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Supplementary Methods

Determination of dialysis withdrawal

The definition of dialysis withdrawal was carefully considered, and was based on examining > 20 different possible combinations of responses to questions 12, 13, and 14 on the USRDS Death Notification form (CMS 2746). As we sought to study elective dialysis withdrawal, rather than cessation of dialysis before imminent death in the setting of acute illness, our strategy emphasized specificity. For the primary definition, we required that providers attribute the cause of death to "withdrawal from dialysis/uremia" (death code 104) in any position on question 12, and, to increase specificity, to also answer "yes" to question 13 ("Renal replacement therapy discontinued prior to death: Yes/No") and "yes" to question 14 ("Was discontinuation of renal replacement therapy after patient/family request to stop dialysis?").

We further refined the withdrawal definition by excluding patients who died on the day of, or within 3 days of, the date of withdrawal, reasoning that these patients likely faced imminent death and did not truly withdraw (as withdrawal is commonly understood). Likewise, we excluded patients who lived longer than 90 days after withdrawal, since they likely had never required dialysis.

We also required specificity for the definition of non-withdrawal death. If code 104 was not present in any position in question 12 (including responses with code 99, for "unknown" cause of death); the answer to question 13 was "no"; and question 14 showed "no," "unknown," "not applicable," or a blank space, the death was considered a non-withdrawal death. Other combinations resulted in ambiguity regarding whether the death was truly a withdrawal, so these deaths were excluded from the primary analysis.

For a sensitivity analysis, we liberalized the definitions of both withdrawal and non-withdrawal death. Patients with code 99 ("unknown" cause of death) alone in question 12 were added to the withdrawal group. Additionally, all patients with ambiguous causes of death were added to the non-withdrawal death group.

The date of withdrawal was operationalized as the date of the last maintenance dialysis treatment. Since place of withdrawal is not a requested field on the ESRD Death Notification form, we operationalized location of withdrawal as follows: if the last dialysis treatment occurred in the hospital, those withdrawals were considered inpatient withdrawals.

Medical Events

Medical events included hospitalizations for the indications listed in **Supplementary Table S1** using discharge codes. The subset of hospitalizations for myocardial infarction, stroke, amputation/critical limb ischemia, sepsis, or fractures constituted "major medical events." Medical events were identified from inpatient claims for each month of the 6-month period preceding death. Event rates were calculated on a monthly basis, with each event counted individually.

Disability proxy score

We developed a disability proxy score specifically for use with dialysis patient claims data designed, in part, to attempt to identify disability. While this score has not been validated by medical records review, we have used it in several investigations; details of the development of the score and an example of its application have been previously published (Wetmore et al. *Clin J Am Soc Nephrol.* 2016;11:1413-21; Wetmore et al. *Am J Kidney Dis.* 2018;71:831-41). In

brief, established scores, such as the Fried Frailty Score, are excellent tools, but are imperfect for our use because typical measures that might be proxies for frailty, functional status, and disability are not, unfortunately, available in Medicare claims data. We attempted to develop claims-based measures that can potentially assess for disability which (1) use medical claims data and (2) are tailored to dialysis patients. Specifically, we assessed putative disability using evidence of particular diagnoses and the Medicare durable medical equipment (DME) files.

Potential markers of disability from the DME files were chosen by first limiting to those with prevalence greater than 1%, and then further limiting to those with an association with fracture, hospitalization, or mortality. Proportional hazards models were first used to investigate unadjusted associations of these markers with death, and adjusted associations (adjusted for demographics, comorbidity, erythropoietin dose, hemoglobin). The resulting potential markers of disability were: bed, oxygen, wheelchair, continuous positive airway pressure (CPAP) device, nebulizer, walker, commode, dressings, enteral supplies, diabetic shoes, diabetic supplies, suction canister, home health claim, hospice claim, skilled nursing facility claim, rehab claim, myocardial infarction, history of stroke, depression, visual impairment, hip fracture, history of thyroid disease, and dementia.

Using this list, we constructed another proportional hazards model, with mortality as the outcome, to determine the additional contribution of these potential disability markers beyond demographic characteristics and comorbidity. The model was then reduced, and the following variables remained significant for mortality in the model, after adjusting for other patient characteristics and comorbidity:

- hospital bed
- wheelchair

- walker

- commode

- home oxygen

- CPAP device

- suction canister

- wound dressings

- enteral supplies

- home health claims

- hospice claims

- skilled nursing facility claims

- acute myocardial infarction (AMI)

- stroke

- hip fracture

- visual impairment

- dementia

- depression

Use of hospital bed, wheelchair, walker, commode, home oxygen, CPAP device, suction canister, wound dressings, and enteral supplies was ascertained from Medicare DME claim files based on Healthcare Common Procedure Coding System (HCPCS) codes. To define AMI, stroke, hip fracture, visual impairment, dementia, and depression, we required one or more inpatient, skilled nurse facility, home health, or hospice claims with a corresponding diagnosis code or two or more outpatient/Part B claims with corresponding diagnosis codes within a year.

The HCPCS and International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis codes are listed in Table S2.

The disability proxy score was created by taking parameter estimates from the adjusted proportional hazards model (including demographics, comorbid conditions, and the above potential markers of disability), multiplying the parameter estimates by 10, setting to zero if between -0.5 and +0.5, rounding to integer, and summing. The C-statistic in the developmental cohort was 0.736. While the score was developed using hemodialysis patients who were incident in 2008, the performance characteristics of the score were assessed by applying the resulting score to a separate validation Medicare cohort. The validation cohort consisted of patients initiating hemodialysis the following year (that is, incident to dialysis in 2009), who therefore had virtually identical underlying case-mix characteristics. The resulting C-statistic in the validation cohort was 0.741.

The final score was calculated using the following formula: based on presence/absence of disease and/or equipment use: score = 1 × hospital bed + 1 × wheelchair – 1 × walker – 1 × commode + 3 × oxygen – 2 × CPAP device + 2 × suction canister + 1 × wound dressings + 3 × enteral feedings + 1 × home health claim + 10 × hospice service claim + 2 × SNF claim + 2 × AMI + 1 × history of stroke + 1 × hip fracture + 2 × dementia + 2 × depression.

Given the nature of DME as a durable good, the mean monthly disability proxy score was calculated using data from a rolling 3-month window. In other words, the proxy disability score generated, for example, over the 6 months before death requires one to ascertain relevant claims accumulated over the previous 3 months; the score for a given month therefore reflects claims generated over the previous 3 months.

Statistical analysis detail: creation of the illness trajectories

To determine the trajectories of interest (medical events, hospitalizations and skilled nursing facility stays, and putative disability) prior to death, we used the SAS procedure known as Proc TRAJ. Use of the Proc TRAJ process in clinical studies requires balancing algorithmically defined groupings with meaningful clinical context; because we sought the optimal balance of descriptive richness and parsimony, we determined that two major groups appeared to provide the optimal balance of descriptive richness and parsimony. A logistic model was computed to determine the factors related to trajectory grouping.

Statistical analysis detail: assessment of setting of death

We assessed setting of death (hospital versus out-of-hospital, intensive care unit [ICU] versus non-ICU); a logistic model was used to identify factors related to setting of death. In these models, individual comorbid conditions were collapsed, for the sake of parsimony, to categories of the Liu comorbidity index, as has been done previously [1-3].

1. Wetmore JB, Liu J, Wirtz HS, Gilbertson DT, Cooper K, Nieman KM, et al. Geovariation in fracture risk among patients receiving hemodialysis. *Clin J Am Soc Nephrol.* 2016 Aug;11(8):1413-21.

2. Liu J, Huang Z, Gilbertson DT, Foley RN, Collins AJ. An improved comorbidity index for outcome analyses among dialysis patients. *Kidney Int.* 2010 Jan;77(2):141-51.

3. Slinin Y, Guo H, Li S, Ensrud K, Gilbertson DT, Collins AJ, et al. Hemodialysis patient outcomes: provider characteristics. *Am J Nephrol.* 2014 May;39(5):367-75.

Supplementary Table S1. Event Codes

Medical Events	Principle Diagnosis Codes
Myocardial infarction	ICD-9-CM: 410, 411, 413
Heart failure	ICD-9-CM: 398.91, 402.x1, 404.x1, 404.x3, 425.xx 428.xx, V42.1, 276.6
Stroke	430, 431, 432, 433, 434, 436, 852.0, 852.2, 852.4, 853
Amputation/critical limb ischemia	ICD-9-CM: 443.1, 443.22, 443.81, 443.89, 443.9; 440.0, 440.20, 440.21, 440.29, 440.30, 440.31, 440.32, 440.4, 440.8, 440.9; 249.70, 249.71, 250.70, 250.71, 250.72, 250.73; 707.06, 707.07; 447.1; 729.5 with 440.20, 440.21, 440.22, 440.23, 440.24; 785.4; 707.1, 707.10, 707.13, 707.14, 707.15, 707.19, 707.9 with 440.20, 440.21, 440.22, 440.23, 440.24; 440.22,440.23,440.24; 00.40, 00.41, 00.42, 00.43, 00.44, 39.50. CPT: 354542, 35454, 35456, 35459, 35470, 35472, 35473, 35474. ICD-9-CM: 39.25, 39.29. CPT: 35500, 35521, 35533, 35537, 35538, 35539, 35540, 35541, 35546, 35548, 35549, 35551, 35556, 35558, 35563, 35565, 35566, 35583, 35585, 35587, 35621, 35623, 35646, 35647, 35651, 35654, 35656, 35661, 35663, 35665, 35666, 35671, 35681, 35682, 35700. ICD-9-CM: 39.90, 00.45, 00.46, 00.47, 00.48, 00.55; 84.10, 84.12, 84.14, 84.15, 85.17, 84.3, 84.91, 84.11 CPT: 27590, 27591, 27592, 27594, 27596, 27599, 27880, 27881, 27882, 27888, 27889, 28800, 28805, 28810, 28820, 28825
Sepsis	038.xx
Pneumonia	ICD-9-CM: 480-488 in primary position, or 786 or 518 in primary position and 480 in secondary position
Vascular access infection	ICD-9-CM: 996.62
Gastrointestinal bleeding	ICD-9-CM: 569.85; 531.0, 531.1, 531.2, 531.4, 531.5, 531.6; 532.0, 532.1, 532.2, 532.4, 532.5, 532.6; 533.0, 533.1, 533.2, 533.4, 533.5, 533.6; 534.0, 534.1, 534.2, 534.4, 534.5, 534.6; 530.7; 530.21; 535.x1; 537.83, 537.84; 578.x; 456.0, 456.20
Hip/pelvis, femur fracture	Hip/pelvis, ICD-9-CM: 733.14, 808.xx, 820.xx CPT: 27193-27248, and required for Part B claims, service place "inpatient" Femur, ICD-9-CM: 733.15, 821.xx CPT: 27500-27514, 27520-27540, 29850-29856, and required for Part B claims, service place "inpatient"

CPT, Current Procedural Terminology; ICD-9-CM, International Classification of Diseases,

Ninth Revision, Clinical Modification.

Supplementary Table S2. HCPCS and ICD-9-CM diagnosis codes used to define the disability

proxy score

Equipment Use/Disease	HCPCS/ICD-9-CM Diagnosis codes
Hospital bed	E0250, E0251, E0255, E0256, E0260, E0261, E0265, E0266, E0270, E0290-E0297, E0301-E0304
Wheelchair	A0130, E0971, E0973, E1089, E1090, E1250, E1260, E1285, E1290, E2365, E2601, K0001, K0003-K0007, K0010, K0011, K0195, K0813-K0898
Walker	E0100, E0105, E0130, E0135, E0140, E0141, E0143, E0144, E0147-E0149
Commode	E0163, E0165, E0168, E0170, E0171, E0275, E0276
Home oxygen	E0425, E0430, E0431, E0433-E0435, E0439, E0440, E1390, K0738, K0741
CPAP device	A7027, A7034-A7039, A7044-A7046, E0470, E0561, E0562, E0601, E0618, E0619
Suction canister	A7000-A7002
Dressings	A6021-A6024, A6196-A6205, A6209-A6214, A6216-A6239, A6242-A6247, A6251-A6259, A6266, A6402-A6404, A6442-A6456
Enteral supplies	B3034-B3036, B4081-4083, B4087, B4088, B4100, B4102, B4104, B4149, B4150, B4152-B4155, B4157, B9000, B9002
AMI	410.x1
Stroke	430, 431, 432, 434.x1, 436.xx, V12.54
Hip fracture	733.14, 808.xx, 820.xx
Visual impairment	361.xx, 362.xx, 365.xx, 366.xx, 369.xx
Dementia	290.xx
Depression	296.xx, 298.0, 300.4, 301.1x, 309.0, 309.1, 311

AMI, acute myocardial infarction; CPAP, continuous positive airway pressure.

Table S3. Factors associated with the setting of death

Variable	Hospital vs. Non-Hospital Death		ICU vs. Non-ICU Death	
	Odds Ratio (95% CI)	*P*	Odds Ratio (95% CI)	*P*
Intercept	0.08 (0.08-0.09)	< 0.0001	0.06 (0.05-0.06)	< 0.0001
Death from withdrawal				
No	1.00 (ref)		1.00 (ref)	
Yes	0.27 (0.26-0.29)	< 0.0001	0.30 (0.28-0.32)	< 0.0001
Age, years				
18-44	0.86 (0.81-0.91)	< 0.0001	0.90 (0.85-0.96)	0.0005
45-64	1.00 (ref)		1.00 (ref)	
65-74	1.12 (1.09-1.15)	< 0.0001	1.01 (0.98-1.04)	0.3766
75-84	1.12 (1.08-1.15)	< 0.0001	0.90 (0.87-0.93)	< 0.0001
≥ 85	1.00 (0.96-1.04)	0.9628	0.71 (0.68-0.74)	< 0.0001
Sex				
Female	1.15 (1.12-1.18)	< 0.0001	1.10 (1.08-1.13)	< 0.0001
Male	1.00 (ref)		1.00 (ref)	
Race/ethnicity				
White	1.00 (ref)		1.00 (ref)	
Black	1.03 (1.01-1.06)	0.014	1.05 (1.02-1.08)	0.0003
Asian	1.21 (1.13-1.30)	< 0.0001	1.34 (1.25-1.44)	< 0.0001
Native Americans	1.15 (1.04-1.27)	0.0064	1.21 (1.09-1.34)	0.0003
Other/unknown	1.16 (1.03-1.31)	0.0112	1.29 (1.15-1.45)	< 0.0001
Hispanic	1.24 (1.20-1.29)	< 0.0001	1.26 (1.21-1.31)	< 0.0001
Dialysis duration, years				
< 2	0.99 (0.95-1.02)	0.393	1.00 (0.97-1.04)	0.916
2-< 5	1.00 (ref)		1.00 (ref)	
≥ 5		< 0.0001	1.06 (1.03-1.08)	< 0.0001
Primary cause of ESRD	1.06 (1.04-1.09)			
Diabetes	1.00 (ref)		1.00 (ref)	
Hypertension	1.05 (1.02-1.07)	0.001	1.05 (1.03-1.08)	0.0002
Glomerulonephritis	1.11 (1.06-1.17)	< 0.0001	1.11 (1.06-1.16)	< 0.0001
Other cause	1.09 (1.05-1.13)	< 0.0001	1.06 (1.02-1.10)	0.0028
Institutional stay, days				
0	1.00 (ref)		1.00 (ref)	
1-< 10	16.69 (15.76-17.67)	< 0.0001	11.40 (10.66-12.19)	< 0.0001
10-< 25	20.47 (19.30-21.71)	< 0.0001	14.43 (13.47-15.45)	< 0.0001
25-< 58	22.39 (21.06-23.79)	< 0.0001	15.14 (14.11-16.24)	< 0.0001
≥ 58	21.19 (19.92-22.55)	< 0.0001	13.99 (13.03-15.03)	< 0.0001
Urbanicity				
Urban	1.00 (ref)		1.00 (ref)	
Large rural city/town	0.93 (0.90-0.97)	0.0002	0.87 (0.84-0.90)	< 0.0001
Small rural town	0.89 (0.85-0.93)	< 0.0001	0.89 (0.84-0.93)	< 0.0001
Isolated small rural town	0.91 (0.86-0.97)	0.002	0.86 (0.81-0.92)	< 0.0001
Missing	0.86 (0.79-0.95)	0.0015	0.65 (0.59-0.71)	< 0.0001
Medicaid coverage				
No	1.00 (ref)		1.00 (ref)	
Yes	0.93 (0.91-0.95)	< 0.0001	1.01 (0.98-1.03)	0.5717
Liu comorbidity index				

0	1.00 (ref)		1.00 (ref)	
1-4	0.87 (0.82-0.93)	< 0.0001	0.87 (0.82-0.93)	< 0.0001
5-7	0.63 (0.60-0.68)	< 0.0001	0.69 (0.65-0.73)	< 0.0001
≥ 8	0.61 (0.58-0.65)	< 0.0001	0.66 (0.62-0.70)	< 0.0001
Disability proxy score				
≤ 0	1.00 (ref)		1.00 (ref)	
1-2	1.29 (1.25-1.34)	< 0.0001	1.23 (1.18-1.27)	< 0.0001
3-4	1.19 (1.15-1.23)	< 0.0001	1.16 (1.12-1.20)	< 0.0001
5-6	1.11 (1.06-1.16)	< 0.0001	1.11 (1.07-1.16)	< 0.0001
≥ 7	0.33 (0.32-0.35)	< 0.0001	0.42 (0.41-0.44)	< 0.0001

CI, confidence interval; ESRD, end-stage renal disease; ICU, intensive care unit.

Supplementary Table S4. Odds ratio for death from withdrawal vs. death from other causes,

sensitivity analysis using alternative definitions of withdrawal and non-withdrawal death

Variable	Odds Ratio (95% CI)	P
Intercept	0.02 (0.02-0.03)	< 0.0001
Age, years		
18-44	0.78 (0.67-0.91)	0.0011
45-64	1.00 (ref)	
65-74	1.33 (1.26-1.40)	< 0.0001
75-84	1.69 (1.60-1.78)	< 0.0001
≥ 85	2.13 (2.00-2.27)	< 0.0001
Sex		
Female	1.16 (1.12-1.20)	< 0.0001
Male	1.00 (ref)	
Race/ethnicity		
White	1.00 (ref)	
Black	0.50 (0.48-0.53)	< 0.0001
Asian	0.64 (0.56-0.72)	< 0.0001
Native Americans	1.15 (0.98-1.34)	0.0837
Other/unknown	0.76 (0.61-0.96)	0.0183
Hispanic	0.69 (0.65-0.74)	< 0.0001
Dialysis duration, years		
< 2	0.99 (0.94-1.04)	0.5724
2-< 5	1.00 (ref)	
≥ 5	1.04 (1.00-1.08)	0.0816
Primary cause of ESRD		
Diabetes	1.00 (ref)	
Hypertension	0.94 (0.89-0.98)	0.0094
Glomerulonephritis	1.10 (1.02-1.19)	0.0178
Other cause	1.09 (1.02-1.16)	0.0059
Institutional stay, days		
0	1.00 (ref)	
1-< 10	0.86 (0.80-0.92)	< 0.0001
10-< 25	1.02 (0.95-1.10)	0.5051
25-< 58	1.02 (0.95-1.10)	0.5077
≥ 58	1.02 (0.95-1.10)	0.6404
Urbanicity		
Urban	1.00 (ref)	
Large rural city/town	1.13 (1.07-1.20)	< 0.0001
Small rural town	1.17 (1.09-1.26)	< 0.0001
Isolated small rural town	1.31 (1.21-1.42)	< 0.0001
Missing	0.66 (0.54-0.81)	< 0.0001
Medicaid coverage		
No	1.00 (ref)	
Yes	0.93 (0.89-0.97)	0.0006
Comorbid conditions		
ASHD	0.90 (0.86-0.94)	< 0.0001
CHF	0.75 (0.72-0.79)	< 0.0001

CVA/TIA	0.98 (0.94-1.02)	0.3138
PVD	1.00 (0.97-1.04)	0.8796
Other cardiac disease	0.87 (0.83-0.90)	< 0.0001
COPD	0.73 (0.71-0.76)	< 0.0001
GI bleeding	1.03 (0.98-1.09)	0.2972
Liver disease	1.00 (0.94-1.07)	0.926
Dysrhythmia	1.00 (0.96-1.04)	0.8537
Cancer	0.84 (0.80-0.89)	< 0.0001
Diabetes	0.89 (0.85-0.93)	< 0.0001
Disability proxy score		
≤ 0	1.00 (ref)	
1-2	1.61 (1.45-1.78)	< 0.0001
3-4	1.90 (1.72-2.10)	< 0.0001
5-6	2.43 (2.18-2.71)	< 0.0001
≥ 7	20.75 (19.02-22.63)	< 0.0001

ASHD, atherosclerotic heart disease; CHF, congestive heart failure; CI, confidence interval;

COPD, chronic obstructive pulmonary disease; CVA/TIA, cerebrovascular accident/transient

ischemic attack; ESRD, end-stage renal disease; PVD, peripheral vascular disease.

Supplementary Table S5. Odds ratio for death from withdrawal vs. death from other causes,

sensitivity analysis substituting disability trajectory for proxy disability score category

Variable	Odds Ratio (95% CI)	*P*
Intercept	0.06 (0.05-0.06)	< 0.0001
Age, years		
18-44	0.61 (0.52-0.72)	< 0.0001
45-64	1.00 (ref)	
65-74	1.54 (1.45-1.62)	< 0.0001
75-84	2.24 (2.12-2.37)	< 0.0001
≥ 85	3.17 (2.98-3.38)	< 0.0001
Sex		
Female	1.20 (1.16-1.25)	< 0.0001
Male	1.00 (ref)	
Race/ethnicity		
White	1.00 (ref)	
Black	0.40 (0.38-0.42)	< 0.0001
Asian	0.54 (0.48-0.62)	< 0.0001
Native Americans	1.03 (0.88-1.20)	0.7396
Other/unknown	0.68 (0.54-0.85)	0.0006
Hispanic	0.65 (0.61-0.69)	<.0001
Dialysis duration, years		
< 2	0.95 (0.90-1.00)	0.0385
2-< 5	1.00 (ref)	
≥ 5	1.03 (0.99-1.07)	0.1269
Primary cause of ESRD		
Diabetes	1.00 (ref)	
Hypertension	0.93 (0.88-0.97)	0.003
Glomerulonephritis	1.12 (1.03-1.21)	0.0062
Other cause	1.09 (1.03-1.16)	0.0057
Institutional stay, days		
0	1.00 (ref)	
1-< 10	1.03 (0.96-1.11)	0.4005
10-< 25	1.49 (1.39-1.60)	< 0.0001
25-< 58	1.56 (1.46-1.68)	< 0.0001
≥ 58	1.32 (1.22-1.42)	< 0.0001
Urbanicity		
Urban	1.00 (ref)	
Large rural city/town	1.15 (1.09-1.22)	< 0.0001
Small rural town	1.16 (1.08-1.25)	< 0.0001
Isolated small rural town	1.31 (1.21-1.42)	< 0.0001
Missing	0.55 (0.45-0.68)	< 0.0001
Medicaid coverage		
No	1.00 (ref)	
Yes	0.86 (0.83-0.90)	< 0.0001
Comorbid conditions		
ASHD	0.85 (0.82-0.89)	< 0.0001
CHF	0.71 (0.68-0.74)	< 0.0001

|		
CVA/TIA	0.98 (0.93-1.02)	0.2782
PVD	0.98 (0.94-1.02)	0.2609
Other cardiac disease	0.85 (0.82-0.89)	< 0.0001
COPD	0.66 (0.63-0.69)	< 0.0001
GI bleeding	1.01 (0.96-1.07)	0.6797
Liver disease	1.07 (1.01-1.14)	0.0338
Dysrhythmia	0.94 (0.90-0.98)	0.0043
Cancer	1.16 (1.10-1.22)	< 0.0001
Diabetes	0.83 (0.79-0.87)	< 0.0001
Disability proxy score		
Trajectory 1	1.00 (ref)	
Trajectory 2	5.41 (5.19-5.64)	< 0.0001

ASHD, atherosclerotic heart disease; CHF, congestive heart failure; CI, confidence interval;

COPD, chronic obstructive pulmonary disease; CVA/TIA, cerebrovascular accident/transient

ischemic attack; ESRD, end-stage renal disease; PVD, peripheral vascular disease.

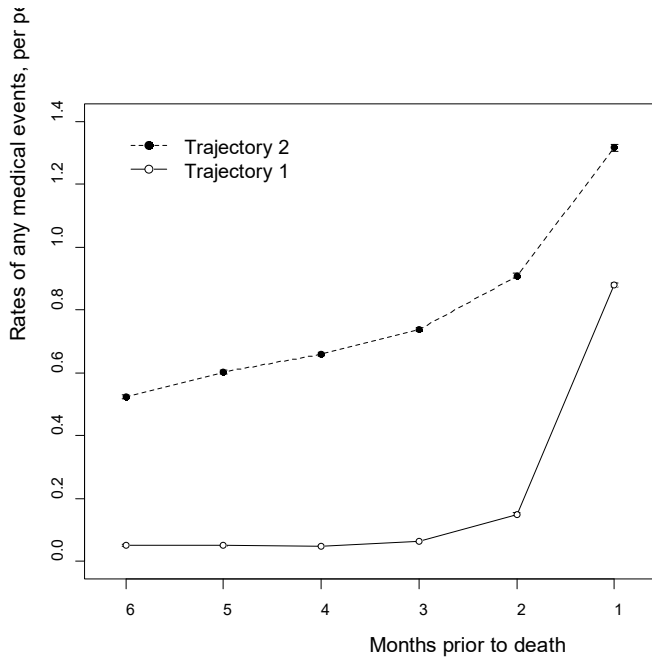Figure S1. Creation of the study sample. ESRD, end-stage renal disease.
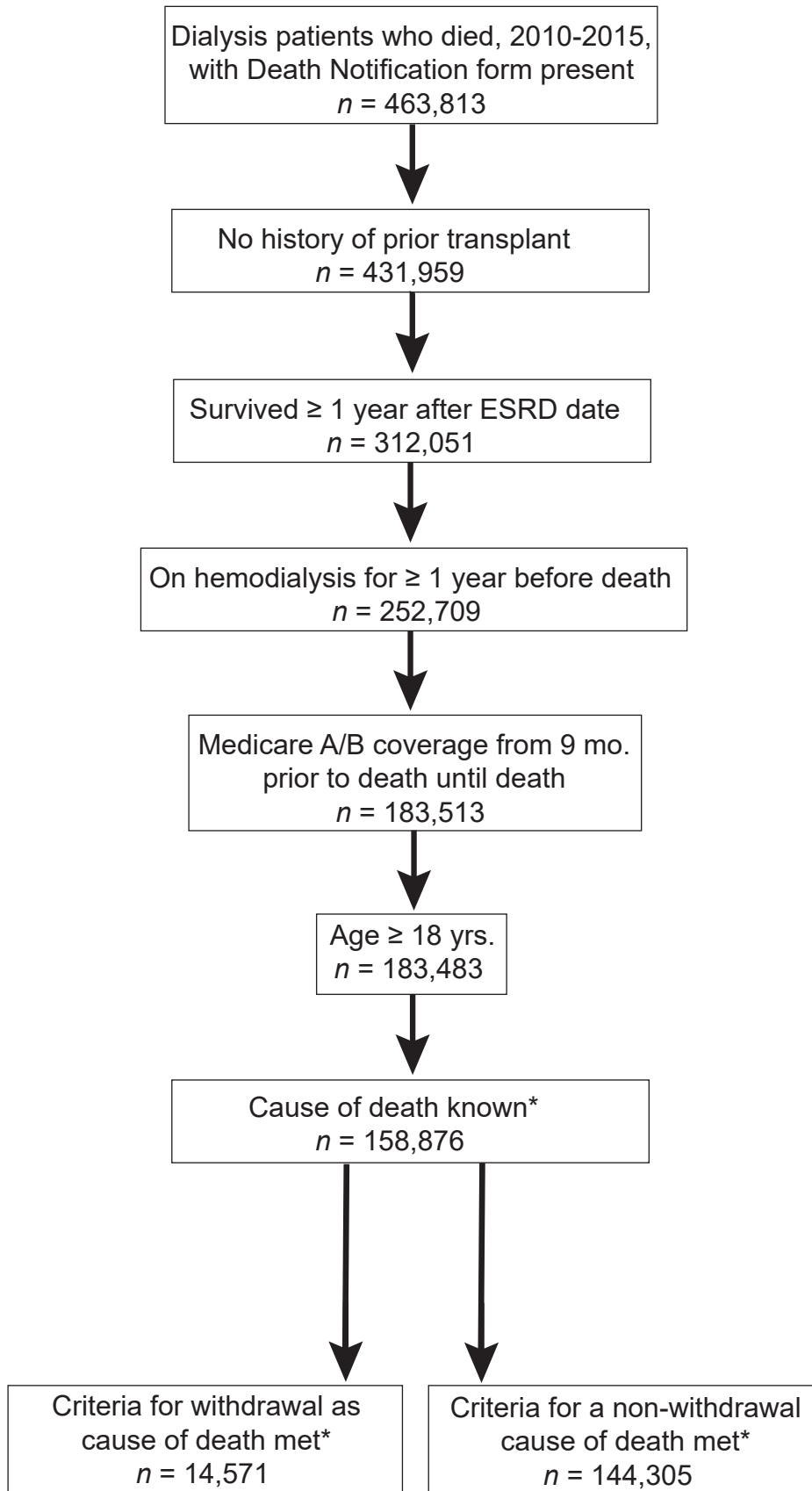
*See text for details.

Figure S2. Illness trajectories (the patterns of medical events, hospitalizations and skilled nursing facility stays, and putative disability in the months prior to death) for patients who died. Trajectory 1 is "healthier" pattern, and trajectory 2 a "sicker" pattern.

A

B