Published in final edited form as:

Hemodial Int. 2019 April ; 23(2): 261–272. doi:10.1111/hdi.12723.

Early Withdrawal and Non-Withdrawal Death in the Months Following Hemodialysis Initiation: A Retrospective Cohort Analysis

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Abstract

Background: Whether and how factors associated with elective hemodialysis withdrawal differ from those associated with non-withdrawal death soon after maintenance hemodialysis initiation have not been well studied

Methods: A retrospective cohort analysis was performed using USRDS data from 2011–2014. Patients were randomly categorized 2:1 into training and validation samples. Elective withdrawal deaths were identified using the Death Notification form. Multinomial logistic regression was used to fit a prediction model for three outcome categories (withdrawal, non-withdrawal death, survival at 6 months) as a function of demographic, comorbidity, and functional status.

Findings: The training sample comprised 80,284 hemodialysis patients. Mean age was 71.7 ± 11.4 years, 44.9% were female, 72.9% were white, and 22.8% were black. Within 6 months, 19.1% died, of whom 2099 (2.6%) withdrew and 13,223 (16.5%) died of a non-withdrawal cause; 13.7% of all deaths were withdrawals. Baseline characteristics and event rates were similar among the 40,142 patients in the validation sample. The model was calibrated adequately and could discriminate moderately well between withdrawal and survival (area under ROC curve [AUC]: 0.77) and between non-withdrawal death and survival (AUC: 0.73). However, discrimination between withdrawal and non-withdrawal death was relatively low (AUC: 0.62). Older age and white, compared with non-white, race were each associated with greater odds of death, and these associations were stronger for withdrawal than for non-withdrawal death.

Discussion: Advanced age and white, as opposed to black, race were most strongly associated with early elective hemodialysis withdrawal compared with non-withdrawal death. However, it is difficult to differentiate between patients who will experience early withdrawal versus non-withdrawal death, as many factors are similarly associated with both outcomes.

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Conflict of Interest Statement: The authors report no conflicts of interest.

Keywords

Dialysis; ESRD; withdrawal; Medicare

Introduction

The end-of-life experience for patients receiving maintenance dialysis is an increasingly important area of study. The growth in the prevalent dialysis population has been driven mainly by increases in longevity.^{1,2} Consequently, appropriate use of conservative care for end-stage renal disease (ESRD),^{3–6} palliative care in nephrology,^{7–12} and elective withdrawal from dialysis^{13–19} are issues currently engaging the nephrology community.

Many patients who initiate maintenance dialysis die soon thereafter. In the US, at least 7% of new hemodialysis patients die within 3 months of initiation, and approximately 20% die within 12 months.¹ Patients who die soon after initiation are important to study because non-initiation may have been an appropriate option for them. This may be especially true for patients who electively withdraw soon after dialysis initiation; the burden imposed by dialysis, often a principle factor in the decision to withdraw, might be avoided by maintaining quality of life through a conservative approach to care.

Several studies have sought to risk-stratify dialysis initiators for all-cause mortality,^{20–26} while others have examined the factors associated with dialysis withdrawal.^{14,15,19,27,28} However, few if any studies have rigorously examined early withdrawal in incident dialysis patients. Using a large sample of patients from a national registry,¹ we sought to examine how patients who elected to withdraw, as well as those who died of a non-withdrawal cause soon after initiation, differed from survivors. We were interested in determining whether patients who withdrew early might be distinguished from those who experienced early death, because the former may represent a unique group of individuals who, if sensitively and informatively counselled, might elect not to initiate dialysis. We reasoned that understanding the factors associated with early death, whether due to elective withdrawal or not, might inform patients and providers about outcomes in the early post-initiation period.

Materials and Methods

Data sources

Data from 2011 to 2014 in the United States Renal Data System (USRDS) ESRD database, which includes data from the ESRD Medical Evidence Report, the ESRD Death Notification (form CMS-2746), and Medicare Parts A and B claims, were used. We used Medicare billing claims data to determine the presence of comorbid conditions and to generate a putative marker of functional status based in part on claims for use of durable medical equipment (DME; further described below).

Study design

This study used a retrospective design. Patients initiating hemodialysis between January 1, 2011, and July 1, 2014 (permitting at least 6 months of follow-up), who had an ESRD

Medical Evidence Report were identified. All patients were required to have been insured by Medicare Parts A and B for at least 1 year prior to hemodialysis initiation and to have been aged at least 18 years. Patients were followed for 6 months (3 months in a sensitivity analysis) from the first date of dialysis to the earliest of date of death, kidney transplant, or December 31, 2014.

Demographic and comorbidity variables

Variables selected for analysis were based on clinical insights and concordance with previous studies.^{14,15,19} Age, race, sex, and cause of ESRD (derived from the USRDS standard analytic files) were included, as were major comorbid conditions, ascertained over the year preceding hemodialysis initiation by the presence of one or more inpatient or two or more outpatient/Part B claims separated by at least 30 days.^{29,30} The conditions assessed and the associated identification approach are shown in Supplementary Methods S1 and Table S1. We also included duration of nephrology care prior to hemodialysis initiation, initial hemodialysis access, and time spent hospitalized or in a skilled nursing (SNF) facility in the year preceding hemodialysis initiation. Additionally, we included two markers of the rate of kidney function decline: presence of a claim for stage 3 chronic kidney disease (CKD) in the previous year, or a claim for acute kidney injury (AKI) in the 10 days preceding hemodialysis initiation (Table 1).

To create a score that might reflect difficult-to-define phenomena such as impaired functional status, we employed a variation of a previously developed claims-based algorithm,^{19,29} which eliminated a history of myocardial infarction or stroke from the score (as these were accounted for separately as model covariates).

Determination of withdrawal and non-withdrawal death

Deaths were identified using the Death Notification form. Details of our definition of dialysis withdrawal, adapted from our previous work¹⁹ appear in Supplementary Methods S2. In brief, presence of code 104 in the first or second position of question 12 on the Death Notification form, plus a “yes” answer to question 14 (“Was discontinuation of renal replacement therapy after patient/family request to stop dialysis?”), was required. We also required death to occur at least 3 days after withdrawal in order to exclude (as withdrawers) patients who likely faced imminent death and did not truly withdraw as withdrawal is commonly understood. All other deaths were considered non-withdrawal deaths. Given that the majority of deaths were non-withdrawal deaths, and the likely strong incentive to code a withdrawal death affirmatively as a withdrawal (as opposed to leaving the field blank), we considered unknown/missing deaths to be non-withdrawal deaths.

Inclusions and exclusions

Construction of the study sample is shown in Figure 1. Patients without a known initial hemodialysis access type, or who died on their first day of dialysis, were excluded. Of patients who withdrew, those without a known withdrawal date and those who survived longer than 90 days after withdrawal were excluded. The remaining patients were randomly split 2:1 into training and validation samples.

Statistical analysis

Descriptive statistics (counts [*n*], percentages [%]) were used to characterize the maintenance hemodialysis patients in the training sample stratified by the three outcome categories of interest (withdrawal, non-withdrawal death, survival by 6 months). Multinomial logistic regression was used to fit a prediction model for the three outcome categories as a function of the demographic, comorbidity, and functional status covariates in the training sample. This model simultaneously estimated two sets of risk equations on the log scale, one for the ratio of the probability of withdrawal to the probability of survival (base event) and the other for the ratio of the probability of non-withdrawal death to the probability of survival, with the constraint that predicted probabilities for the three outcome categories sum to 1. The exponential of each regression coefficient can be interpreted as a generalized odds ratio (OR).

Risk prediction performance of the model was assessed in the validation sample using measures of discrimination and calibration (Supplementary Methods S3).

Additional sensitivity analyses were conducted. First, because patients initiating dialysis due to AKI may have been misclassified as having ESRD, we refit the primary model after excluding 14,028 patients with AKI and no history of CKD in the previous year. Second, we refit the primary model with outcomes assessed in the first 3 months after hemodialysis initiation. Third, because kidney function at the time of dialysis initiation is likely an important predictor of early prognosis, we refit the original model additionally adjusting for estimated glomerular filtration rate (eGFR; $< \text{or } 10 \text{ mL/min/1.73m}^2$) as calculated from the USRDS Medical Evidence Report, which uses the CKD-EPI formula³¹; 17,606 patients were excluded from this analysis because their serum creatinine values were measured after hemodialysis initiation or more than 10 days before. Fourth, the preceding sensitivity analysis was refit after excluding 117 patients with implausibly high initiating eGFR values ($> 45 \text{ mL/min/1.73m}^2$). Additional sensitivity analyses considered only the results of question 14 (irrespective of whether withdrawal was explicitly listed in question 12), used a 12-month follow-up period, and included only patients aged 66 years or older upon hemodialysis initiation.

Compliance and protection of human research participants

The research protocol was approved by the institutional review board at Hennepin Healthcare Systems. Data Use Agreements (DUA) between the Hennepin Healthcare Research Institute and the USRDS and CMS were in place.

Results

Characteristics of the patients comprising the training sample are shown in Table 1. Of these 80,284 patients, 19.1% died within 6 months; 2099 (2.6%) withdrew and 13,223 (16.5%) died of a non-withdrawal cause. Thus, 13.7% of all deaths were withdrawals. On average, patients who withdrew or who died of a non-withdrawal cause were older and more likely to be white, rather than black or of other non-white race. Sex distributions differed little between the three groups. Percentages of individual comorbid conditions were generally

lower for patients who withdrew than those who died of a non-withdrawal cause, although there were exceptions.

The performance of the risk prediction model was assessed in the validation sample using measures of discrimination and calibration. Considering the outcome categories in a pairwise fashion, the model discriminated moderately well between withdrawal and survival by 6 months (area under the receiver operating characteristic curve [AUC]: 0.77) and between non-withdrawal death and survival by 6 months (AUC: 0.73) (Table 2, Figure 2). However, discrimination between withdrawal and non-withdrawal death by 6 months was relatively low (AUC: 0.62). The overall multi-class model discrimination (i.e., the ability to correctly distinguish two patients from two randomly selected outcome categories) was also quite modest (*M*-index: 0.68). The model was well calibrated on average, as reflected by close agreement between observed and predicted event rates (Table 3, Figure S1) and calibration intercepts near zero (Table S2); calibration slopes were close to 1, suggesting the model was neither overfitted nor underfitted.

The factors associated with withdrawal (relative to survival) and with non-withdrawal death (relative to survival) within 6 months of hemodialysis initiation are shown in Table 4. Because the primary aim of the model-building exercise was creation of a multivariable prediction model, the coefficients of the prediction model, shown as ORs, cannot be interpreted as causal effect estimates. In general, however, patterns of the factors associated with withdrawal and with non-withdrawal death were similar: older age, white race, AKI, dialysis initiation with an access other than fistula, and increasing functional status score (indicating poorer functional status) were associated with a similarly increased risk of withdrawal and of death from a non-withdrawal cause. However, age was more strongly associated with withdrawal than with non-withdrawal death, while non-white, compared with white, race was substantially less strongly associated with withdrawal than with non-withdrawal death. Notably, for predialysis nephrology care of 12 months or shorter, (compared with longer than 12 months), the odds of death from a non-withdrawal cause relative to survival were increased, but there was no corresponding association with withdrawal. Increased SNF time (≥ 31 days in the year preceding dialysis initiation) was associated only with increased odds of withdrawal (compared with less SNF time, but not with increased odds of non-withdrawal death).

Example predicted risk profiles for 6-month outcomes are shown in Figure 3. The four scenarios illustrated demonstrate varying predicted probabilities of the various outcomes. Case A represents the predicted probabilities for a relatively young and healthy person who initiated hemodialysis with a fistula having received a year of predialysis nephrology care; in this scenario, the predicted survival probability was 98.7% and the probability of withdrawal only 0.1%. At the other extreme is Case D, representing an elderly individual with many comorbid conditions, no predialysis care, and initiation with a catheter; predicted survival probability is only 41.8%. Intermediate Cases B and C show how the predicted probabilities of withdrawal and non-withdrawal death vary by scenario (8.2% for withdrawal versus 18.6% for non-withdrawal death for Case B; 1.9% versus 14.5%, respectively, for Case C).

Multiple sensitivity analyses were conducted. To reduce the likelihood of AKI being misclassified as ESRD, we excluded 6730 patients with AKI and no history of CKD in the previous year; the results of the model were nearly identical (Table S3). Next, we modeled 3-month mortality; a slightly higher proportion of all deaths were attributed to withdrawal at 3 (14.9%) than at 6 (13.7%) months, but results were nearly identical to the primary model (Table S4). Next, we accounted for eGFR at dialysis initiation ($\leq$ or $>$ 10 mL/min/1.73m²); this was not originally part of the main model since eGFRs for a large number of patients were measured well before dialysis initiation, rendering this value suspect. Nonetheless, results were nearly identical (Table S5). Additional sensitivity analyses excluded patients initiating with eGFR $\leq$ 45 mL/min/1.73m², classified only patients for whom the answer to question 14 on the Death Notification form was “yes” (irrespective of whether withdrawal was listed as a cause of death in question 12), examined 12-month mortality as the outcome, and considered only patients aged 66 years or older at time of hemodialysis initiation; for all, results were nearly identical (not shown).

Discussion

In this study, we examined factors associated with elective dialysis withdrawal and with non-withdrawal death within 6 months of hemodialysis initiation. While other studies have examined factors associated with all-cause mortality in incident dialysis patients,^{20–26} none, to our knowledge, have specifically examined early elective withdrawal. We found that overall discrimination was modest at best, and discrimination between withdrawal and non-withdrawal death in particular was relatively poor. Despite substantial overlap in the factors associated with withdrawal and with non-withdrawal death, several factors appeared to be relatively more strongly associated with early withdrawal than with early non-withdrawal death, namely advanced age, white race, and more intensive SNF care prior to dialysis initiation. These findings could inform discussions between physicians and patients facing ESRD onset and, more generally, contribute to the understanding of mortality in the months after dialysis initiation.

Mortality rates soon after initiation are high worldwide,^{21,32} suggesting that dialysis initiation may not best serve the needs of certain patients, such as those for whom dialysis is likely to be especially burdensome or life expectancy short. Elective withdrawal from dialysis represents a special case of early mortality, as these patients may be uniquely receptive to discussions about alternative care options if their future course were at least partially predictable. For such patients, non-initiation of dialysis or palliative ESRD care may be appropriate. Thus, consideration of early death as a whole, without regard to whether the patient participated in the elective withdrawal process, may not adequately reflect the totality of experience for patients newly initiated on hemodialysis.

Because the focus of this study was to create a multivariable prediction model rather than to specifically identify factors causally related to withdrawal and non-withdrawal death, coefficients from the prediction model should not be interpreted as precise causal effect estimates.³³ Nonetheless, some clinical insights are possible. Heavy disease burden, which often characterizes patients receiving hemodialysis, prompts both death and elective withdrawal, so it was unsurprising that many factors were associated with both withdrawal

and non-withdrawal death. As with studies examining death regardless of cause, increasing age,^{21–23,25,26} dialysis initiation with a catheter in the absence of a developing fistula or graft,²⁵ major comorbid conditions such as heart failure^{23,25,26} or cancer,^{22,23,25,26} poorer functional status,²³ and increased use of hospitalization prior to dialysis initiation^{25,26} were associated with both forms of death in our study. As such, our model, overall, had a very modest ability to discriminate between patients who withdrew within 6 months from those who died of another cause.

However, there were some important distinctions between patients who withdrew and those who died of a non-withdrawal cause. Although age would be expected to be associated with death of any etiology, including withdrawal,¹⁹ the strength of association of older age was greater for withdrawal relative to survival than for non-withdrawal death relative to survival. A very recent study using patient medical records also found that older age was associated with elective withdrawal, although this study was not confined to an examination of new initiates.³⁴ This suggests that the possibility of elective withdrawal in the months after dialysis initiation should be especially emphasized when counselling older patients about what the post-initiation period might hold. Time spent institutionalized in a SNF in the year preceding hemodialysis initiation also appeared to be associated with early withdrawal in a graded fashion, although no clear trend was observed for non-withdrawal death. Heavy use of predialysis institutionalization may therefore be at least a modest marker for individuals at increased risk for early elective withdrawal, and be relevant when counselling patients.

Perhaps most striking were the findings associated with race. While non-whites (blacks and members of other racial groups) demonstrated a modest 6-month survival advantage compared with whites, they were less than half as likely as whites to withdraw within 6 months. This finding was also concordant with the results of a recent study in which whites were much more likely to withdraw than non-whites.³⁴ As a percentage of all early deaths, withdrawal was nearly twice as frequent in whites as in blacks. The reasons are uncertain; it has been speculated in the case of prevalent dialysis patients¹⁹ that members of racial minorities have a relatively higher “threshold” for elective withdrawal than whites, perhaps due to cultural or societal factors. Other, poorly defined barriers to withdrawal may also exist, including the possibility that nephrologists do not discuss elective withdrawal in the same terms, or with the same frequency or intensity, with black or other minority patients as with white patients. Racial differences in end-of-life care requires further study.

One unexpected finding concerned the association of outcomes with duration of predialysis nephrology care. While longer duration was associated with decreased risk of non-withdrawal death, as might be expected on the basis of other studies,^{21,25} this was not the case for withdrawal. *A priori*, we had expected that shorter duration of predialysis nephrology care would also be associated with early withdrawal, since patients would presumably have had fewer opportunities to receive predialysis counselling about how dialysis initiation transpires. That this did not appear to be the case suggests that nephrologists may not routinely discuss withdrawal after initiation as a possible scenario. Whether and how nephrologists discuss elective dialysis withdrawal with their patients should be further studied.

Our study is subject to several important limitations. First, we studied only US patients insured by Medicare, so our findings may be less pertinent to patients in other countries where the criteria for initiating dialysis, and the sociocultural milieu involving withdrawal from dialysis, differ from in the US. Second, our definition of dialysis withdrawal, while carefully considered in this and other studies to attempt to truly identify elective dialysis withdrawal, is likely subject to some degree of misclassification. Since our definition emphasized specificity, it seems more likely that we misclassified some patients who truly withdrew as non-withdrawers than the reverse. Fourth, early death appears to be missed in the USRDS data²¹; it is uncertain how these apparent deaths are apportioned between elective withdrawal and non-withdrawal death. Finally, factors such as socioeconomic status or social support (e.g., living with others in the home) were not explicitly considered and might have helped to improve the performance of the prediction model.

In conclusion, the present study may be the first to comprehensively analyze early elective withdrawal in a large patient registry. Nearly one in seven patients who died within 6 months of hemodialysis initiation electively withdrew. Our work demonstrates the difficulty of predicting early withdrawal; our model had relatively low ability to discriminate between withdrawal and non-withdrawal death because many factors are similarly associated with both outcomes. Nevertheless, advanced age and substantial time in a SNF prior to dialysis initiation were more strongly associated with early withdrawal than with non-withdrawal death; these factors may be appropriate to consider when advising patients about the post-initiation experience. Blacks and members of other racial minorities were substantially less likely to withdraw early after dialysis initiation than whites, a finding that may reflect sociocultural differences in end-of-life care or differential interactions with the healthcare system. Longer duration of predialysis nephrology care, while associated with lower risk of non-withdrawal death, was not associated with decreased likelihood of withdrawal, a finding that can likely be understood only by studying how nephrologists counsel patients as ESRD approaches.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Chronic Disease Research Group colleagues Anne Shaw for manuscript preparation and Nan Booth, MSW, MPH, ELS, for manuscript editing.

Funding Statement: This study was funded by NIH grants #DK104006 and HL132373 to JBW. The data reported here have been supplied by the United States Renal Data System (USRDS) (DUA#2015–25, 2016–63, 2016–63a). The funding agency had no role in the study design; collection, analysis, and interpretation of data; writing the report; or the decision to submit the report for publication. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the US government.

Reference List

- (1). United States Renal Data System. US Renal Data System 2017 Annual Data Report: Epidemiology of Kidney Disease in the United States. *Am J Kidney Dis* 2018;71(3, Suppl 1):S1-S676.

- (2). Weinhandl E, Constantini E, Everson S et al. Peer Kidney Care Initiative 2014 report: dialysis care and outcomes in the United States. *Am J Kidney Dis* 2015;65(6 Suppl 1):S1-S140.
- (3). Murtagh FE, Cohen LM, Germain MJ. The “no dialysis” option. *Adv Chronic Kidney Dis* 2011;18(6):443–449. [PubMed: 22098664]
- (4). Murtagh FE, Burns A, Moranne O, Morton RL, Naicker S. Supportive care: comprehensive conservative care in end-stage kidney disease. *Clin J Am Soc Nephrol* 2016;11(10):1909–1914. [PubMed: 27510453]
- (5). Davison SN, Jassal SV. Supportive care: integration of patient-centered kidney care to manage symptoms and geriatric syndromes. *Clin J Am Soc Nephrol* 2016;11(10):1882–1891. [PubMed: 27510454]
- (6). Morton RL, Kurella TM, Coast J, Davison SN. Supportive care: economic considerations in advanced kidney disease. *Clin J Am Soc Nephrol* 2016;11(10):1915–1920. [PubMed: 27510455]
- (7). O’Connor NR, Kumar P. Conservative management of end-stage renal disease without dialysis: a systematic review. *J Palliat Med* 2012;15(2):228–235. [PubMed: 22313460]
- (8). Muthalagappan S, Johansson L, Kong WM, Brown EA. Dialysis or conservative care for frail older patients: ethics of shared decision-making. *Nephrol Dial Transplant* 2013;28(11):2717–2722. [PubMed: 23787549]
- (9). Van Biesen W, van de Luijngaarden MW, Brown EA et al. Nephrologists’ perceptions regarding dialysis withdrawal and palliative care in Europe: lessons from a European Renal Best Practice survey. *Nephrol Dial Transplant* 2015;30(12):1951–1958. [PubMed: 26268713]
- (10). Fung E, Slesnick N, Kurella TM, Schiller B. A survey of views and practice patterns of dialysis medical directors toward end-of-life decision making for patients with end-stage renal disease. *Palliat Med* 2016;30(7):653–660. [PubMed: 26814215]
- (11). Lazenby S, Edwards A, Samuriwo R, Riley S, Murray MA, Carson-Stevens A. End-of-life care decisions for haemodialysis patients - ‘We only tend to have that discussion with them when they start deteriorating’. *Health Expect* 2017;20(2):260–273. [PubMed: 26968338]
- (12). Couchoud C, Bello AD, Lobbedez T et al. Access to and characteristics of palliative care-related hospitalization in the management of end-stage renal disease patients on renal replacement therapy in France. *Nephrology (Carlton)* 2017;22(8):598–608. [PubMed: 27192045]
- (13). Kurella TM, Goldstein MK, Perez-Stable EJ. Preferences for dialysis withdrawal and engagement in advance care planning within a diverse sample of dialysis patients. *Nephrol Dial Transplant* 2010;25(1):237–242. [PubMed: 19734137]
- (14). Chan HW, Clayton PA, McDonald SP, Agar JW, Jose MD. Risk factors for dialysis withdrawal: an analysis of the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, 1999–2008. *Clin J Am Soc Nephrol* 2012;7(5):775–781. [PubMed: 22461540]
- (15). Ellwood AD, Jassal SV, Suri RS, Clark WF, Na Y, Moist LM. Early dialysis initiation and rates and timing of withdrawal from dialysis in Canada. *Clin J Am Soc Nephrol* 2013;8(2):265–270. [PubMed: 23085725]
- (16). O’Hare AM, Vig EK, Hebert PL. Initiation of dialysis at higher levels of estimated GFR and subsequent withdrawal. *Clin J Am Soc Nephrol* 2013;8(2):179–181. [PubMed: 23349332]
- (17). Aggarwal Y, Baharani J. End-of-life decision making: withdrawing from dialysis: a 12-year retrospective single centre experience from the UK. *BMJ Support Palliat Care* 2014;4(4):368–376.
- (18). Findlay MD, Donaldson K, Doyle A et al. Factors influencing withdrawal from dialysis: a national registry study. *Nephrol Dial Transplant* 2016;31(12):2041–2048. [PubMed: 27190373]
- (19). Wetmore JB, Yan H, Hu Y, Gilbertson DT, Liu J. Factors associated with withdrawal from maintenance dialysis: a case-control analysis. *Am J Kidney Dis* 2018;71(6):831–841. [PubMed: 29331476]
- (20). Foote C, Ninomiya T, Gallagher M et al. Survival of elderly dialysis patients is predicted by both patient and practice characteristics. *Nephrol Dial Transplant* 2012;27(9):3581–3587. [PubMed: 22565061]
- (21). Foley RN, Chen SC, Solid CA, Gilbertson DT, Collins AJ. Early mortality in patients starting dialysis appears to go unregistered. *Kidney Int* 2014;86(2):392–398. [PubMed: 24522495]

- (22). Floege J, Gillespie IA, Kronenberg F et al. Development and validation of a predictive mortality risk score from a European hemodialysis cohort. *Kidney Int* 2015;87(5):996–1008. [PubMed: 25651366]
- (23). Couchoud CG, Beuscart JB, Aldigier JC, Brunet PJ, Moranne OP. Development of a risk stratification algorithm to improve patient-centered care and decision making for incident elderly patients with end-stage renal disease. *Kidney Int* 2015;88(5):1178–1186. [PubMed: 26331408]
- (24). Kanda E, Bieber BA, Pisoni RL, Robinson BM, Fuller DS. Importance of simultaneous evaluation of multiple risk factors for hemodialysis patients' mortality and development of a novel index: dialysis outcomes and practice patterns study. *PLoS One* 2015;10(6):e0128652.
- (25). Thamer M, Kaufman JS, Zhang Y, Zhang Q, Cotter DJ, Bang H. Predicting Early Death Among Elderly Dialysis Patients: Development and Validation of a Risk Score to Assist Shared Decision Making for Dialysis Initiation. *Am J Kidney Dis* 2015;66(6):1024–1032. [PubMed: 26123861]
- (26). Wick JP, Turin TC, Faris PD et al. A Clinical Risk Prediction Tool for 6-Month Mortality After Dialysis Initiation Among Older Adults. *Am J Kidney Dis* 2017;69(5):568–575. [PubMed: 27856091]
- (27). Leggat JE Jr, Bloembergen WE, Levine G, Hulbert-Shearon TE, Port FK. An analysis of risk factors for withdrawal from dialysis before death. *J Am Soc Nephrol* 1997;8(11):1755–1763. [PubMed: 9355079]
- (28). Fissell RB, Bragg-Gresham JL, Lopes AA et al. Factors associated with “do not resuscitate” orders and rates of withdrawal from hemodialysis in the international DOPPS. *Kidney Int* 2005;68(3):1282–1288. [PubMed: 16105062]
- (29). Wetmore JB, Liu J, Wirtz HS et al. Geovariation in Fracture Risk among Patients Receiving Hemodialysis. *Clin J Am Soc Nephrol* 2016;11(8):1413–1421. [PubMed: 27269611]
- (30). Slinin Y, Guo H, Li S et al. Hemodialysis patient outcomes: provider characteristics. *Am J Nephrol* 2014;39(5):367–375. [PubMed: 24776789]
- (31). Inker LA, Schmid CH, Tighiouart H et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med* 2012;367(1):20–29. [PubMed: 22762315]
- (32). Robinson BM, Zhang J, Morgenstern H et al. Worldwide, mortality risk is high soon after initiation of hemodialysis. *Kidney Int* 2014;85(1):158–165. [PubMed: 23802192]
- (33). Westreich D, Greenland S. The table 2 fallacy: presenting and interpreting confounder and modifier coefficients. *Am J Epidemiol* 2013;177(4):292–298. [PubMed: 23371353]
- (34). Chen JC, Thorsteinsdottir B, Vaughan LE et al. End of life, withdrawal, and palliative care utilization among patients receiving maintenance hemodialysis therapy. *Clin J Am Soc Nephrol* 2018;13(8):1172–1179. [PubMed: 30026285]

Figure 1.
Study design. ESRD, end-stage renal disease.

Figure 2.
Discrimination plot.

Figure 3.

Example predicted risk profiles for 6-month outcomes. *Case A:* Black female aged 18–44 years, ESRD from GN, predialysis care > 12 months, CKD stage 3 within the past year but no AKI, no other comorbidity, best functional status score, < 14 hospital days and no nursing facility care, starting hemodialysis as an outpatient with a mature AVF. Corresponding percentages at 6 months: survival 98.7%, non-withdrawal death 1.2%, elective withdrawal 0.1%. *Case B:* White female aged 85 years or older; ESRD from hypertension; predialysis care > 12 months; CKD stage 3 but no AKI within the past year;

history of arrhythmia, atherosclerotic heart disease, and gastrointestinal bleeding; moderately poor functional status score (category 3); < 14 hospital days but 31 nursing facility days; starting hemodialysis as an inpatient with a catheter but with a maturing AVF or graft. Corresponding percentages at 6 months: survival 73.2%, non-withdrawal death 18.6%, elective withdrawal 8.2%. *Case C:* Black female aged 75–84 years; ESRD from hypertension; predialysis care 6–12 months, CKD stage 3 but no AKI within the past year; history of arrhythmia, atherosclerotic heart disease, and gastrointestinal bleeding; moderately poor functional status score (category 3); < 14 hospital days but 31 nursing facility days; starting hemodialysis as an inpatient with a catheter but with a maturing AVF or graft. Corresponding percentages at 6 months: survival 73.2%, non-withdrawal death 18.6%, elective withdrawal 8.2%. *Case D:* White female aged 85 years or older; ESRD from hypertension; predialysis care < 6 months; CKD stage 3 with AKI in the past year; history of arrhythmia, atherosclerotic heart disease, stroke, PVD, and COPD; poor functional status (category 4), 14 hospital days but < 31 days in a nursing facility, starting hemodialysis as an inpatient with a catheter and no maturing access. Corresponding percentages at 6 months: survival 41.8%, non-withdrawal death 48.9%, withdrawal 9.4%. AKI, acute kidney injury; AVF, arteriovenous fistula; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; GN, glomerulonephritis; PVD, peripheral vascular disease;; SNF, skilled nursing facility.

Table 1.Baseline characteristics by 6-month outcome category, ESRD training sample ($n = 80,284$)

	Outcome within 6 Months			
	All	Withdrawal	Non-Withdrawal Death	Survival
	$n = 80,284$	$n = 2099$	$n = 13,223$	$n = 64,962$
Age, years	71.7 (11.4)	77.7 $\pm$ 9.0	75.4 $\pm$ 10.0	70.8 $\pm$ 11.5
Age category, years				
18–44	< 2102 (2.6)	< 11 (< 0.5) *	123 (0.9)	1968 (3.0)
45–64	> 14,728 (18.3)	> 134 (> 6.4)	1444 (10.9)	13,150 (20.2)
65–74	28,207 (35.1)	523 (24.9)	4060 (30.7)	23,624 (36.4)
75–84	26,349 (32.8)	935 (44.5)	5240 (39.6)	20,174 (31.1)
85	8898 (11.1)	496 (23.6)	2356 (17.8)	6046 (9.3)
Sex				
Male	44,218 (55.1)	1151 (54.8)	7346 (55.6)	35,721 (55.0)
Female	36,066 (44.9)	948 (45.2)	5877 (44.4)	29,241 (45.0)
Race				
White	58,533 (72.9)	1845 (87.9)	10,336 (78.2)	46,352 (71.4)
Black	18,309 (22.8)	213 (10.1)	2449 (18.5)	15,647 (24.1)
Other	3442 (4.3)	41 (2.0)	438 (3.3)	2963 (4.6)
Nephrologist care, months				
> 12	23,900 (29.8)	547 (26.1)	2700 (20.4)	20,653 (31.8)
6–12	14,123 (17.6)	335 (16.0)	1955 (14.8)	11,833 (18.2)
< 6	10,884 (13.6)	278 (13.2)	1852 (14.0)	8754 (13.5)
None/unknown	31,377 (39.1)	939 (44.7)	6716 (50.8)	23,722 (36.5)
Primary cause of ESRD				
Diabetes	36,367 (45.3)	733 (34.9)	5115 (38.7)	30,519 (47.0)
Hypertension	26,943 (33.6)	729 (34.7)	4750 (35.9)	21,464 (33.0)
Glomerulonephritis	4004 (5.0)	95 (4.5)	493 (3.7)	3416 (5.3)
Other	12,970 (16.2)	542 (25.8)	2865 (21.7)	9563 (14.7)
AKI in past 10 days	23,836 (29.7)	817 (38.9)	5342 (40.4)	17,677 (27.2)
Stage 3 CKD in past year	27,950 (34.8)	805 (38.4)	5482 (41.5)	21,663 (33.3)
Hemodialysis initial access				
AVF	13,801 (17.2)	172 (8.2)	892 (6.7)	12,737 (19.6)
AVG	2611 (3.3)	50 (2.4)	239 (1.8)	2322 (3.6)
Catheter, maturing AVF/AVG	15,449 (19.2)	307 (14.6)	1831 (13.8)	13,311 (20.5)
Catheter without plan	48,423 (60.3)	1570 (74.8)	10,261 (77.6)	36,592 (56.3)
Dialysis initiation as inpatient	41,586 (51.8)	1171 (55.8)	7391 (55.9)	33,024 (50.8)
Comorbid conditions				
ASHD	40,342 (50.2)	1212 (57.7)	8278 (62.6)	30,852 (47.5)
Congestive heart failure	41,676 (51.9)	1276 (60.8)	8728 (66.0)	31,672 (48.8)

	Outcome within 6 Months			
	All	Withdrawal	Non-Withdrawal Death	Survival
	<i>n</i> = 80,284	<i>n</i> = 2099	<i>n</i> = 13,223	<i>n</i> = 64,962
Arrhythmia	32,128 (40.0)	1143 (54.5)	7577 (57.3)	23,408 (36.0)
Stroke	14,659 (18.3)	467 (22.2)	3076 (23.3)	11,116 (17.1)
Other cardiac disease	28,843 (35.9)	928 (44.2)	6432 (48.6)	21,483 (33.1)
PVD	28,356 (35.3)	911 (43.4)	5916 (44.7)	21,529 (33.1)
Hypertension	74,512 (92.8)	1975 (94.1)	12,469 (94.3)	60,068 (92.5)
Diabetes	53,148 (66.2)	1266 (60.3)	8501 (64.3)	43,381 (66.8)
COPD	26,061 (32.5)	797 (38.0)	5646 (42.7)	19,618 (30.2)
Gastrointestinal bleeding	2907 (3.6)	105 (5.0)	728 (5.5)	2074 (3.2)
Liver disease	4059 (5.1)	160 (7.6)	1162 (8.8)	2737 (4.2)
Cancer	11,211 (14.0)	447 (21.3)	2625 (19.9)	8139 (12.5)
Days in a hospital in past year				
None	27,800 (34.6)	547 (26.1)	3011 (22.8)	24,242 (37.3)
< 14	27,118 (33.8)	714 (34.0)	4069 (30.8)	22,335 (34.4)
14	25,366 (31.6)	838 (39.9)	6143 (46.5)	18,385 (28.3)
Days in a SNF in past year				
None	76,417 (95.2)	1916 (91.3)	12,176 (92.1)	62,325 (95.9)
< 31	2164 (2.7)	97 (4.6)	597 (4.5)	1470 (2.3)
31	1703 (2.1)	86 (4.1)	450 (3.4)	1167 (1.8)
Days in a hospital in past year	13.4 (21.1)	16.4 ± 21.4	20.1 ± 25.9	11.9 ± 19.6
Days in a SNF in past year	2.0 (13.8)	3.7 ± 17.3	3.3 ± 18.3	1.7 ± 12.5
Functional status score				
0	49,657 (61.9)	1027 (48.9)	6382 (48.3)	42,248 (65.0)
1–2	15,808 (19.7)	497 (23.7)	3076 (23.3)	12,235 (18.8)
3–4	10,404 (13.0)	389 (18.5)	2454 (18.6)	7561 (11.6)
5–6	3234 (4.0)	135 (6.4)	954 (7.2)	2145 (3.3)
7	1181 (1.5)	51 (2.4)	357 (2.7)	773 (1.2)

Note: Values are mean ± standard deviation or *n* (%).

* Subject to the terms of the Data Use Agreement, cells with *n* < 11 are suppressed. The cells below and adjacent are also suppressed to prevent the ability to subtract the known values from the total to determine the missing cell value.

AKI, acute kidney injury; ASHD, atherosclerotic heart disease; AVF, arteriovenous fistula; AVG, arteriovenous graft; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; PVD, peripheral vascular disease; SNF, skilled nursing facility.

Table 2.

Risk model discrimination, ESRD training and validation samples

	Training sample (<i>n</i> = 80,284)	Validation sample (<i>n</i> = 40,142)
Multi-class discrimination (<i>M</i> -index)		
<i>M</i> -index	0.68	0.68
Pairwise discrimination (AUC)		
Withdrawal vs. survival	0.76	0.77
Non-withdrawal death vs. survival	0.73	0.73
Withdrawal vs. non-withdrawal death	0.63	0.62

ESRD, end-stage renal disease; AUC, area under ROC curve.

Table 3.Difference between average observed and predicted event rates, ESRD validation sample ($n = 40,142$)

Outcome	Observed Event Rate	Predicted Event Rate	Difference
Withdrawal	0.020	0.027	-0.007
Non-withdrawal death	0.165	0.161	0.004
Survival	0.809	0.812	-0.003

ESRD, end-stage renal disease.

Table 4.

Odds ratios and 95% confidence intervals for withdrawal and death from a non-withdrawal cause, compared with survival, within 6 months of dialysis initiation, training sample ($n = 80,284$)

	Withdrawal by 6 months vs. survival	Non-withdrawal death by 6 months vs. survival
Age category, years		
18–44	0.25 (0.13–0.49)	0.43 (0.35–0.52)
45–64	0.50 (0.42–0.61)	0.66 (0.62–0.71)
65–74	1 (Ref)	1 (Ref)
75–84	1.97 (1.76–2.20)	1.43 (1.36–1.50)
85	3.16 (2.77–3.61)	1.95 (1.83–2.08)
Female	0.98 (0.90–1.08)	0.92 (0.89–0.96)
Race		
White	1 (Ref)	1 (Ref)
Black	0.47 (0.40–0.54)	0.88 (0.84–0.93)
Other	0.41 (0.30–0.56)	0.81 (0.72–0.90)
Nephrologist care, months		
> 12	1 (Ref)	1 (Ref)
6–12	0.98 (0.85–1.12)	1.11 (1.04–1.18)
< 6	0.99 (0.85–1.15)	1.29 (1.20–1.38)
None/unknown	1.07 (0.95–1.20)	1.46 (1.39–1.54)
Primary cause of ESRD		
Diabetes	1 (Ref)	1 (Ref)
Hypertension	1.02 (0.90–1.15)	1.05 (1.00–1.11)
Glomerulonephritis	1.11 (0.88–1.39)	0.92 (0.82–1.02)
Other	1.57 (1.37–1.79)	1.28 (1.21–1.36)
AKI in past 10 days	1.18 (1.07–1.30)	1.19 (1.14–1.24)
Stage 3 CKD in past year	0.94 (0.86–1.04)	1.00 (0.95–1.04)
Hemodialysis initial access		
AVF	1 (Ref)	1 (Ref)
AVG	1.57 (1.14–2.16)	1.31 (1.12–1.52)
Catheter with maturing AVF/AVG	1.54 (1.27–1.87)	1.54 (1.41–1.68)
Catheter without plan	2.33 (1.97–2.76)	2.50 (2.31–2.70)
Dialysis initiation as inpatient	1.12 (1.02–1.22)	1.11 (1.07–1.16)
Comorbid conditions		
ASHD	0.95 (0.85–1.05)	1.13 (1.07–1.18)
Congestive heart failure	1.10 (0.98–1.24)	1.22 (1.16–1.28)
Arrhythmia	1.28 (1.15–1.42)	1.37 (1.31–1.43)
Stroke	1.13 (1.01–1.26)	1.08 (1.03–1.14)
Other cardiac disease	1.02 (0.92–1.13)	1.11 (1.06–1.16)
PVD	1.17 (1.06–1.28)	1.14 (1.10–1.20)
Hypertension	0.89 (0.72–1.09)	0.81 (0.74–0.89)

	Withdrawal by 6 months vs. survival	Non-withdrawal death by 6 months vs. survival
Diabetes	0.93 (0.83–1.04)	0.91 (0.86–0.95)
COPD	1.01 (0.91–1.11)	1.13 (1.08–1.18)
Gastrointestinal bleeding	1.15 (0.93–1.41)	1.13 (1.03–1.25)
Liver disease	1.89 (1.59–2.25)	1.87 (1.73–2.02)
Cancer	1.42 (1.27–1.59)	1.41 (1.33–1.48)
Days hospitalized in past year		
None	1 (Ref)	1 (Ref)
< 14	1.05 (0.92–1.19)	1.00 (0.94–1.05)
14	1.07 (0.92–1.24)	1.17 (1.10–1.26)
Days in SNF in past year		
None	1 (Ref)	1 (Ref)
< 31	1.20 (0.97–1.50)	1.12 (1.01–1.24)
31	1.41 (1.11–1.78)	1.05 (0.93–1.18)
Functional status score		
0	1 (Ref)	1 (Ref)
1–2	1.41 (1.25–1.58)	1.27 (1.20–1.34)
3–4	1.60 (1.40–1.82)	1.41 (1.33–1.49)
5–6	1.79 (1.46–2.19)	1.68 (1.54–1.84)
7	1.83 (1.35–2.48)	1.67 (1.45–1.92)

AKI, acute kidney injury; ASHD, atherosclerotic heart disease; AVF, arteriovenous fistula; AVG, arteriovenous graft; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; PVD, peripheral vascular disease; SNF, skilled nursing facility.