomial regression with adjustment for age, sex, Davies comorbidity score, estimated glomerular filtration rate, and primary kidney disease.
[b] Including psychiatry, rehabilitation medicine, dermatology, and ophthalmology.
[c] Including planned and non-planned in-hospital days.

During follow-up, 4,646 in-hospital days occurred overall: 924 in patients who chose conservative care and 3,722 in patients who chose dialysis. The overall incidence of in-hospital days in the conservative care group was 6.0 per person year compared with 9.8 per person year in the dialysis group. The incidence rate ratio, adjusted for age, sex, Davies comorbidity score, eGFR, and primary kidney disease, was 0.50 (95% confidence interval: 0.29 to 0.88). Patients who chose dialysis had more in-hospital days compared to conservative care patients at the departments of internal medicine, surgery, and neurology, but less in-hospital days at gastro-enterology.

Similar results on outpatient and inpatient hospital utilization were found in sensitivity analyses based on categorization of both patient groups according to the most recent documented treatment plan at the end of study or at the time of death (Supplementary Table S1). Only different than in the main analyses, the sensitivity analyses showed that patients who chose dialysis had more outpatient visits and in-hospital days to the departments of gynaecology and urology than patients who chose conservative care instead of similar. Furthermore, no difference in in-hospital days at the department of gastro-enterology was observed between both patient groups in the sensitivity analyses.

Hospital costs

Table 3 shows the results on hospital costs. Overall, €11,691,079 was incurred during follow-up measured from original treatment decision: €897,483 in patients who chose conservative care and €10,793,596 in patients who chose dialysis. The overall cost rate in the conservative care group was €5,859 per person year compared with €28,354 per person year in the dialysis group, comprising both the predialysis and dialysis period. In the dialysis group, the overall cost rate of the predialysis period was €6,692 per person year (n = 162) and €54,906 per person year for the dialysis period (n = 84). The cost rate ratio between the patients who chose conservative care or dialysis was 0.42 (95% confidence interval: 0.27 to 0.65), adjusted for age, sex, Davies comorbidity score, eGFR, and primary kidney disease. Patients who chose dialysis had higher costs on dialysis sessions, outpatient care, inpatient care, laboratory tests, and medical imaging. Results were similar in sensitivity analyses fitting generalised linear models with log-gamma or Poisson distribution. The results on hospital costs were also similar in sensitivity analyses based on categorization of both patient groups according to the most recent documented treatment plan at the end of study or at the time of death (Supplementary Table S2).

Hospital utilization and costs near the end of life

Figures 2-4 and Table 4 show the results on outpatient and inpatient hospital utilization, place of death, and costs near the end of life in 124 patients who died after a minimum follow-up time of four months. The dialysis group was subdivided into a group of predialysis patients and a group of patients receiving dialysis per corresponding time period. Patients on conservative care had similar hospital utilization and costs near the end of life compared to predialysis patients. However, compared to patients receiving dialysis, patients on conservative care had less outpatient visits in the final month of life (Figure 2) and less in-hospital days in the final two months of life (Figure 3). The

hospitalization rate in the final month of life and the number of hospital deaths were lowest in patients on conservative care (Table 4). Patients on conservative care and predialysis patients both had lower overall costs and non-dialysis-sessions-related costs near the end of life compared to patients receiving dialysis (Figure 4, and Supplementary Table S3 and S4 for details on statistics).

Table 3. Mean annual hospital costs in patients selecting either conservative care or dialysis, measured from original treatment decision until death or end of study

	Choice for conservative care *n* = 100 Crude rate	**Choice for dialysis** *n* = 162 Crude rate	**Cost ratio (95% CI)**[a]	***P* value**[a]
Costs per person year	€ 5,859	€ 28,354	0.42 (0.27 to 0.65)	< 0.001
Dialysis sessions	€ 702[b]	€ 17,686[c]	0.11 (0.02 to 0.68)	0.02
Inpatient care	€ 3,084	€ 5,577	0.44 (0.20 to 0.97)	0.04
Laboratory tests	€ 591	€ 1,832	0.53 (0.35 to 0.78)	0.002
Outpatient care	€ 671	€ 1,351	0.71 (0.55 to 0.93)	0.01
Medical interventions[d]	€ 435	€ 893	0.69 (0.32 to 1.52)	0.36
Medical imaging[e]	€ 280	€ 843	0.47 (0.28 to 0.81)	0.01
Functional tests	€ 97	€ 172	0.58 (0.28 to 1.23)	0.16

[a] Negative binomial regression with adjustment for age, sex, Davies comorbidity score, estimated glomerular filtration rate, and primary kidney disease.

[b] Three patients changed their original treatment decision in favour of conservative care into dialysis and started with dialysis during follow-up; analysis was based on original treatment decision.

[c] Costs on dialysis sessions measured from original treatment decision, comprising both the predialysis and dialysis period, and as incurred by the overall group of patients who chose dialysis, including patients preparing for dialysis (*n* = 78) and patients started with dialysis (*n* = 84, including 64 on hemodialysis and 20 on peritoneal dialysis).

[d] Including surgical operations and other invasive interventions.

[e] Including imaging by radiology and nuclear medicine.

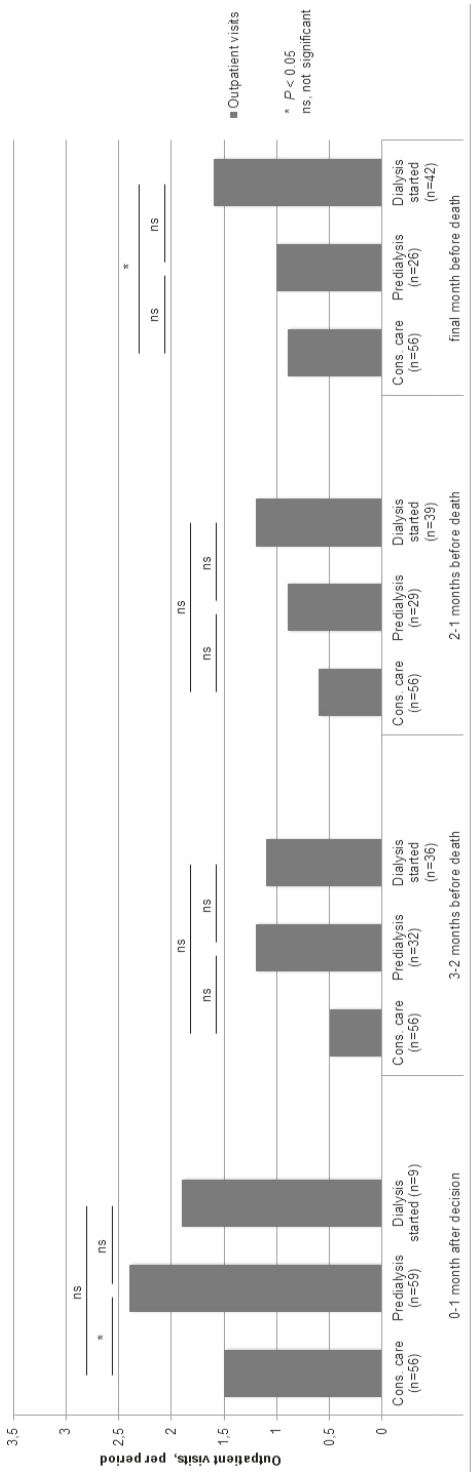

Figure 2. Outpatient visits near the end of life in patients on conservative care versus patients preparing dialysis versus patients started with dialysis (see Supplementary Table S3 for more details).

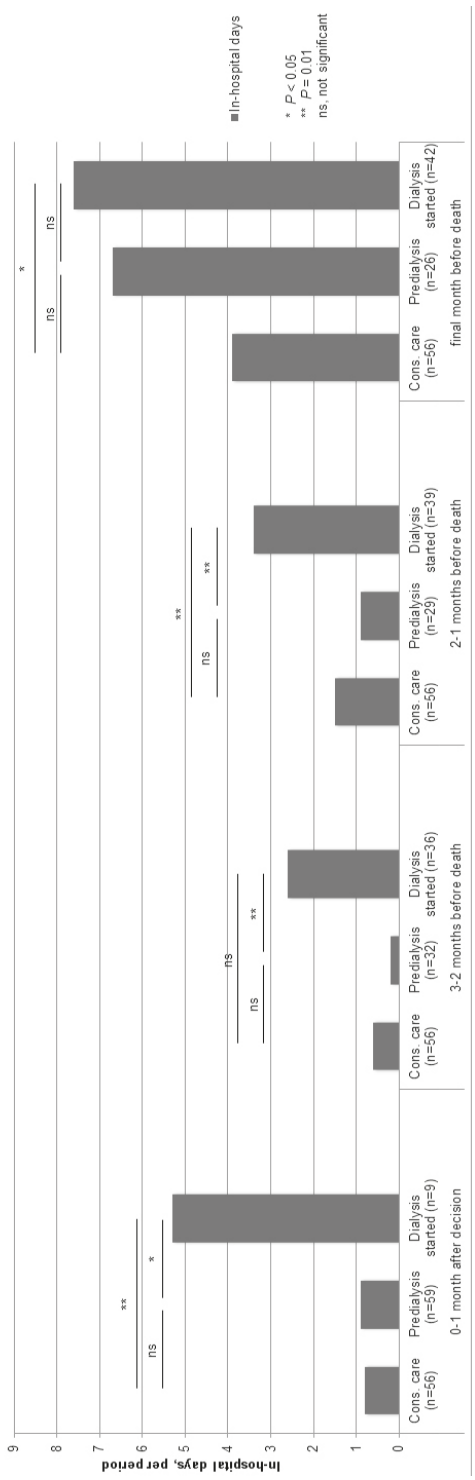

Figure 3. In-hospital days near the end of life in patients on conservative care versus patients preparing dialysis versus patients started with dialysis (see Supplementary Table S3 for more details).

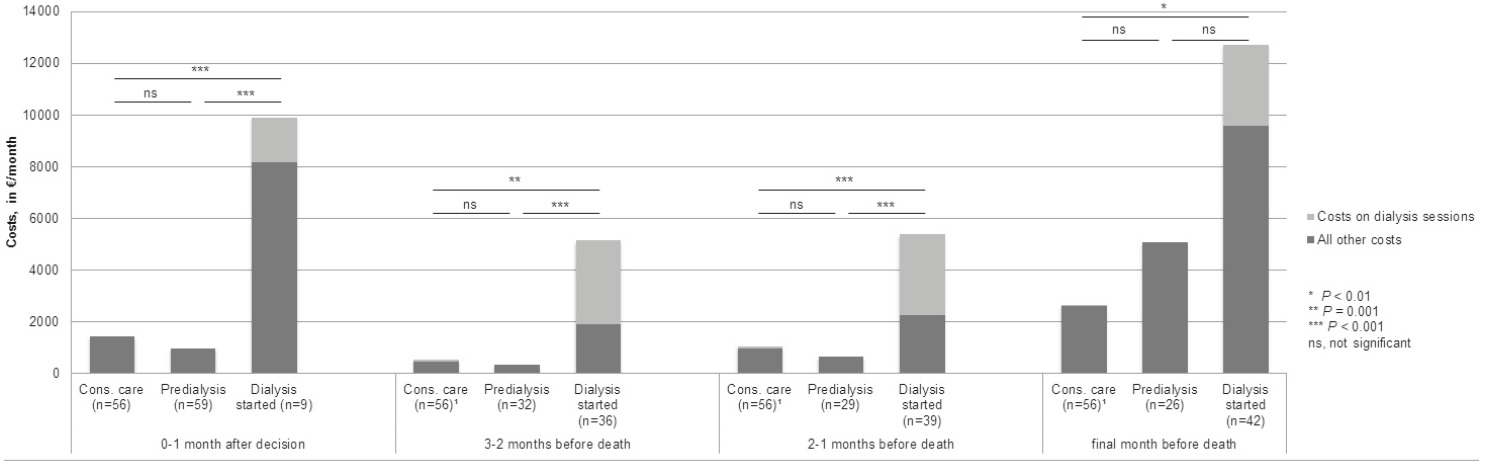

Figure 4. Hospital costs near the end of life in patients on conservative care versus patients preparing dialysis versus patients started with dialysis, comprising both hemodialysis and peritoneal dialysis. Significance of overall cost ratios is indicated (see Supplementary Table S4 for more details).

[1] One patient who initially was on a conservative care pathway switched to dialysis during follow-up.

Table 4. Hospitalization rates near the end of life (part A) and place of death (part B) in patients on conservative care versus patients preparing dialysis versus patients started with dialysis

A: Hospitalization rate	**Conservative care** *n* (%)	**Predialysis** *n* (%)	**Dialysis started** *n* (%)	**Hazard ratio** (95% CI)[a]	***P* value**[a]
0-1 month after treatment decision	7/56 (12.5%)	12/59 (20.3%)	6/9 (66.7%)	0.28 (0.09 to 0.93)[b] 0.14 (0.04 to 0.51)[c] 0.04 (0.01 to 0.22)[d]	0.04 0.003 < 0.001
3-2 months before death	9/56 (16.1%)	3/32 (9.4%)	13/36 (36.1%)	2.89 (0.69 to 12.14)[b] 0.16 (0.04 to 0.58)[c] 0.45 (0.15 to 1.39)[d]	0.15 0.01 0.17
2-1 months before death	10/56 (17.9%)	5/29 (17.2%)	14/39 (35.9%)	1.40 (0.42 to 4.61)[b] 0.28 (0.10 to 0.82)[c] 0.39 (0.14 to 1.13)[d]	0.58 0.02 0.08
1-0 months before death	26/56 (46.4%)	14/26 (53.8%)	33/42 (78.6%)	0.77 (0.37 to 1.59)[b] 0.52 (0.27 to 0.99)[c] 0.40 (0.22 to 0.74)[d]	0.47 0.047 0.003
B: Place of death	**Conservative care** *n* (%)	**Predialysis** *n* (%)	**Dialysis started** *n* (%)	**Odds ratio (95% CI)**[f]	***P* value**[f]
Hospital death[e]	18/56 (32.1%)	11/26 (42.3%)	30/42 (71.4%)	0.63 (0.21 to 1.89)[b] 0.28 (0.10 to 0.81)[c] 0.18 (0.06 to 0.51)[d]	0.41 0.02 0.001

[a] Cox regression on first event of hospitalization with adjustment for age, sex, Davies comorbidity score, and primary kidney disease.
[b] Conservative care vs. Predialysis.
[c] Predialysis vs. Dialysis started.
[d] Conservative care vs. Dialysis started.
[e] Defined as hospital death versus non-hospital death (at home, hospice, nursery home).
[f] Logistic regression with adjustment for age, sex, and Davies comorbidity score.

DISCUSSION

In this retrospective observational study, we determined hospital utilization and costs in a relatively large group of older patients who chose conservative care or dialysis after a shared decision-making process. Patients who chose conservative care had less intensive hospital utilization patterns than patients who chose dialysis, including less outpatient visits and in-hospital days at the departments of internal medicine, surgery, and neurology. Hospital costs were also lower in patients on a conservative care pathway compared to patients on a dialysis pathway, including lower costs on dialysis sessions, outpatient care, inpatient care, laboratory tests, and medical imaging. The lower hospital utilization and costs observed in patients on conservative care were also found near the end of life. These findings suggest that patients who decide to forego dialysis and choose conservative care, despite being generally older and more frail, have no higher hospital

resource needs but, on the contrary, have substantial less intensive patterns of hospital utilization and associated costs compared to patients on a dialysis pathway.

Especially when considering conservative care, it is relevant to have insight if such treatment pathway is associated with higher hospital utilization to treat symptoms that are normally targeted by dialysis, like dyspnea due to fluid overload [15-18]. Also, patients who select conservative care are generally older and have more comorbidities which could result in higher needs of hospital resources. Consistent with the limited available data, we observed that patients on conservative care had less intensive hospital utilization than those who chose dialysis [20-24]. Our analysis adds that differences were observed in both outpatient and inpatient utilization, at which hospital departments, and in the final months of life. Only two smaller studies found more emergency hospitalizations in patients on a conservative care pathway compared to patients treated with peritoneal dialysis [25], or predialysis patients [26], although the predialysis patients were significantly younger and less frail.

To the best of our knowledge, only three studies have compared costs of a conservative care pathway to a dialysis pathway. One included a comparison of bills for hospital admissions in a small patient sample [22], and two included the development of simulation models to analyze cost-effectiveness of different treatment pathways [33, 34]. Despite methodological issues [14], all three studies found lower costs for conservative care or conservative care-like pathways compared to dialysis pathways. Our observational data confirm these findings and suggest that conservative care is associated with lower hospital costs, including lower dialysis-sessions-related costs and non-dialysis-related costs, also near the end of life.

There are several explanations possible for the lower hospital utilization and costs observed in patients on conservative care compared to patients on a dialysis pathway. First, differences could be related to the more intensive treatment regimen of dialysis, its preparation trajectory including a shunt operation or peritoneal dialysis catheter insertion, and possible occurrence of complications. Suggestive for this explanation is that the main differences in outpatient and inpatient utilization were seen at internal medicine and surgery, and in costs on dialysis sessions, although further exploration would be needed to determine whether hospital resources use was dialysis-related or not. Second, detection bias could be present because patients on a dialysis pathway are

seen more often in hospital, which may result in easier use of more hospital resources ("care generates care"). Also, decisions on care in dialysis patients may be influenced by a tendency to do everything possible as dialysis is perceived as an active treatment modus [17]. A possible consequence, however, is that the patient's life and death could become more medicalized when being on a dialysis pathway, which is suggested by the higher hospital resource need observed overall and near the end of life in the dialysis patient group, including more in-hospital deaths [21, 35, 36]. Third, patients who decided to forego dialysis and chose conservative care might consider other treatment options for chronic kidney disease-related symptoms or for comorbidities unpreferred as well. Also, healthcare providers could feel that they have nothing to offer patients who chose conservative care [37, 38]. We observed, however, no lower hospital utilization rates at most departments or less costs on medical interventions in the conservative care group, which emphasizes that conservative care is an active treatment pathway as well.

A limitation of our study is its observational design, which brings the potential risks of treatment allocation bias and confounding. To overcome this problem, we adjusted for several confounders in the multivariable regression models. However, there may be residual confounding, for example, in cognitive function or nutritional status. Although the overall patient cohort was relatively large, particularly the subgroup analysis on hospital resource use near the end of life may have been underpowered. We therefore performed no other subgroup analyses, for example, on dialysis modality. Also, we might underestimate the cost differences between conservative care and dialysis because dialysis transportation costs were not available. A major strength of our study is the availability of a cohort of patients who chose conservative care or dialysis. Our findings might not be generalizable to centers with different approaches to conservative care and dialysis, to centers with different cost prices, or to countries with a different healthcare structure. Comparative evaluations of non-hospital data, including primary care, nursing homes, and hospice care, are also needed.

To conclude, we observed less intensive outpatient and inpatient hospital utilization patterns in patients aged ≥70 years old who chose conservative care compared to a dialysis pathway, including less intensive hospital utilization near the end of life. Furthermore, both overall and non-dialysis-related costs were lower in patients on a conservative care pathway. These findings suggest that a conservative care pathway could reduce the treatment burden and hospital costs associated with resource-intensive care

that may not be aligned with a patient's values and preferences. Value of care could therefore be generated in selected older patients with conservative care as alternative to dialysis considering its previously recognized potential to achieve reasonable patient-relevant outcomes, such as survival and health-related quality of life [8-13], in balance with treatment burden and costs. This emphasizes the need for a shared decision-making process on preferred treatment for end-stage kidney disease that focuses on what matters to the patient.

REFERENCES

1. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. Kidney Int. 2011;80(12):1258-70.
2. Xie Y, Bowe B, Mokdad AH, et al. Analysis of the Global Burden of Disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. Kidney Int. 2018;94(3):567-81.
3. Germain MJ. Should dialysis be offered to all elderly patients? Blood Purif. 2015;39(1-3):55-7.
4. Kooman JP, Cornelis T, van der Sande FM, Leunissen KM. Renal replacement therapy in geriatric end-stage renal disease patients: a clinical approach. Blood Purif. 2012;33(1-3):171-6.
5. 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(3):447-59.
6. Williams AW, Dwyer AC, Eddy AA, et al. Critical and honest conversations: the evidence behind the "Choosing Wisely" campaign recommendations by the American Society of Nephrology. Clin J Am Soc Nephrol. 2012;7(10):1664-72.
7. Farrington K, Covic A, Aucella F, et al. Clinical Practice Guideline on management of older patients with chronic kidney disease stage 3b or higher (eGFR <45 mL/min/1.73 m2). Nephrol Dial Transplant. 2016;31(suppl 2):ii1-ii66.
8. O'Connor NR, Kumar P. Conservative management of end-stage renal disease without dialysis: a systematic review. J Palliat Med. 2012;15(2):228-35.
9. Brown MA, Collett GK, Josland EA, Foote C, Li Q, Brennan FP. CKD in elderly patients managed without dialysis: survival, symptoms, and quality of life. Clin J Am Soc Nephrol. 2015;10(2):260-8.
10. Verberne WR, Geers AB, Jellema WT, Vincent HH, van Delden JJ, Bos WJ. Comparative Survival among Older Adults with Advanced Kidney Disease Managed Conservatively Versus with Dialysis. Clin J Am Soc Nephrol. 2016;11(4):633-40.
11. 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(1):205.
12. Da Silva-Gane M, Wellsted D, Greenshields H, Norton S, Chandna SM, Farrington K. Quality of life and survival in patients with advanced kidney failure managed conservatively or by dialysis. Clin J Am Soc Nephrol. 2012;7(12):2002-9.
13. Foote C, Kotwal S, Gallagher M, Cass A, Brown M, Jardine M. 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(3):241-53.
14. Morton RL, Kurella Tamura M, Coast J, Davison SN. Supportive Care: Economic Considerations in Advanced Kidney Disease. Clin J Am Soc Nephrol. 2016;11(10):1915-20.
15. Verberne WR, Konijn WS, Prantl K, et al. Older patients' experiences with a shared decision-making process on choosing dialysis or conservative care for advanced chronic kidney disease: a survey study. BMC Nephrol. 2019;20(1):264.
16. Morton RL, Tong A, Howard K, Snelling P, Webster AC. The views of patients and carers in treatment decision making for chronic kidney disease: systematic review and thematic synthesis of qualitative studies. BMJ. 2010;340:c112.
17. Hussain JA, Flemming K, Murtagh FE, Johnson MJ. Patient and health care professional decision-making to commence and withdraw from renal dialysis: a systematic review of qualitative research. Clin J Am Soc Nephrol. 2015;10(7):1201-15.
18. Verberne WR, Das-Gupta Z, Allegretti AS, et al. Development of an International Standard Set of Value-Based Outcome Measures for Patients With Chronic Kidney Disease: A Report of the International Consortium for Health Outcomes Measurement (ICHOM) CKD Working Group. Am J Kidney Dis. 2019;73(3):372-84.

19. Urquhart-Secord R, Craig JC, Hemmelgarn B, et al. Patient and Caregiver Priorities for Outcomes in Hemodialysis: An International Nominal Group Technique Study. Am J Kidney Dis. 2016;68(3):444-54.
20. 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(4):1313-7.
21. Carson RC, Juszczak M, Davenport A, Burns A. Is maximum conservative management an equivalent treatment option to dialysis for elderly patients with significant comorbid disease? Clin J Am Soc Nephrol. 2009;4(10):1611-9.
22. Teo BW, Ma V, Xu H, Li J, Lee EJ, Group NCR. Profile of hospitalisation and death in the first year after diagnosis of end-stage renal disease in a multi-ethnic Asian population. Ann Acad Med Singapore. 2010;39(2):79-87.
23. Hussain JA, Mooney A, Russon L. Comparison of survival analysis and palliative care involvement in patients aged over 70 years choosing conservative management or renal replacement therapy in advanced chronic kidney disease. Palliat Med. 2013;27(9):829-39.
24. Raman M, Middleton RJ, Kalra PA, Green D. Outcomes in dialysis versus conservative care for older patients: A prospective cohort analysis of stage 5 Chronic Kidney Disease. PLoS One. 2018;13(10):e0206469.
25. Shum CK, Tam KF, Chak WL, Chan TC, Mak YF, Chau KF. Outcomes in older adults with stage 5 chronic kidney disease: comparison of peritoneal dialysis and conservative management. J Gerontol A Biol Sci Med Sci. 2014;69(3):308-14.
26. Rodriguez Villarreal I, Ortega O, Hinostroza J, et al. Geriatric assessment for therapeutic decision-making regarding renal replacement in elderly patients with advanced chronic kidney disease. Nephron Clin Pract. 2014;128(1-2):73-8.
27. Phair G, Agus A, Normand C, et al. Healthcare use, costs and quality of life in patients with end-stage kidney disease receiving conservative management: results from a multi-centre observational study (PACKS). Palliat Med. 2018;32(8):1401-9.
28. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145(4):247-54.
29. Davies SJ, Russell L, Bryan J, Phillips L, Russell GI. Comorbidity, urea kinetics, and appetite in continuous ambulatory peritoneal dialysis patients: their interrelationship and prediction of survival. Am J Kidney Dis. 1995;26(2):353-61.
30. Sedgwick P. Incidence rate ratio. BMJ. 2010;341:c4804.
31. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? BMJ. 2000;320(7243):1197-200.
32. Mihaylova B, Briggs A, O'Hagan A, Thompson SG. Review of statistical methods for analysing healthcare resources and costs. Health Econ. 2011;20(8):897-916.
33. Lee CP, Chertow GM, Zenios SA. A simulation model to estimate the cost and effectiveness of alternative dialysis initiation strategies. Med Decis Making. 2006;26(5):535-49.
34. Teerawattananon Y, Mugford M, Tangcharoensathien V. Economic evaluation of palliative management versus peritoneal dialysis and hemodialysis for end-stage renal disease: evidence for coverage decisions in Thailand. Value Health. 2007;10(1):61-72.
35. Wong SPY, Yu MK, Green PK, Liu CF, Hebert PL, O'Hare AM. End-of-Life Care for Patients With Advanced Kidney Disease in the US Veterans Affairs Health Care System, 2000-2011. Am J Kidney Dis. 2018;72(1):42-9.
36. Morton RL, Webster AC, McGeechan K, et al. Conservative Management and End-of-Life Care in an Australian Cohort with ESRD. Clin J Am Soc Nephrol. 2016;11(12):2195-203.
37. Ladin K, Pandya R, Kannam A, et al. Discussing Conservative Management With Older Patients With CKD: An Interview Study of Nephrologists. Am J Kidney Dis. 2018;71(5):627-35.
38. Ladin K, Pandya R, Perrone RD, et al. Characterizing Approaches to Dialysis Decision Making with Older Adults: A Qualitative Study of Nephrologists. Clin J Am Soc Nephrol. 2018;13(8):1188-96.

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Sensitivity analysis on annual rates of outpatient visits and in-hospital days in patients selecting either conservative care or dialysis, measured from original treatment decision until death or end of study. Analysis was based on categorization of both patient groups according to the most recent documented treatment plan at the end of study or at the time of death.

	Choice for conservative care *n* = 107 Crude incidence rate	**Choice for dialysis** *n* = 155 Crude incidence rate	**Incidence rate ratio**[a] (95% CI)	***P* value**[a]
Outpatient visits per person year	6.9	10.9	0.64 (0.52 to 0.78)	< 0.001
Internal medicine	3.8	6.1	0.64 (0.53 to 0.79)	< 0.001
Surgery	0.5	1.8	0.26 (0.17 to 0.39)	< 0.001
Cardiology	0.8	0.8	0.95 (0.54 to 1.67)	0.87
Pulmonology	0.2	0.4	0.82 (0.30 to 2.25)	0.70
Gastro-enterology	0.1	0.3	0.90 (0.36 to 2.25)	0.82
Neurology	0.1	0.3	0.37 (0.17 to 0.83)	0.02
Gynaecology and Urology	0.3	0.5	0.69 (0.48 to 0.98)	0.04
Other[b]	1.0	0.8	0.93 (0.48 to 1.80)	0.83
In-hospital days per person year[c]	5.9	10.0	0.44 (0.26 to 0.74)	0.002
Internal medicine	3.1	5.5	0.32 (0.16 to 0.67)	0.002
Surgery	0.5	1.7	0.31 (0.15 to 0.63)	0.001
Cardiology	0.8	1.2	0.57 (0.20 to 1.63)	0.30
Pulmonology	0.5	0.6	0.69 (0.03 to 13.77)	0.81
Gastro-enterology	0.7	0.3	6.99 (0.69 to 70.43)	0.10
Neurology	0.1	0.3	0.05 (0.004 to 0.68)	0.03
Gynaecology and Urology	0.2	0.3	0.40 (0.25 to 0.66)	< 0.001
Other[b]	<0.1	0.1	0.17 (0.02 to 1.93)	0.15

[a] Negative binomial regression with adjustment for age, sex, Davies comorbidity score, estimated glomerular filtration rate, and primary kidney disease.
[b] Including psychiatry, rehabilitation medicine, dermatology, and ophthalmology.
[c] Including planned and non-planned in-hospital days.

Supplementary Table S2. Sensitivity analysis on mean annual hospital costs in patients who chose either conservative care or dialysis, measured from original treatment decision until death or end of study. Analysis was based on categorization of both patient groups according to the most recent documented treatment plan at the end of study or at the time of death.

	Choice for conservative care *n* = 107 Crude rate	**Choice for dialysis** *n* = 155 Crude rate	**Cost ratio** (95% CI)[a]	***P* value**[a]
Costs per person year	€ 4,945	€ 29,674	0.31 (0.20 to 0.47)	< 0.001
Dialysis sessions	€ 0	€ 18,688[b]	-	-
Inpatient care	€ 2,956	€ 5,735	0.38 (0.18 to 0.81)	0.01
Laboratory tests	€ 557	€ 1,897	0.44 (0.30 to 0.65)	< 0.001
Outpatient care	€ 680	€ 1,374	0.69 (0.54 to 0.90)	0.005
Medical interventions[c]	€ 393	€ 930	0.55 (0.25 to 1.21)	0.14
Medical imaging[d]	€ 260	€ 875	0.38 (0.22 to 0.65)	< 0.001
Functional tests	€ 99	€ 174	0.77 (0.38 to 1.55)	0.47

[a] Negative binomial regression with adjustment for age, sex, Davies comorbidity score, estimated glomerular filtration rate, and primary kidney disease.
[b] Costs on dialysis sessions measured from original treatment decision, comprising both the predialysis and dialysis period, and as incurred by the overall group of patients who chose dialysis, including patients preparing for dialysis (*n* = 68) and patients started with dialysis (*n* = 87, including 67 on hemodialysis and 20 on peritoneal dialysis).
[c] Including surgical operations and other invasive interventions.
[d] Including imaging by radiology and nuclear medicine.

Supplementary Table S3. Outpatient visits and in-hospital days near the end of life in patients on conservative care versus patients preparing dialysis versus patients started with dialysis

	Conservative care Incidence rate	**Predialysis** Incidence rate	**Dialysis started** Incidence rate	**Incidence rate ratio**[a] (95% CI)	***P* value**[a]
Outpatient visits per period					
0-1 month after treatment decision	1.5 (*n* = 56)	2.4 (*n* = 59)	1.9 (*n* = 9)	0.69 (0.49 to 0.97)[b]	0.03
				1.26 (0.75 to 2.14)[c]	0.38
				0.87 (0.48 to 1.58)[d]	0.64
3-2 months before death	0.5 (*n* = 56)	1.2 (*n* = 32)	1.1 (*n* = 36)	0.66 (0.38 to 1.17)[b]	0.15
				0.96 (0.60 to 1.55)[c]	0.87
				0.64 (0.36 to 1.13)[d]	0.12
2-1 months before death	0.6 (*n* = 56)	0.9 (*n* = 29)	1.2 (*n* = 39)	0.97 (0.51 to 1.87)[b]	0.94
				0.62 (0.35 to 1.10)[c]	0.10
				0.60 (0.33 to 1.11)[d]	0.10
1-0 months before death	0.9 (*n* = 56)	1.0 (*n* = 26)	1.6 (*n* = 42)	0.86 (0.43 to 1.73)[b]	0.68
				0.55 (0.30 to 1.00)[c]	0.05
				0.47 (0.26 to 0.87)[d]	0.02
In-hospital days per period					
0-1 month after treatment decision	0.8 (*n* = 56)	0.9 (*n* = 59)	5.3 (*n* = 9)	0.40 (0.08 to 2.00)[b]	0.26
				0.05 (0.004 to 0.63)[c]	0.02
				0.02 (0.001 to 0.42)[d]	0.01
3-2 months before death	0.6 (*n* = 56)	0.2 (*n* = 32)	2.6 (*n* = 36)	5.48 (0.66 to 45.47)[b]	0.12
				0.05 (0.01 to 0.39)[c]	0.01
				0.26 (0.05 to 1.40)[d]	0.12
2-1 months before death	1.5 (*n* = 56)	0.9 (*n* = 29)	3.4 (*n* = 39)	2.03 (0.35 to 11.79)[b]	0.43
				0.06 (0.01 to 0.47)[c]	0.01
				0.13 (0.03 to 0.63)[d]	0.01
1-0 months before death	3.9 (*n* = 56)	6.7 (*n* = 26)	7.6 (*n* = 42)	0.48 (0.17 to 1.36)[b]	0.17
				0.77 (0.29 to 2.08)[c]	0.61
				0.37 (0.14 to 0.96)[d]	0.04

[a] Negative binomial regression with adjustment for age, sex, Davies comorbidity score, and primary kidney disease.
[b] Conservative care vs. Predialysis.
[c] Predialysis vs. Dialysis started.
[d] Conservative care vs. Dialysis started.

Supplementary Table S4. Hospital costs near the end of life in patients on conservative care versus patients preparing dialysis versus patients started with dialysis (including hemodialysis and peritoneal dialysis)

	Conservative care Crude rate	**Predialysis** Crude rate	**Dialysis started** Crude rate	**Cost ratio**[a] (95% CI)	***P* value**[a]
Overall costs per period					
0-1 month after treatment decision	€ 1,436 (*n* = 56)	€ 976 (*n* = 59)	€ 9,907 (*n* = 9)	0.90 (0.41 to 1.99)[b] 0.07 (0.02 to 0.23)[c] 0.06 (0.02 to 0.24)[d]	0.79 < 0.001 < 0.001
3-2 months before death	€ 543 (*n* = 56)	€ 336 (*n* = 32)	€ 5,132 (*n* = 36)	3.17 (0.79 to 12.74)[b] 0.03 (0.01 to 0.12)[c] 0.11 (0.03 to 0.39)[d]	0.10 < 0.001 0.001
2-1 months before death	€ 1,053 (*n* = 56)	€ 647 (*n* = 29)	€ 5,369 (*n* = 39)	1.99 (0.57 to 6.97)[b] 0.03 (0.01 to 0.13)[c] 0.07 (0.02 to 0.21)[d]	0.28 < 0.001 < 0.001
1-0 months before death	€ 2,655 (*n* = 56)	€ 5,077 (*n* = 26)	€ 12,692 (*n* = 42)	0.48 (0.11 to 2.07)[b] 0.34 (0.10 to 1.20)[c] 0.16 (0.05 to 0.58)[d]	0.32 0.09 0.005
Costs on dialysis sessions per period					
0-1 month after treatment decision	€ 0 (*n* = 56)	€ 0 (*n* = 59)	€ 1,731 (*n* = 9)	-	-
3-2 months before death	€ 78[e] (*n* = 56)	€ 0 (*n* = 32)	€ 3,239 (*n* = 36)	-	-
2-1 months before death	€ 85[e] (*n* = 56)	€ 0 (*n* = 29)	€ 3,130 (*n* = 39)	-	-
1-0 months before death	€ 54[e] (*n* = 56)	€ 0 (*n* = 26)	€ 3,103 (*n* = 42)	-	-
All other costs per period					
0-1 month after treatment decision	€ 1,436 (*n* = 56)	€ 976 (*n* = 59)	€ 8,176 (*n* = 9)	0.90 (0.41 to 1.99)[b] 0.08 (0.03 to 0.27)[c] 0.07 (0.02 to 0.28)[d]	0.79 < 0.001 < 0.001
3-2 months before death	€ 464 (*n* = 56)	€ 336 (*n* = 32)	€ 1,893 (*n* = 36)	2.62 (0.64 to 10.66)[b] 0.10 (0.03 to 0.38)[c] 0.26 (0.07 to 0.93)[d]	0.18 0.001 0.04
2-1 months before death	€ 968 (*n* = 56)	€ 647 (*n* = 29)	€ 2,240 (*n* = 39)	1.91 (0.53 to 6.93)[b] 0.10 (0.02 to 0.38)[c] 0.18 (0.06 to 0.59)[d]	0.32 0.001 0.005
1-0 months before death	€ 2,601 (*n* = 56)	€ 5,077 (*n* = 26)	€ 9,589 (*n* = 42)	0.43 (0.10 to 1.94)[b] 0.46 (0.13 to 1.67)[c] 0.20 (0.06 to 0.73)[d]	0.28 0.24 0.02

[a] Negative binomial regression with adjustment for age, sex, Davies comorbidity score, and primary kidney disease.
[b] Conservative care vs. Predialysis.
[c] Predialysis vs. Dialysis started.
[d] Conservative care vs. Dialysis started.
[e] One patient who initially was on a conservative care pathway switched to dialysis during follow-up.