**Supplemental Information**

# Association between duration of predialysis care and mortality after dialysis start

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**Supplemental Material**

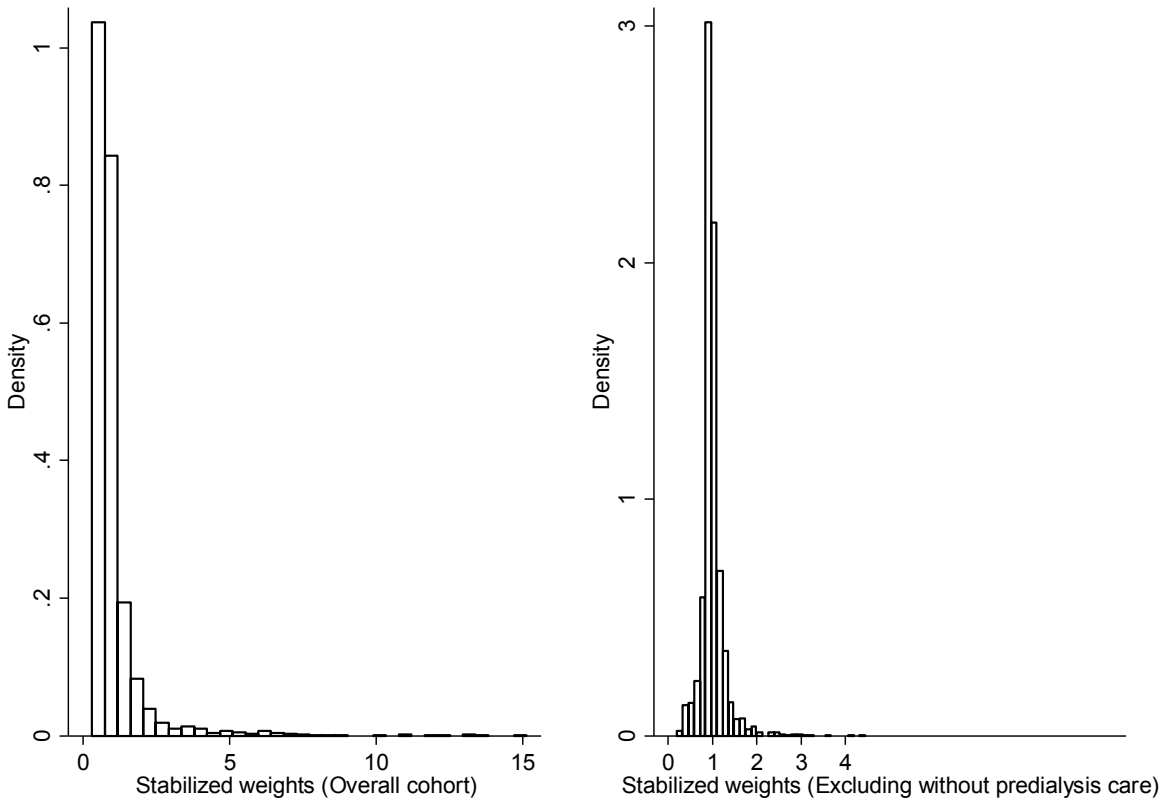
**Text.** Further details of statistical analysis

*Weight-generating models*. We estimated the stabilized inverse probability of treatment weights (IPTWs) using two multinomial, logistic regression models of predialysis care duration (e.g. 0-119, 120-364, and ≥365 days for overall analyses; 1-119, 120-364, and ≥365 days for analyses restricted to people who received predialysis care) - the first without covariates, and the second including markers of disease course and all covariates considered in the standard Cox model. We calculated the stabilized IPTWs for each participant as the ratio of the predicted probability of receiving the duration of predialysis care from the first model, divided by the probability of the observed duration of predialysis care from the second model. We assessed whether the covariates were balanced across levels of the exposure in the weighted sample using standardized difference (1).

*Methods for multiple imputation*. We used multivariate normal, multiple imputation for missing values of serum albumin and creatinine, which were missing in 3% and 0.4% of the cohort, respectively. We did regression analyses in two ways: with case-wise deletion for missing values (i.e., complete-case analysis; sensitivity analyses), and using multiple imputation in the full cohort by replacing each missing datum with 10 potential imputed values (obtained using the multiple imputation procedure command 'mi' in STATA). We carried out these analyses 10 times, once with each set of imputed values, and the regression estimates and standard errors were combined in the standard way.

*Power analysis.* We estimated the power of detecting an association between duration of predialysis care (120-364 or ≥365 versus 0-119 days) and mortality based on the following considerations. A sample of about 3,000 (the study sample at the time when this study was designed would have a power of at least 85% to detect a significant, 30% reduction in the risk of death in people with longer predialysis care (2). We assumed a yearly mortality rate of 15% in the reference group, allowing different allocation ratios from 1:2 to 2:1, and considered an overall two-sided *P* value of 0.05 for statistical significance.

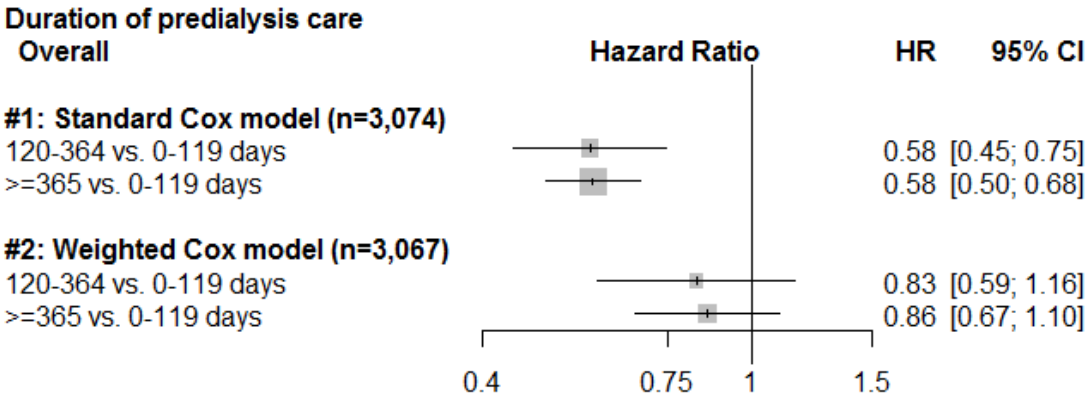
**Supplemental Figure 1.** Distribution of stabilized weights



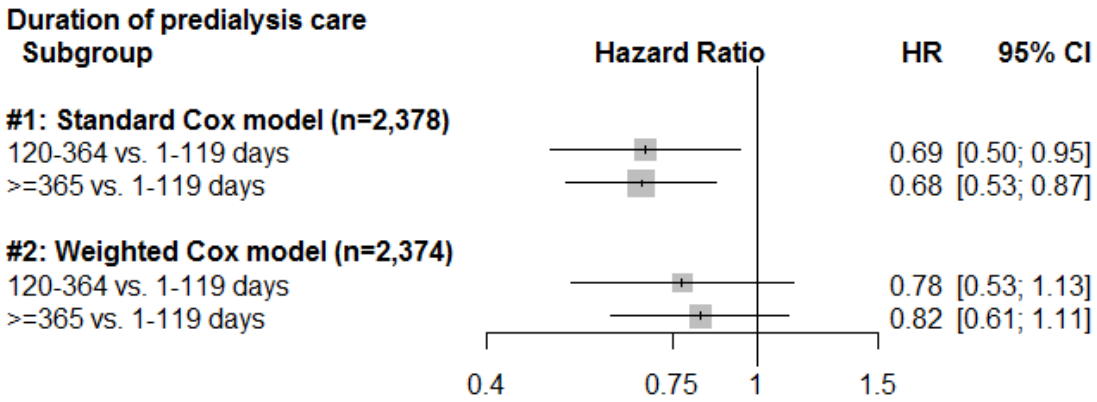

In the overall cohort (n=3,152), mean (standard deviation) of stabilized weights: 1.02 ± 1.03, median 0.76, range 0.30-15.14; in the sub-cohort excluding people without predialysis care (n=2,414), mean (standard deviation) of stabilized weights: 1.00 ± 0.28, median 0.96, range 0.20-4.45.

**Supplemental Figure 2.** Hazard ratios (HRs) and 95% confidence intervals (95% CIs) for mortality associated with duration of predialysis care: complete-case analysis

(A) All participants




(B) Participants with predialysis care



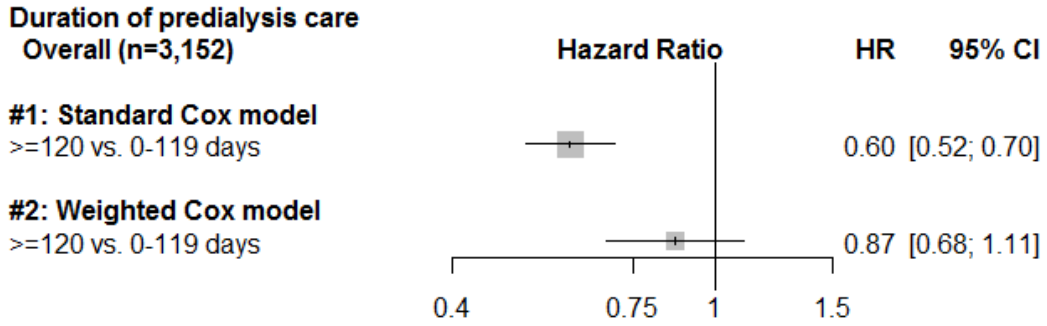

Models included all participants (A); models included participants with predialysis care (B)

#1: Standard Cox model adjusted for age at initiating dialysis, sex, dialysis programs, serum albumin, and 10 comorbidities (diabetes, congestive heart failure, cancer, other cardiac disease, cerebrovascular disease, coronary artery disease, peripheral vascular disease, chronic obstructive lung disease, polycystic kidney disease, and gastrointestinal bleeding).

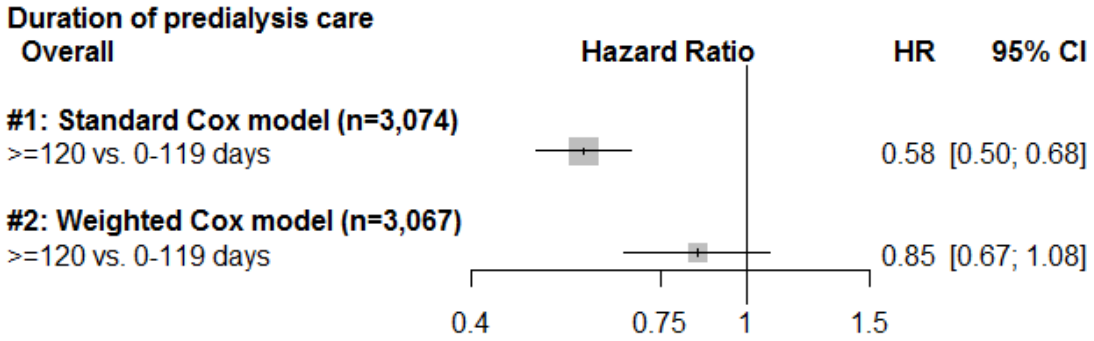
#2: Inverse-probability-of-treatment-weighted Cox model accounting for the same covariates as in the above Cox model and markers of disease course (inpatient or outpatient of dialysis start, the last available estimated glomerular filtration rate prior to starting dialysis).

**Supplemental Figure 3.** Hazard ratios (HRs) and 95% confidence intervals (95% CIs) for mortality associated with duration of predialysis care: ≥120 vs. 0-119 days

(A) Multiple imputed data




(B) Complete-case analysis




Models included multiple imputed data (A); models included completed data only (B)

#1: Standard Cox model adjusted for age at initiating dialysis, sex, dialysis programs, serum albumin, and 10 comorbidities (diabetes, congestive heart failure, cancer, other cardiac disease, cerebrovascular disease, coronary artery disease, peripheral vascular disease, chronic obstructive lung disease, polycystic kidney disease, and gastrointestinal bleeding).

#2: Inverse-probability-of-treatment-weighted Cox model accounting for the same covariates as in the above Cox model and markers of disease course (inpatient or outpatient of dialysis start, the last available estimated glomerular filtration rate prior to starting dialysis).

**Supplemental Table 1.** Primary reason for admission on inpatient dialysis starts, by duration of predialysis care (n=1,752)

| Primary reason for admission | Duration of predialysis care (days) | | |
|---|---|---|---|
| | 0-119 (n = 876) | 120-364 (n = 136) | ≥365 (n = 740) |
| *Kidney disease* | 304 (35) | 65 (48) | 378 (51) |
| Complications of kidney disease requiring urgent initiation of dialysis | 291 (33) | 62 (46) | 353 (48) |
| Others (admission to start dialysis, outpatient peritoneal dialysis could not be performed due to peritonitis or poor inflow/outflow, uremic symptoms) | 13 (1) | 3 (2) | 25 (3) |
| *Cardiovascular disease* | 144 (16) | 25 (19) | 147 (20) |
| Congestive heart failure | 50 (6) | 18 (13) | 69 (9) |
| Coronary artery disease | 42 (5) | 5 (4) | 64 (9) |
| Others (abdominal aortic aneurysm, cerebrovascular disease, peripheral vascular disease, other) | 52 (6) | 2 (1.5) | 14 (2) |
| *Gastrointestinal disease* | 50 (6) | 7 (5) | 30 (4) |
| *Infection* | 120 (14) | 10 (7) | 64 (9) |
| *Malignancy* | 37 (4) | 1 (0.7) | 10 (1) |
| *Elective surgery* (cardiac, gastrointestinal, malignancy, musculoskeletal, vascular, other) | 77 (9) | 7 (5) | 21 (3) |
| *Others* (endocrine, genitourinary, hematological, other neurological, respiratory/thoracic disorder, other) | 142 (16) | 20 (15) | 86 (12) |
| Missing | 2 | 1 | 4 |

**Supplemental Table 2.** Comparison of means or proportions of covariates across duration of predialysis care in the weighted sample (n=3,152)

| Covariates | Duration of predialysis care (day) | | | Standardized difference across duration of predialysis care (day) | | |
|---|---|---|---|---|---|---|
| | 0-119 | 120-364 | ≥365 | 120-364 vs. 0-119 | ≥365 vs. 0-119 | ≥365 vs. 120-364 |
| Age (mean, years) | 65 | 64 | 64 | 0.02 | 0.05 | 0.03 |
| Male | 0.63 | 0.60 | 0.60 | 0.06 | 0.06 | 0.00 |
| Dialysis programs | | | | | | |
| A | 0.20 | 0.21 | 0.20 | 0.03 | 0.00 | 0.03 |
| B | 0.31 | 0.32 | 0.32 | 0.01 | 0.01 | 0.00 |
| C | 0.26 | 0.28 | 0.29 | 0.05 | 0.08 | 0.04 |
| D | 0.11 | 0.10 | 0.09 | 0.03 | 0.05 | 0.03 |
| E | 0.12 | 0.09 | 0.10 | 0.10 | 0.09 | 0.01 |
| Serum albumin (mean, g/dL) | 3.2 | 3.2 | 3.1 | 0.02 | 0.06 | 0.08 |
| *Presence of comorbidities* | | | | | | |
| Diabetes | 0.55 | 0.53 | 0.53 | 0.04 | 0.04 | 0.00 |
| Coronary artery disease | 0.36 | 0.36 | 0.33 | 0.01 | 0.06 | 0.05 |
| Congestive heart failure | 0.30 | 0.31 | 0.30 | 0.03 | 0.01 | 0.04 |
| Other cardiac disease | 0.27 | 0.30 | 0.28 | 0.06 | 0.03 | 0.03 |
| Cerebrovascular disease | 0.17 | 0.15 | 0.16 | 0.05 | 0.03 | 0.02 |
| Peripheral vascular disease | 0.18 | 0.16 | 0.16 | 0.05 | 0.03 | 0.02 |
| Cancer | 0.17 | 0.21 | 0.20 | 0.08 | 0.06 | 0.03 |
| Chronic obstructive lung disease | 0.07 | 0.06 | 0.07 | 0.03 | 0.01 | 0.02 |
| Polycystic kidney disease | 0.04 | 0.03 | 0.04 | 0.05 | 0.01 | 0.02 |
| Gastrointestinal bleeding | 0.09 | 0.09 | 0.10 | 0.00 | 0.02 | 0.02 |
| *Markers of disease course* | | | | | | |
| Inpatient dialysis start | 0.51 | 0.56 | 0.56 | 0.11 | 0.11 | 0.01 |
| eGFR (mean, ml/min/1.73m$^2$) | 8.7 | 8.7 | 8.9 | 0.00 | 0.03 | 0.05 |

eGFR, estimated glomerular filtration rate

**Supplemental Table 3.** Comparison of means or proportions of covariates across duration of predialysis care in the weighted sample (n=2,414)

| Covariates | Duration of predialysis care (day) | | | Standardized difference across duration of predialysis care (day) | | |
|---|---|---|---|---|---|---|
| | 1-119 | 120-364 | ≥365 | 120-364 vs. 1-119 | ≥365 vs. 1-119 | ≥365 vs. 120-364 |
| Age (mean, years) | 65 | 65 | 65 | 0.02 | 0.01 | 0.00 |
| Male | 0.62 | 0.59 | 0.60 | 0.06 | 0.04 | 0.03 |
| Dialysis programs | | | | | | |
| A | 0.21 | 0.23 | 0.22 | 0.05 | 0.03 | 0.02 |
| B | 0.32 | 0.33 | 0.33 | 0.03 | 0.02 | 0.00 |
| C | 0.24 | 0.23 | 0.25 | 0.03 | 0.02 | 0.05 |
| D | 0.11 | 0.11 | 0.10 | 0.00 | 0.04 | 0.03 |
| E | 0.12 | 0.10 | 0.10 | 0.06 | 0.08 | 0.01 |
| Serum albumin (mean, g/dL) | 3.3 | 3.3 | 3.3 | 0.05 | 0.04 | 0.01 |
| *Presence of comorbidities* | | | | | | |
| Diabetes | 0.58 | 0.57 | 0.57 | 0.02 | 0.02 | 0.01 |
| Coronary artery disease | 0.36 | 0.34 | 0.34 | 0.04 | 0.04 | 0.00 |
| Congestive heart failure | 0.28 | 0.30 | 0.29 | 0.05 | 0.02 | 0.03 |
| Other cardiac disease | 0.24 | 0.27 | 0.26 | 0.08 | 0.06 | 0.02 |
| Cerebrovascular disease | 0.17 | 0.16 | 0.16 | 0.02 | 0.01 | 0.01 |
| Peripheral vascular disease | 0.17 | 0.16 | 0.17 | 0.03 | 0.00 | 0.03 |
| Cancer | 0.16 | 0.19 | 0.19 | 0.07 | 0.06 | 0.01 |
| Chronic obstructive lung disease | 0.06 | 0.06 | 0.06 | 0.03 | 0.03 | 0.00 |
| Polycystic kidney disease | 0.05 | 0.04 | 0.04 | 0.05 | 0.02 | 0.02 |
| Gastrointestinal bleeding | 0.08 | 0.09 | 0.09 | 0.03 | 0.01 | 0.01 |
| *Markers of disease course* | | | | | | |
| Inpatient dialysis start | 0.40 | 0.43 | 0.43 | 0.07 | 0.06 | 0.02 |
| eGFR (mean, ml/min/1.73m$^2$) | 8.4 | 8.2 | 8.2 | 0.04 | 0.05 | 0.02 |

eGFR, estimated glomerular filtration rate

*References for supplemental material*

1. Austin PC, Stuart EA: Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med* 34:3661-3679, 2015
2. Smart NA, Dieberg G, Ladhani M, Titus T: Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease. *Cochrane Database Syst Rev* 6:CD007333, 2014