Chapter 8: Transition of Care in Chronic Kidney Disease

- In every age group, from 18-34 to 75 years and older, incidence rates for Department of Veterans Affairs (VA) patients were 20% to 40% lower than in the United States (U.S.) in general. Because VA patients are disproportionately male and non-white, the relative advantage to VA patients is even greater.
- Mortality rates continued to be highest in the first several months upon transition to dialysis, among both the 100,000 U.S. Veterans and 9,000 members of Kaiser Permanente of Southern California who transitioned to end-stage renal disease (ESRD) between 2007 and 2015.
- Over 20% of the more than 100,000 U.S. Veterans who transitioned to ESRD over a 7.5-year period (10/2007-3/2015) received antidepressant medications prior to transition (prelude period). After transition to ESRD (vintage period), the antidepressant prescription rate increased to almost 30%. Among these Veterans, the prevalence of depression and post-traumatic stress disorder exhibited an upward trend over nine consecutive years (2007-2015).
- Among the 90,676 Veterans who transitioned to ESRD with at least one documented comorbidity, 64% had congestive heart failure (CHF), 53% had diabetes mellitus (DM) with complications, and 55% had chronic obstructive pulmonary disease (COPD). Over a quarter of all these Veteran patients had a diagnosis of cancer (CA), and 33% had a prior myocardial infarction (MI).
- Among the 50,786 Veterans who transitioned to ESRD as an inpatient during a hospitalization, the most common primary admission diagnoses (causes) included 23% for acute kidney injury (AKI), 18% for hypertension (HTN), 11% for CHF, and 9% for chronic kidney disease (CKD). Septicemia-related hospital admissions also increased dramatically after ESRD transition.
- Congestive heart failure and AKI were the most common reasons for hospital admission prior to ESRD transition (prelude period), whereas dialysis access complications were the most common cause for hospitalization after ESRD transition (vintage period).
- Prelude trend analyses provided important information about changes in clinical and laboratory measures during the several years prior to transition to ESRD. For the 29,362 Veterans who transitioned to ESRD, measured serum phosphorus in the 36 months (3 years) prelude gradually increased from 4.0 mg/dL to above 5.5 mg/dL immediately prior to transition. After transition to dialysis, serum phosphorus levels dropped to below 5 mg/dL.
- The secular trends observed over nine consecutive years (2007-2015) suggest changes in practice patterns for Veterans with advanced CKD, resulting in lower blood hemoglobin (<9 g/dL) and lower eGFR values (<7 ml/min/1.73m^2) in the finals days prior to transitioning to ESRD.

Introduction

The Transition of Care in Chronic Kidney Disease (TC-CKD) Special Study Center examines the transition of care to renal replacement therapy (RRT; i.e., dialysis or transplantation) in patients with very-late-stage (advanced) non-dialysis dependent (NDD) CKD. These are often people with an estimated glomerular filtration rate (eGFR) <25 ml/min/1.73 m^2.

The primary databases used in these analyses were created from a linkage between the national USRDS data and two large longitudinal databases of NDD-CKD patients—the national Veterans Health Administration (VHA) database and the regional (Southern California) Kaiser Permanente (KP-SC) database. These linkages have allowed us to identify nearly all VHA and KP-SC patients who have transitioned to ESRD from the index point, 2007,

onwards. Each of these linked databases includes thousands of NDD-CKD patients who transitioned to ESRD each year, in whom historical data were examined from up to -5 (minus five) years prior to ESRD ("prelude" period) to +2 (plus two) years after ESRD transition (early "vintage" period).

In this USRDS Special Study operation, we have examined the recent national VHA and KP-SC cohorts of incident ESRD patients. We have provided pre-ESRD (prelude) data on all available ESRD transitions since 10/1/2007 among Veterans, and since 1/1/2007 among KP-SC patients. Analyses that examined 4-year (10/1/2007-9/30/2011) pre- and post-ESRD data of approximately 52,000 incident ESRD Veterans who transitioned to ESRD were presented in 2014 and 2015 Annual Data Report (ADR) chapters. In our 2016 ADR chapter, we presented 6.5-year (10/1/2007-3/31/2014) and 7-year (01/01/2007-12/31/2013) transition-to-ESRD data on approximately 85,000 incident ESRD Veterans across the entire nation and 8,038 KP-SC members in Southern California. In this 2017 ADR, we present 7.5-year pre- and post-ESRD data on more than 100,000 incident ESRD Veterans who transitioned between 10/1/2007 and 3/31/2015. In this year's chapter, we feature, for the first time, several secular trends among pre-ESRD Veterans over nine calendar years, i.e., 2007 through 2015. As in the previous years, this chapter also includes KP-SC data over eight years (01/01/2007-12/31/2014), which includes 9,260 KP-SC members who transitioned to ESRD in Southern California.

As stated in the original goals of this Special Study Center, we have continued to test the hypotheses that a pre-ESRD (prelude) data-driven personalized approach to the transition of care into ESRD in very-late-stage NDD-CKD is associated with more favorable outcomes. We believe this is particularly true if decisions are based on pre-ESRD factors such as clinical and laboratory variables, including the CKD progression rate, comorbid conditions during prelude period, and demographics. We have published some of these concepts and data in the form of abstracts and 12 peer-reviewed manuscripts over the past two years.[1-12] We have also developed and validated a scoring system derived from these pre-ESRD data to better ascertain the extent to which timing, preparation, and modality of ESRD may be associated with better outcomes.

The Veterans Health Administration

There are more than 20 million Veterans in the U.S.; approximately nine million are enrolled in the Veterans Health Administration (VHA), including approximately six million who receive their healthcare in one of the VHA facilities. Whereas approximately 90% of the U.S. Veteran population is presently male, it is estimated that in the next decade the proportion of females will rise to 18-20%.[13-14] Minority Veterans currently comprise about 22% of the overall Veteran population, among whom the majority are of Black or African American race (12% of all Veterans) and Hispanic or Latino ethnicity (7% of all Veterans).[15-16] Each year approximately 13,000 Veterans transition to RRT, mostly in the form of maintenance dialysis treatment.[17] Among the more than 6,000 dialysis units nationwide, there are currently approximately 70 VHA dialysis centers.[17] Given this number of VHA dialysis centers and their limited capacity, only 10% of all incident dialysis Veterans initiate treatment in a VHA center.[17] Although almost 90% of the ESRD Veterans receive dialysis treatment in non-VHA facilities, including large dialysis organizations, the transition data of these and other outsourced Veterans and in particular, their prelude and early vintage analyses and other data, are also included in this chapter. Hence, our transition-of-care data for more than 100,000 (N=102,477) Veterans with ESRD are inclusive and comprehensive.

ESRD Rates among Veterans

As reported in previous ADR chapters on Transition of Care in CKD, on average 13,664 Veterans transitioned to ESRD each year over the period of 2007-2015, with an average national ESRD transition rate of 1,139 Veterans per month (see below for additional data and analyses on secular trend data). In this report, we have also calculated the ESRD incident rates for Veterans in each calendar year (January 1-December 31), instead of federal government fiscal year (October 1-September 30). The most updated U.S. Census data were accessed to obtain annual Veteran population data using the Census Fact Finder site.[6]

We calculated the counts of all Veterans in each year and per age strata (Table 8.1). The USRDS incidence rates for ESRD among U.S. adults were obtained from the 2016 Standard Analysis Files (SAFs)

for comparison. For the seven full calendar years between 2008 and 2014, the crude ESRD incident rates among Veterans were 635.3, 664.1, 646.5, 620.9, 635.6, 669.8, and 665.0 per million Veterans. Given the ESRD incident rates of 488.1, 499.6, 495.7, 482.4, 485.5, 484.7, and 492.0 per million per the general U.S. population (PMP), the calculated crude rate ratios of ESRD incidence among Veterans compared to the U.S. general population were 1.30, 1.33, 1.30, 1.29, 1.31, 1.38, and 1.35 for calendar years 2008 through 2014, suggesting that ESRD is 29-38% more likely to occur among Veterans than in the general U.S. population.

It is important to note, however, that the VHA population is considerably older than the general U.S. population. Hence, as stated in our 2016 ADR chapter, on an age-specific and age-adjusted basis, the VHA rate of ESRD is 25-40% lower than the U.S. rate of ESRD. This lower-than-expected adjusted risk occurs despite the fact that the VHA population is predominantly male and disproportionately non-white. The remarkably lower adjusted rate of ESRD among VHA patients, despite higher crude ESRD incidence rates, is currently unexplained. Is it because the VHA provides an integrated health care system with better care to CKD patients, including Blacks, in whom higher CKD burden is well known? Is it because there is a selection bias of persons entering into military service, through healthier persons or those without preexisting kidney disease being selected to serve? Further research may shed some light on this issue.

vol 1 Table 8.1. Rates and ratio of incident ESRD Veterans among the veteran population and the U.S. adult population for calendar years 2008-2014 across five age strata of 18-34, 35-54, 55-64, 65-74, and 75+ years

(a) 18-34 years

	2008	2009	2010	2011	2012	2013	2014
Incident ESRD Veterans	84	83	81	81	69	84	89
All Veterans	1,704,278	1,660,932	1,743,846	1,759,591	1,825,854	1,625,853	1,656,336
ESRD rate in Veterans, PM	49	50	46	46	38	52	54
Incident ESRD in U.S.	5,532	5,758	5,564	5,497	5,607	5,491	5,619
U.S. Population	71,037,035	71,579,121	71,981,752	72,914,022	73,727,483	74,436,376	74,980,662
ESRD rate in the U.S., PM	78	80	77	75	76	74	75
ESRD rate ratio (Vet: U.S.)*	0.63	0.62	0.60	0.61	0.50	0.70	0.72

(Table 8.1 continued on next page)

vol 1 Table 8.1. Rates and ratio of incident ESRD Veterans among the veteran population and the U.S. adult population for calendar years 2008-2014 across five age strata of 18-34, 35-54, 55-64, 65-74, and 75+ years *(continued)*

(b) 35-54 years

	2008	2009	2010	2011	2012	2013	2014
Incident ESRD Veterans	1,442	1,446	1,277	1,177	1,226	1,051	1,060
All Veterans	5,942,549	5,725,846	5,558,510	5,386,065	5,265,255	4,720,849	4,583,813
ESRD rate in Veterans, PM	243	253	230	219	233	223	231
Incident ESRD in U.S.	25,998	26,691	26,014	25,814	25,962	25,975	26,516
U.S. Population	87,002,075	86,590,351	85,977,283	85,433,299	84,892,906	84,384,863	83,971,984
ESRD rate in the U.S., PM	299	308	303	302	306	308	316
ESRD rate ratio (Vet: U.S.)*	0.81	0.82	0.76	0.72	0.76	0.72	0.73

(c) 55-64 years

	2008	2009	2010	2011	2012	2013	2014
Incident ESRD Veterans	3,342	3,511	3,357	3,247	3,084	2,769	2,610
All Veterans	5,718,302	5,441,739	5,340,529	5,085,647	4,564,636	3,976,482	3,640,087
ESRD rate in Veterans, PM	584	645	629	638	676	696	717
Incident ESRD in U.S.	26,043	27,163	27,661	27,635	28,743	28,598	29,344
U.S. Population	33,669,357	34,868,475	36,785,628	38,090,424	38,614,954	39,343,044	40,077,581
ESRD rate in the U.S., PM	773	779	752	726	744	727	732
ESRD rate ratio (Vet: U.S.)*	0.76	0.83	0.84	0.88	0.91	0.96	0.98

(d) 65-74 years

	2008	2009	2010	2011	2012	2013	2014
Incident ESRD Veterans	3,201	3,405	3,319	3,317	3,759	4,081	4,286
All Veterans	4,148,572	4,152,331	4,294,221	4,420,436	4,798,175	4,720,849	4,891,968
ESRD rate in Veterans, PM	772	820	773	750	783	864	876
Incident ESRD in U.S.	26,073	27,251	27,885	27,169	28,399	29,805	31,188
U.S. Population	20,098,221	20,781,497	21,857,563	22,495,852	24,010,384	25,228,428	26,398,290
ESRD rate in the U.S., PM	1,297	1,311	1,276	1,208	1,183	1,181	1,181
ESRD rate ratio (Vet: U.S.)*	0.59	0.63	0.61	0.62	0.66	0.73	0.74

(Table 8.1 continued on next page)

vol 1 Table 8.1. Rates and ratio of incident ESRD Veterans among the veteran population and the U.S. adult population for calendar years 2008-2014 across five age strata of 18-34, 35-54, 55-64, 65-74, and 75+ years *(continued)*

(e) 75 years or older

	2008	2009	2010	2011	2012	2013	2014
Incident ESRD Veterans	6,178	6,053	6,045	5,502	5,356	5,135	4,750
All Veterans	4,911,012	4,851,671	4,839,173	4,806,688	4,776,945	4,544,552	4,468,254
ESRD rate in Veterans, PM	1,258	1,248	1,249	1,145	1,121	1,130	1,063
Incident ESRD in U.S.	28,849	29,384	29,466	28,605	28,001	27,849	28,011
U.S. Population	18,671,803	18,846,651	18,621,790	18,870,776	19,154,525	19,494,613	19,844,921
ESRD rate in the U.S., PM	1,545	1,559	1,582	1,516	1,462	1,429	1,411
ESRD rate ratio (Vet: U.S.)*	0.81	0.80	0.79	0.76	0.77	0.79	0.75

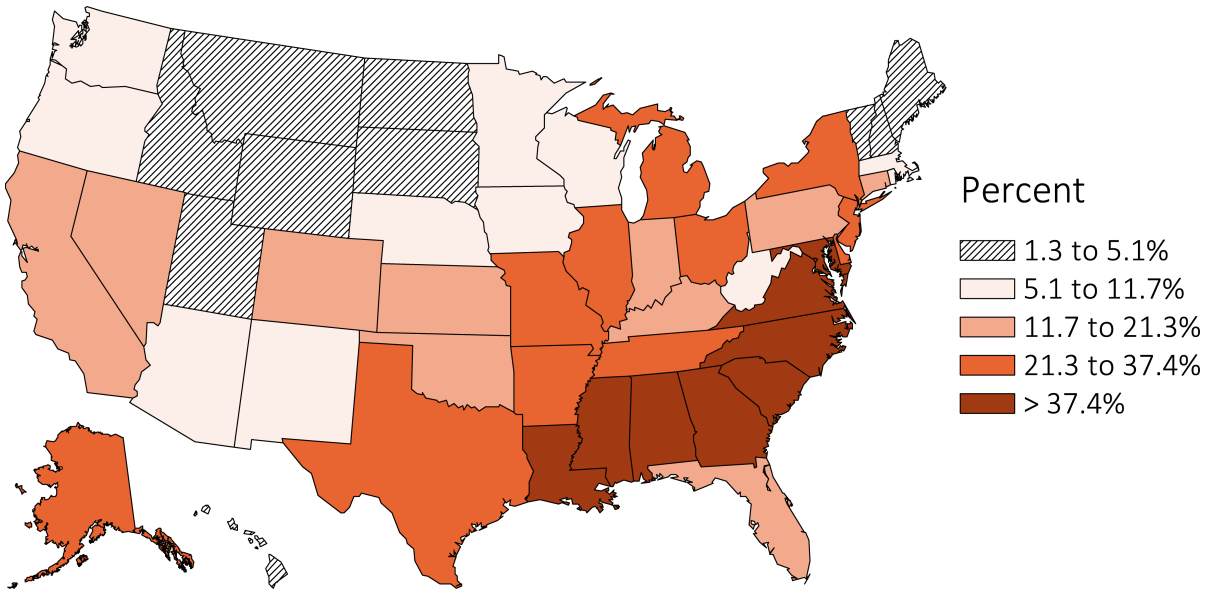
*Data source: VHA Administrative data, USRDS ESRD Database, CMS Medicare Inpatient and Outpatient data, U.S. Census Bureau; data derived from U.S. veteran incident dialysis patients. *Veterans to U.S. rate ratios. Abbreviations: ESRD, end-stage renal disease; PM, per million; Vet, Veterans.*

Highlights of the Incident ESRD Veterans Population between 10/1/2007 and 3/31/2015

Between 10/1/2007 and 3/31/2015 (over 7.5 fiscal years), 102,477 Veterans transitioned to ESRD. The mean ± standard deviation age was 70.2 ±12.0 years, and included 25% patients of Black race and 6% of Hispanic ethnicity. The main causes of ESRD were DM (42%) or HTN (32%).

Across the nation, the distribution of patients with ESRD due to DM varied. Primarily, southwestern states, such as Texas, New Mexico, and Arizona had a higher proportion of patients with ESRD due to DM, while northern states such as Alaska, Oregon, Idaho, and North Dakota had lower proportions of ESRD due to DM (Figure 8.1).

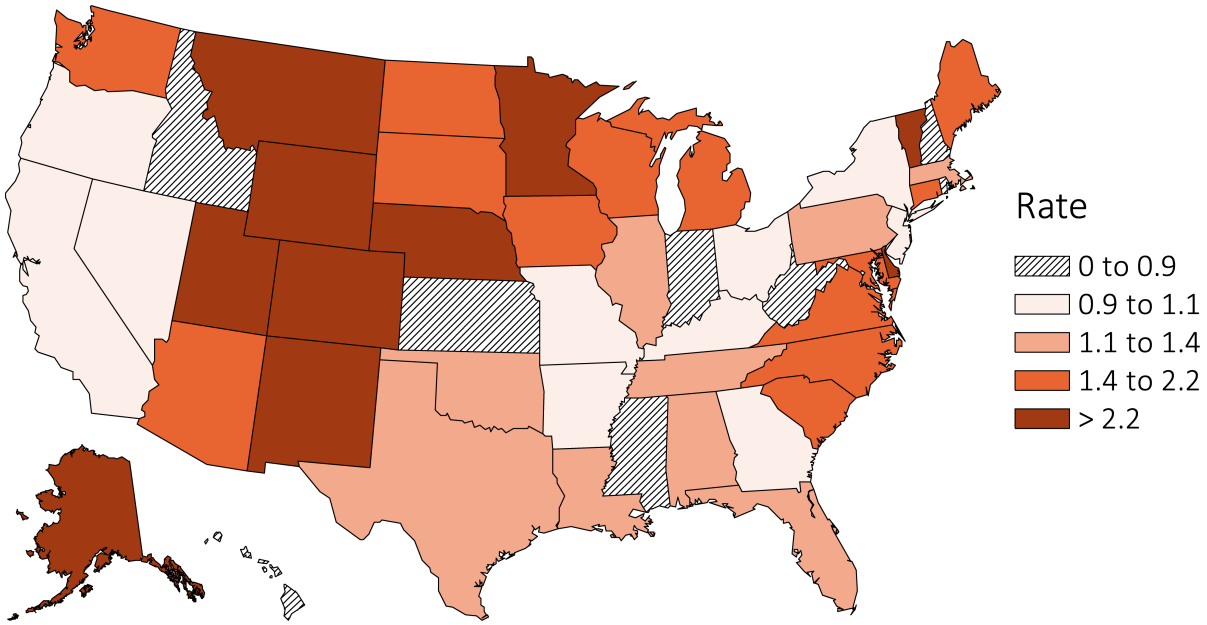
vol 1 Figure 8.1. Distribution of diabetes (%) as the cause of ESRD among 102,477 incident ESRD Veterans across states and territories of the United States, 10/1/2007-3/31/2015



States and territories of the United States of America.

Out of 102,477 Veterans, there were 1,355 preemptive transplantations over 7.5 years in the entire nation. As in the general ESRD population, preemptive transplantation is fairly rare. Figure 8.2 shows the proportions of preemptive kidney transplantation in each state and territory of the U.S. The rates were calculated based on the number of preemptive transplants divided by the total number of the incident ESRD Veterans in that state or territory. The states with the highest preemptive kidney transplant rates among Veterans (>2.2%) were Alaska, Colorado, Delaware, Minnesota, Montana, Nebraska, New Mexico, Utah, Vermont, and Wyoming.

vol 1 Figure 8.2. Distribution of preemptive kidney transplant rates among 102,477 incident ESRD Veterans across states and territories of the United States, 10/1/2007-3/31/2015



States and territories of the United States of America

Nine-Year Secular Trends among Veterans who Transitioned to ESRD

Baseline characteristics of 102,477 incident ESRD Veterans were summarized by calendar year at transition to ESRD, and are shown in Table 8.2. Data were presented as mean ± standard deviation (SD) or median (interquartile range, IQR) for continuous variables, and percentages for categorical variables. Changes may occur in demographics, practice patterns, and clinical measures over a period of several years. In this year's TC-CKD chapter, we examine some of these secular trends.

In addition to renal disease, congestive heart failure (CHF), DM, and chronic obstructive pulmonary disease (COPD) were present in over half of the Veterans. Of note, almost a quarter of all patients had a prior diagnosis of cancer (CA) and over 30% had a prior myocardial infarction (MI). The median (IQR) Charlson Comorbidity Index (CCI) score was 5 (3, 7), and 10% had a CCI of 10 or greater.

Among Veterans who transitioned to ESRD between 10/1/2007 and 3/31/2015, the mean age remained steady over time. The prevalence of Veterans who were Black, divorced, and had mild liver disease increased over time; however, the median CCI was the same each year. The percentage of Veterans who had ischemic heart disease decreased over time compared to earlier years of transition to ESRD.

vol 1 Table 8.2. Baseline characteristics of 102,477 incident ESRD Veterans who transitioned to ESRD between 10/1/2007 and 3/31/2015 according to incidence year at transition to ESRD

		Incidence Year								
	Total	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**
N	102477	3575	14247	14498	14080	13326	13495	13122	12797	3337
Age (years)	70.2±12.0	69.7±12.1	70.1±12.2	70.0±12.2	70.4±12.1	70.3±12.1	70.2±11.9	70.4±11.7	70.1±11.8	70.3±11.6
Female (%)	7	6	6	7	6	7	7	7	7	8
Race (%)										
White	71	73	72	71	72	71	71	69	69	68
Black/African American	25	24	24	25	24	25	25	26	27	27
American Indian or Alaska Native	0.87	0.73	0.90	0.90	0.82	0.83	0.92	0.85	0.95	0.81
Asian	1.09	1.17	1.12	1.10	0.90	0.98	1.11	1.19	1.16	1.41
Native Hawaiian or Pacific Islander	0.07	0.03	0.05	0.08	0.08	0.06	0.05	0.09	0.07	0.21
Other or Multiracial	2.06	1.90	2.16	1.65	1.81	2.11	2.19	2.58	2.09	1.71
Unknown	0.02	0	0.02	0.02	0.02	0.02	0.05	0	0.01	0
Ethnicity (%)										
Hispanic	6	7	6	6	7	7	7	6	7	6
Non-Hispanic	3	3	4	3	3	3	4	4	4	4
Unknown	0.02	0	0.01	0.03	0.01	0	0.04	0.01	0.01	0
Non-Hispanic White	65	67	66	66	66	65	65	64	63	63
Non-Hispanic Black/African-American	25	23	24	25	24	25	25	26	27	27
Marital Status (%)										
Single	8	7	7	8	7	8	8	8	9	8
Married	61	63	62	62	62	61	62	61	60	60
Divorced	21	19	19	20	20	21	21	22	22	23
Widowed	10	11	12	11	11	10	10	9	8	9
Charlson comorbidity index	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)	5 (3,7)

Table 8.2 continued on next page.

vol 1 Table 8.2. Baseline characteristics of 102,477 incident ESRD Veterans who transitioned to ESRD between 10/1/2007 and 3/31/2015 according to incidence year at transition to ESRD *(continued)*

		Incidence Year								
	Total	**2007**	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**
Comorbidity (%)										
Myocardial infarction	33	32	33	34	34	33	34	34	32	30
Congestive heart failure	64	63	64	64	65	64	64	65	63	59
Peripheral vascular disease	53	53	53	53	54	53	53	53	52	51
Dementia	6	6	6	6	6	6	6	6	5	4
Cerebrovascular disease	45	43	45	46	47	46	45	46	44	43
Chronic obstructive pulmonary disease	55	51	53	54	55	55	56	56	55	54
Connective tissue/Rheumatic disease	9	8	8	9	9	9	9	9	9	9
Peptic ulcer disease	12	10	12	12	12	12	11	12	12	10
Mild liver disease	16	14	14	15	16	16	17	17	18	18
Moderate/Severe liver disease	4	3	3	3	4	4	3	4	4	5
Diabetes without complications	19	20	20	19	19	18	18	18	18	19
Diabetes with complications	53	51	50	52	53	53	54	55	56	55
Cancer	27	26	26	27	28	27	26	27	27	28
Metastatic cancer	6	5	6	5	6	6	6	6	5	6
Hemiplegia	6	6	6	6	6	6	6	6	6	7
HIV/AIDS	1.0	0.8	1.1	1.0	0.9	1.1	1.0	1.0	1.2	1.1
Anemia	80	77	79	80	81	80	80	81	82	78
Atrial fibrillation	27	25	27	27	28	27	27	27	27	26
Depression	29	24	25	27	28	29	31	31	33	33
Hyperlipidemia	83	80	80	82	83	84	84	85	85	84
Ischemic heart disease	67	67	67	68	68	67	66	67	65	62
Post-traumatic stress disorder	7	4	5	6	7	7	8	9	10	10
Initial dialysis modality (%)										
Hemodialysis	81	83	82	83	81	81	80	80	80	80
Home hemodialysis	0.51	0.53	0.51	0.37	0.46	0.50	0.64	0.52	0.57	0.72
Peritoneal dialysis	6	5	5	5	6	6	7	7	7	7

Although the mean age remained steady over time, Figure 8.3 shows secular trends and changes in age groups across nine years (2007 through 2015) among the 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015. During this period, the proportion of ESRD-transitioning Veterans decreased in the 40 - <60 year-old age group, but increased in the 60 - <80 year-old age group. Whereas the prevalence of Veterans in the <40 year-old age group remained steady, there was no clear trend among those older than 80 years.

vol 1 Figure 8.3. Secular trends in age stratified by incidence year in 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

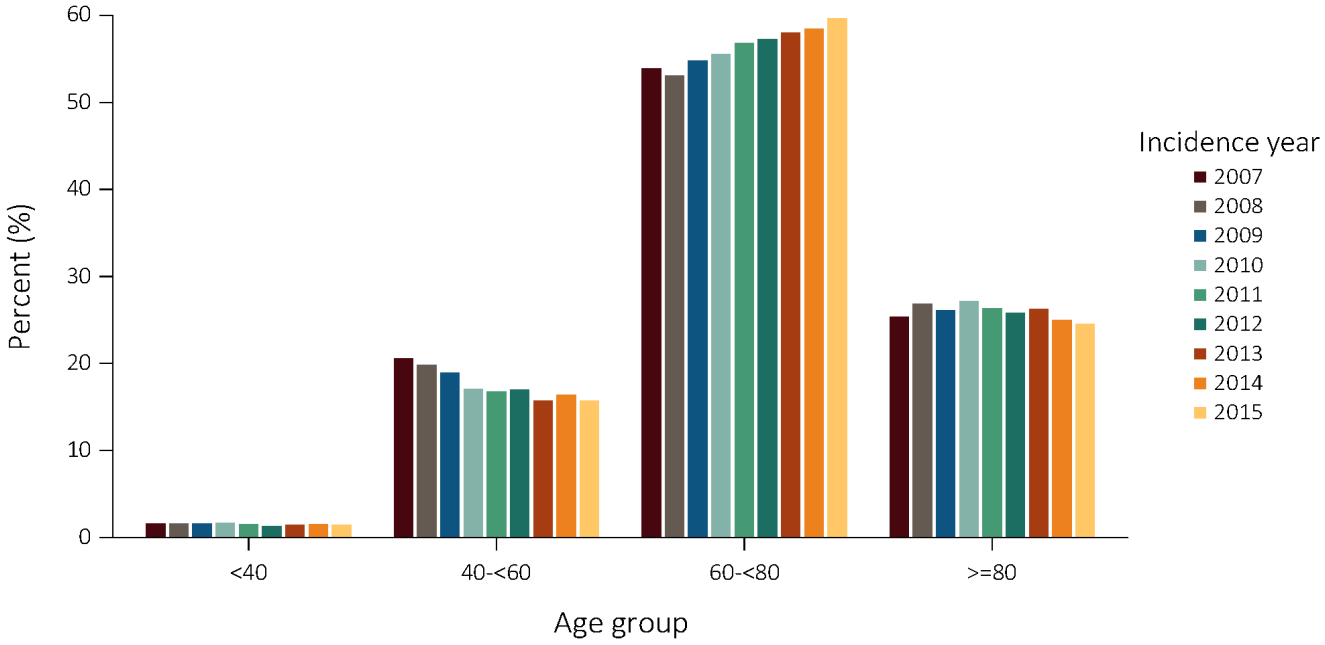
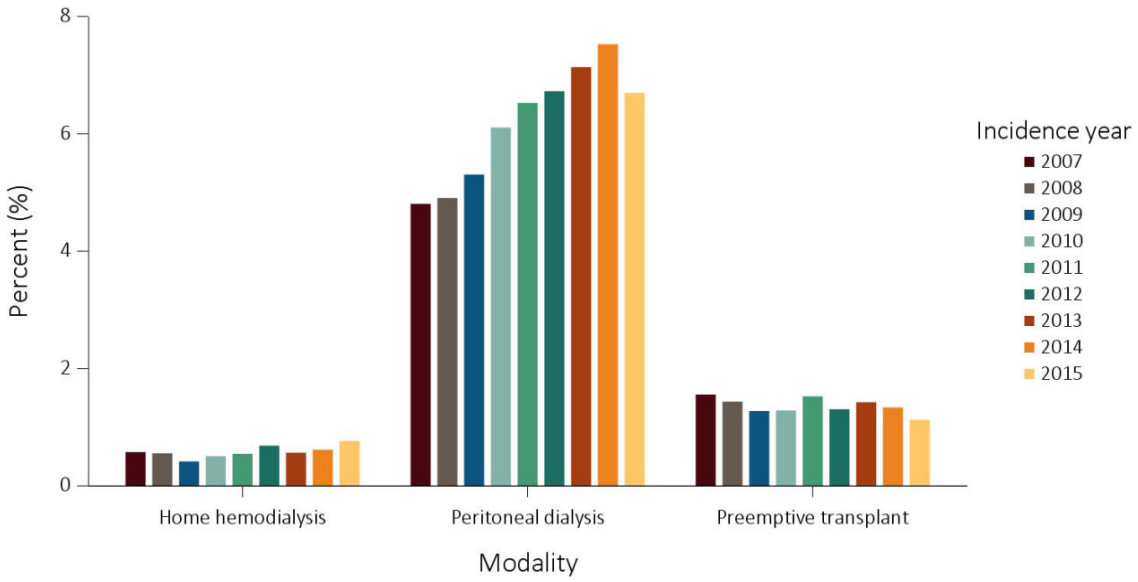


Figure 8.4 shows the secular trends in dialysis modality on the first day of transition to ESRD, across nine incidence years, for 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015. There was an increasing trend in peritoneal dialysis (PD) treatment as the initial modality, except for a decrease in 2015. This was likely due to seasonal variation effect, given that the 2015 data are limited to the first three months of that year. There also appears to be a slight downward trend in the prevalence of preemptive transplant cases, but there was no clear trend in home hemodialysis (HD) use.

vol 1 Figure 8.4. Secular trends in modality on the first day of transition to ESRD, stratified by incidence year in 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.



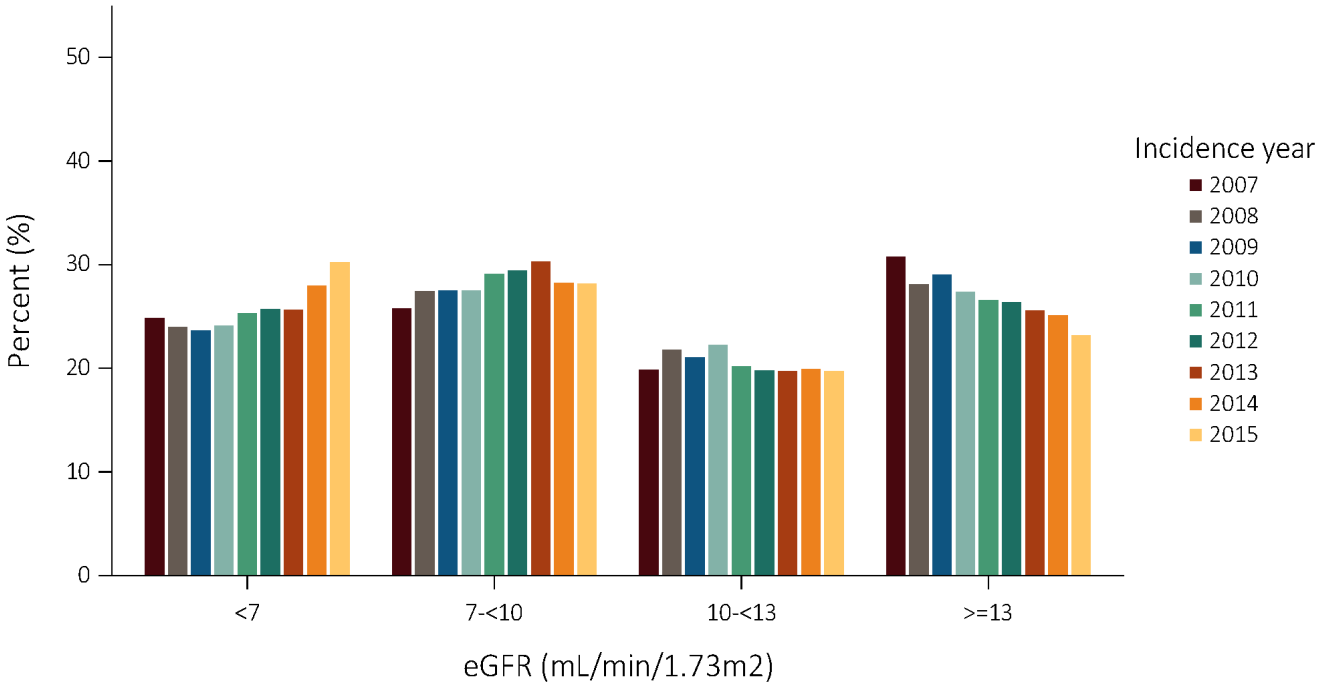
The drop in the prevalence of incident peritoneal dialysis patients in 2015 may have been influenced by the possibility of seasonal variation. Data for 2015 represent only the winter season, which includes months January to March.

Figure 8.5.a shows the secular trends in the pre-ESRD eGFR calculated by the CKD-EPI creatinine equation, for 25,035 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015, and whose eGFR in the final 31 days of the prelude period was available. Over time, there was an upward trend in the proportion of patients with a last-31-day eGFR <7 ml/min/1.73m2, but a downward trend in the group with eGFR ≥13 ml/min/1.73m². These secular trends may reflect changes in practice patterns towards deferred dialysis initiation in Veterans with advanced CKD.

Out of 102,477 patients, there were 55,814 patients who initiated dialysis during a hospitalization; of these, 11,520 and 5,528 had a listed primary cause of hospitalization as AKI and CHF. Figures 8.5.b and 8.5.c illustrate pre-ESRD secular trends of the last 31-day prelude eGFR among patients hospitalized by AKI or CHF at time of transition. Compared to all Veterans (Figure 8.5.a), a greater percentage of Veterans who were hospitalized due to AKI during transition to ESRD (Figure 8.5.b) started dialysis at lower eGFR levels of <7 mL/min/1.73m2. Conversely, a greater percentage of Veterans hospitalized due to CHF during transition to ESRD had a higher last 31-day prelude eGFR level of ≥13 mL/min/1.73 m² (Figure 8.5.c). More analyses are needed to examine such practice pattern alterations over time, including across age and comorbid conditions.

vol 1 Figure 8.5 Secular trends in eGFR in the last 31 days of the prelude (pre-ESRD) time stratified by incidence year in 25,035 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

(a) All Veterans



(b) Veterans hospitalized by AKI at time of transition

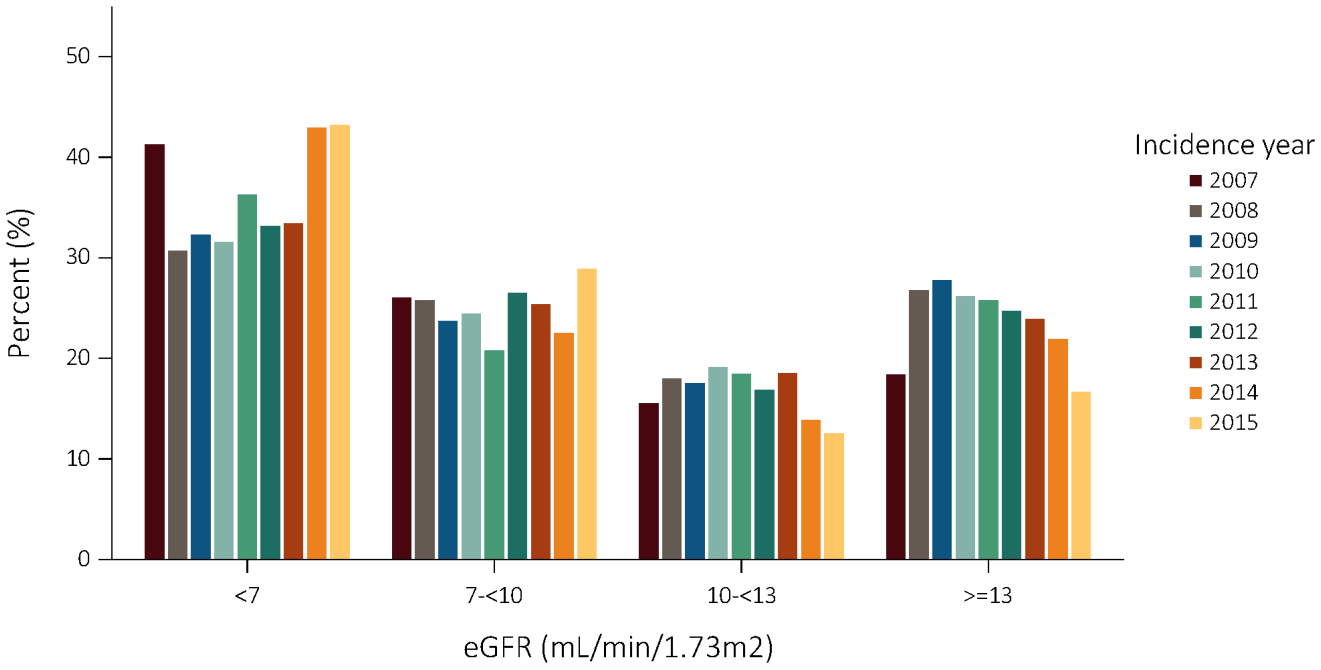


Fig. 8.5 continued on next page.

vol 1 Figure 8.5 Secular trends in eGFR in the last 31 days of the prelude (pre-ESRD) time stratified by incidence year in 2,775 Veterans who were hospitalized during transition to ESRD due to acute kidney injury and who transitioned to ESRD during 10/1/2007-3/31/2015 *(continued).*

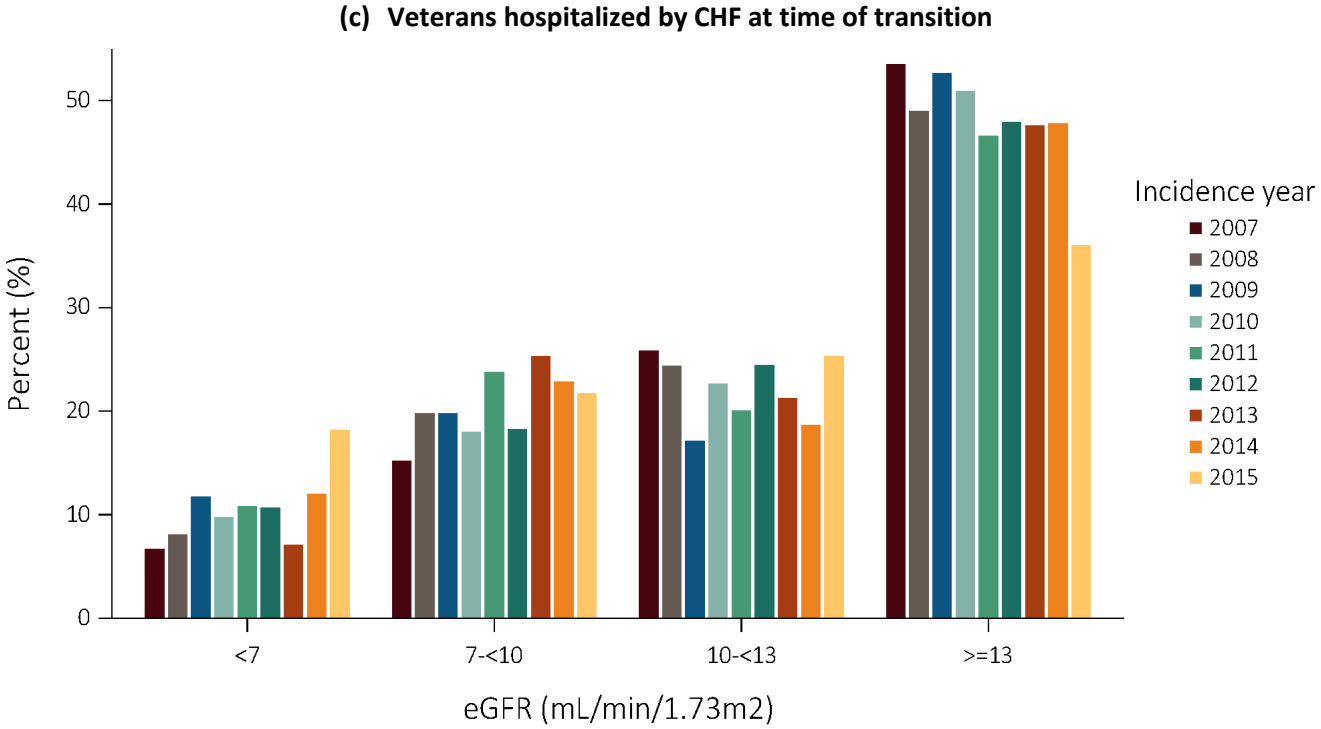
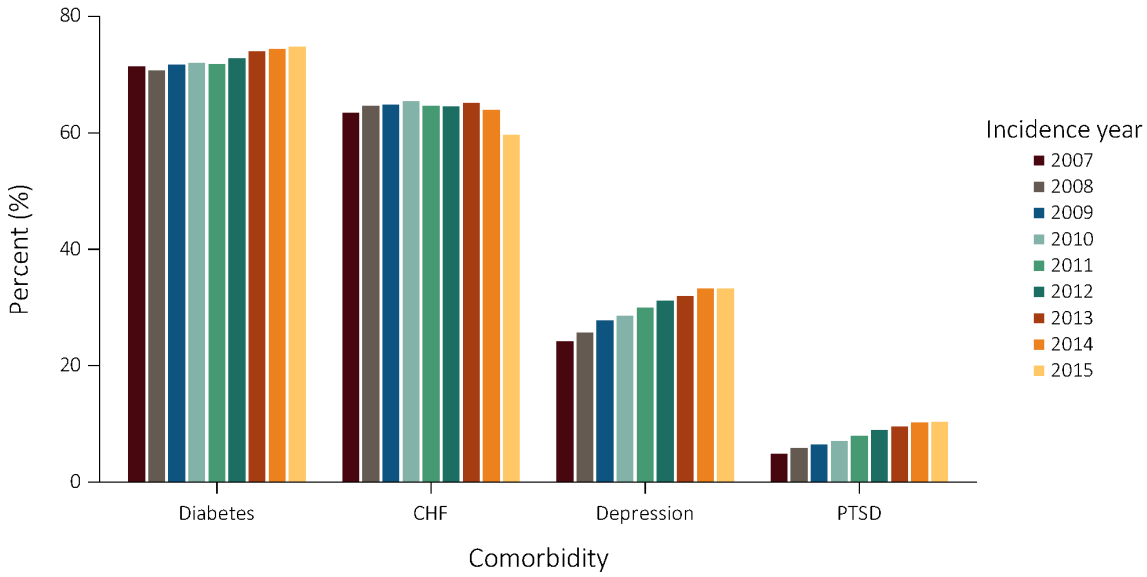


Figure 8.6 shows the secular trends in comorbidities over nine years for 90,676 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015. Data related to comorbid conditions were obtained from multiple VHA and CMS sources, and were based on ICD-9 diagnostic codes. A total of 90,676 Veterans (88.4%) were identified from all sources as being diagnosed with at least one comorbid condition in the prelude period.

Five selected comorbid conditions are shown in Figure 8.6. The prevalence of CHF remained steady, except for a slight drop in 2015. There were substantial upward trends in the frequency of depression and post-traumatic stress disorder, while a less substantial upward trend for diabetes was noticeable.

vol 1 Figure 8.6. Secular trends in comorbidities during the prelude (pre-ESRD) time stratified by calendar year in 90,676 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.



Abbreviations: CHF, Congestive Heart Failure; and PTSD, Post-Traumatic Stress Disorder

Figure 8.7 shows the pre-ESRD secular trends in last 31-day hemoglobin measurement during the prelude period in 23,333 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015. Low hemoglobin levels <9 g/dL immediately prior to transition exhibited a remarkable upward trend, whereas there was a downward trend for hemoglobin levels of 10- <11 and ≥11 g/dL. There was no clear trend in the group with a hemoglobin level of 9- <10 g/dL.

vol 1 Figure 8.7. Secular trends in hemoglobin in the last 31 days of the prelude (pre-ESRD) time stratified by incidence year in 23,333 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

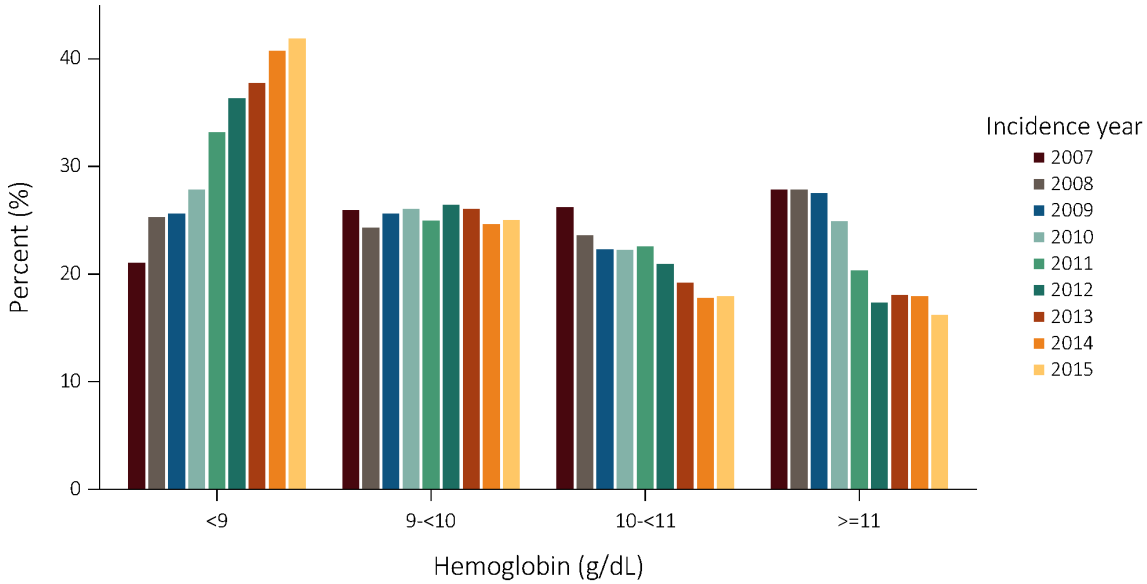


Figure 8.8 shows the secular trends in mortality according to days after transition to ESRD, stratified by calendar year for 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015. The mortality incidence in the first 30 days after transition to ESRD remained consistent among Veterans over the 9-year period. In the first 60, 90 and 365 days after transition to ESRD, there were slight spikes in mortality in years 2008 and 2015.

vol 1 Figure 8.8. Secular trends in mortality according to days after transition to ESRD stratified by incidence year in 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

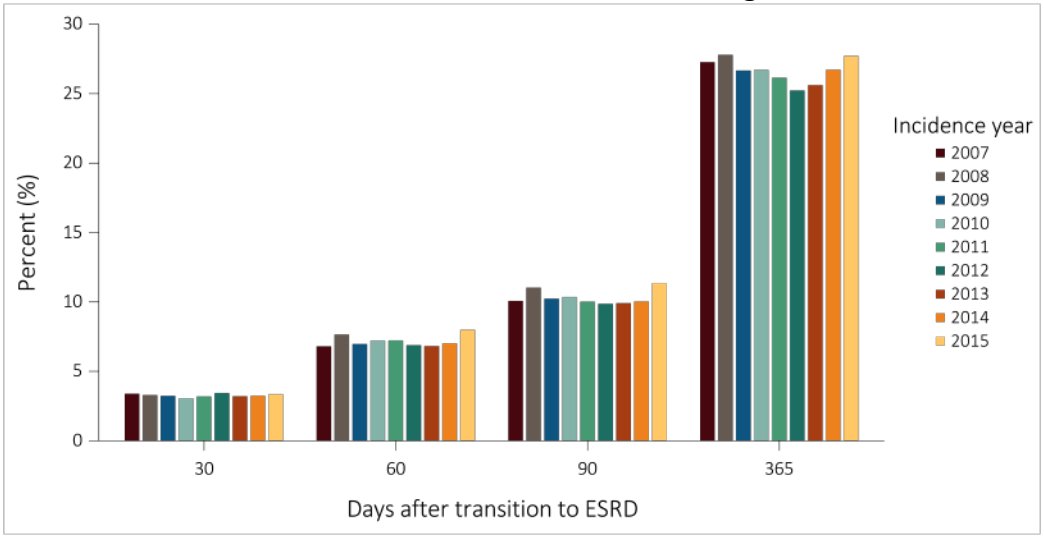
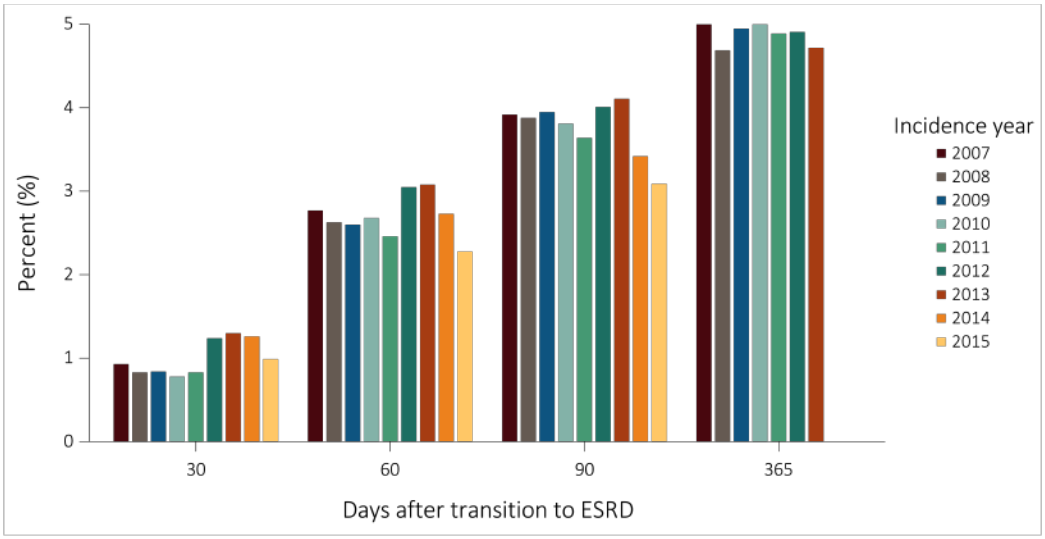


Figure 8.9 shows the secular trends in "recovered-kidney-function" status after transition to ESRD. These were patients who did not need to continue dialysis therapy after having started maintenance dialysis. The analysis was stratified by the number of days after ESRD transition, for 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015. Among Veterans on dialysis, at 30, 60, and 90 days after dialysis initiation downward trends in recovered function were observed from 2013 through 2015. A less remarkable downward trend can be seen among Veterans on dialysis 365 days after transition to ESRD.

vol 1 Figure 8.9. Secular trends in "recovered-kidney-function" according to days after transition to ESRD stratified by incidence year in 102,477 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.



Data for 365 days after transition to ESRD in years 2014 and 2015 were not shown given incomplete longitudinal data.

First Three Months after Transition to ESRD

The status of incident ESRD Veterans during the first three months after transition to ESRD (10/1/2007-3/31/2015) is shown in Table 8.3. At ESRD service initiation, 81.0% and 6.2% of 102,477 Veterans received in-center HD or PD. Nearly the same number of Veterans continued to receive in-center HD or PD in the first 30 and 60 days after transition to ESRD, with a slight decrease of in-center HD use in the latter period. After 90 days of ESRD service, 90.9% and 7.9% of all Veterans receiving any dialysis treatment utilized in-center HD or PD (n=86,137 Veterans).

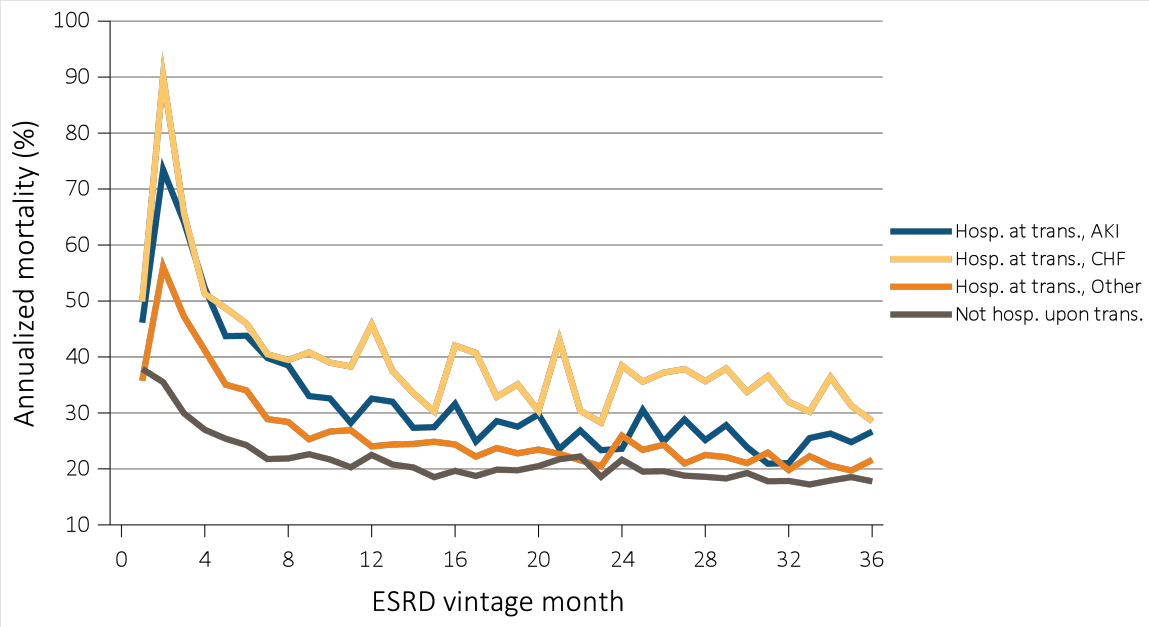
There were 1.3% (n=1,355) registered preemptive kidney transplant recipients at ESRD service initiation. Over the next 30 and 60 days after transition to ESRD, the percentage of kidney transplants remained steady at 1.4% (n=1,405 and n=1,474), but the percentage of deaths doubled from 3.1% (n=3,148) to 7.0% (n=7,135). During the first three months of the transition to ESRD, 10.1% (n=10,324) died, 1.5% (n=1,542) received a kidney transplant, and 3.8% (n=3,877) recovered from ESRD and stopped dialysis therapy. As shown in Figure 8.10, the crude annualized mortality rate among incident ESRD Veterans was higher during the initial months after ESRD transition, across all strata, including those hospitalized for AKI, CHF, or other causes, and those not hospitalized during transition to ESRD. The peaks in annualized mortality rates at about three months reflect the similar early excess mortality that is seen in the general ESRD population. Of note, the highest peak in annualized mortality rate in the early months after ESRD transition was seen in Veterans who were hospitalized due to CHF during transition to ESRD.

vol 1 Table 8.3. Status of 102,477 incident ESRD Veterans on Day 1, Day 30, Day 60, and Day 90 after transition to ESRD, 10/1/2007-3/31/2015

	Day 1		Day 30		Day 60		Day 90	
Modality	**Frequency**	**%**	**Frequency**	**%**	**Frequency**	**%**	**Frequency**	**%**
Hemodialysis	82985	81.0	82994	81.0	82835	80.8	78299	76.4
Home Hemodialysis	527	0.5	527	0.5	526	0.5	591	0.6
Peritoneal Dialysis	6353	6.2	6354	6.2	6352	6.2	6793	6.6
Uncertain Dialysis*	11257	11.0	6653	6.5	805	0.8	454	0.4
Transplant	1355	1.3	1405	1.4	1474	1.4	1542	1.5
Discontinued Dialysis			367	0.4	512	0.5	494	0.5
Death			3148	3.1	7135	7.0	10324	10.1
Lost to Follow-up			34	0.03	73	0.1	103	0.1
Recovered Function			995	1.0	2765	2.7	3877	3.8
Total	102477	100	102477	100	102477	100	102477	100

*Data source: VHA Administrative data, USRDS ESRD Database, CMS Medicare Inpatient and Outpatient data. *Uncertain groups have no known dialysis modality.*

vol 1 Figure 8.10. Annualized unadjusted mortality of incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 and who were followed for up to 36 months, stratified according to cause of hospitalization during transition to ESRD (N=89,527).



**Abbreviations: ESRD, end-stage renal disease; hosp., hospitalization; AKI, acute kidney injury; CHF, congestive heart failure; and trans., transition.*

Data Before, During, and After Transition to ESRD

In the section below, we illustrate the unique aspect of this Special Study Center cohort in the examination of the changes in medication prescriptions, cause of hospitalizations, and laboratory measurements throughout the transition period, including before (prelude), during, and after (vintage) transition. A deeper understanding of these changes can guide the personalized approach to transition of care into ESRD, and help produce outcomes that are more favorable for ESRD patients.

Prescribed Medications upon Transition to ESRD

The Veteran ESRD population utilizes a number of medications, and the patterns of medication use vary before (prelude), during, and after (vintage) transition to ESRD. Both VHA prescription records and CMS Medicare Part D prescription records were used to describe medication use in 6-month intervals before (up to -3 years prelude), during, and after (up to +3 years vintage) ESRD transition. Seven groups of medications were analyzed, including (1) medication used for blood pressure management (alpha blockers, beta blockers, calcium channel blockers, potassium sparing diuretics, loop diuretics, RAAS inhibitors, thiazide diuretics, vasodilators, and central alpha agonists), (2) cholesterol lowering medications (statins and non-statin lipid lowering drugs), (3) diabetes medications (insulin and oral hypoglycemics), (4) anemia medications (erythropoietin stimulating agents [ESA] and iron), (5) mineral and bone disorder medications (native vitamin D, active vitamin D, calcium acetate, cinacalcet, lanthanum, sevelamer), (6) bicarbonate medication, and (7) antidepressants.

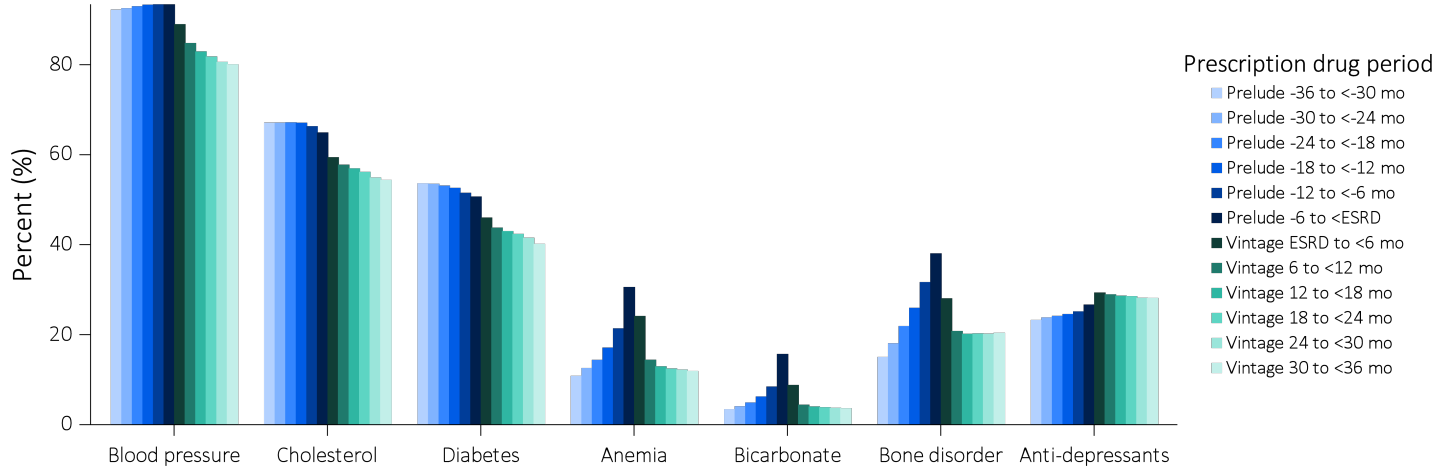
As shown in Figure 8.11, over 90% of patients were prescribed blood pressure lowering medications in the last three years of the prelude period prior to ESRD transition, and this persisted at a slightly lower rate during and throughout the post-transition or vintage period. More granular data on trends in blood pressure medication type are presented in Figure 8.12.a, where it is shown that RAAS inhibitors and loop diuretics were prescribed to over half of Veterans during the prelude time, while the use of thiazides, potassium sparing, and loop diuretics dropped dramatically after transition to ESRD.

Similarly, decreasing trends in the post-transition period were seen for cholesterol lowering drugs and diabetic medications (Figure 8.11). The decrease in diabetic medication prescriptions appears to be driven

by a drop in prescribing oral hypoglycemics in the post-transition period (Figure 8.12.b). Mineral and bone disorder medications (including phosphorous binders) were prescribed at a low rate during the prelude to ESRD, but a major surge was observed in the final prelude months immediately prior to transition to ESRD, followed by a substantial rise during the vintage period. More granular data on trends in mineral and bone disorder medication type are presented in Figure 8.12.c, which shows large surges in prescription of lanthanum and sevelamer after transition to ESRD, and that the calcimimetic agent cinacalcet was mostly prescribed in the vintage, but not prelude period.

Both anemia (ESA and iron) and bicarbonate medications had a modest surge in prescription during ESRD transition, and then rapidly declined post-transition (Figures 8.11 and 8.12.b). However, it should be noted that data on ESA, iron, and active vitamin D medication use in the vintage period after the transition to ESRD do not include these medications being administered in commercial dialysis clinics, and were therefore likely not well-captured by either the CMS or VHA databases. Finally, approximately 22% of Veterans received an antidepressant prescription during the prelude period. Antidepressant prescriptions increased slightly as patients approached ESRD transition, while rates increased approximately 3-5% to almost 30% of all Veterans in the post-transition period.

vol 1 Figure 8.11. Prescribed medication to incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015, with data up to -36 months prior to transition (prelude) and up to +36 months after transition (vintage; data were abstracted from 84,004 Veterans)



Abbreviations: ESRD, end-stage renal disease; mo, month.

vol 1 Figure 8.12. Granular prescribed medication data for incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015, with data up to -36 months prior to transition (prelude) and up to +36 months after transition (vintage; data were abstracted from 84,004 Veterans)

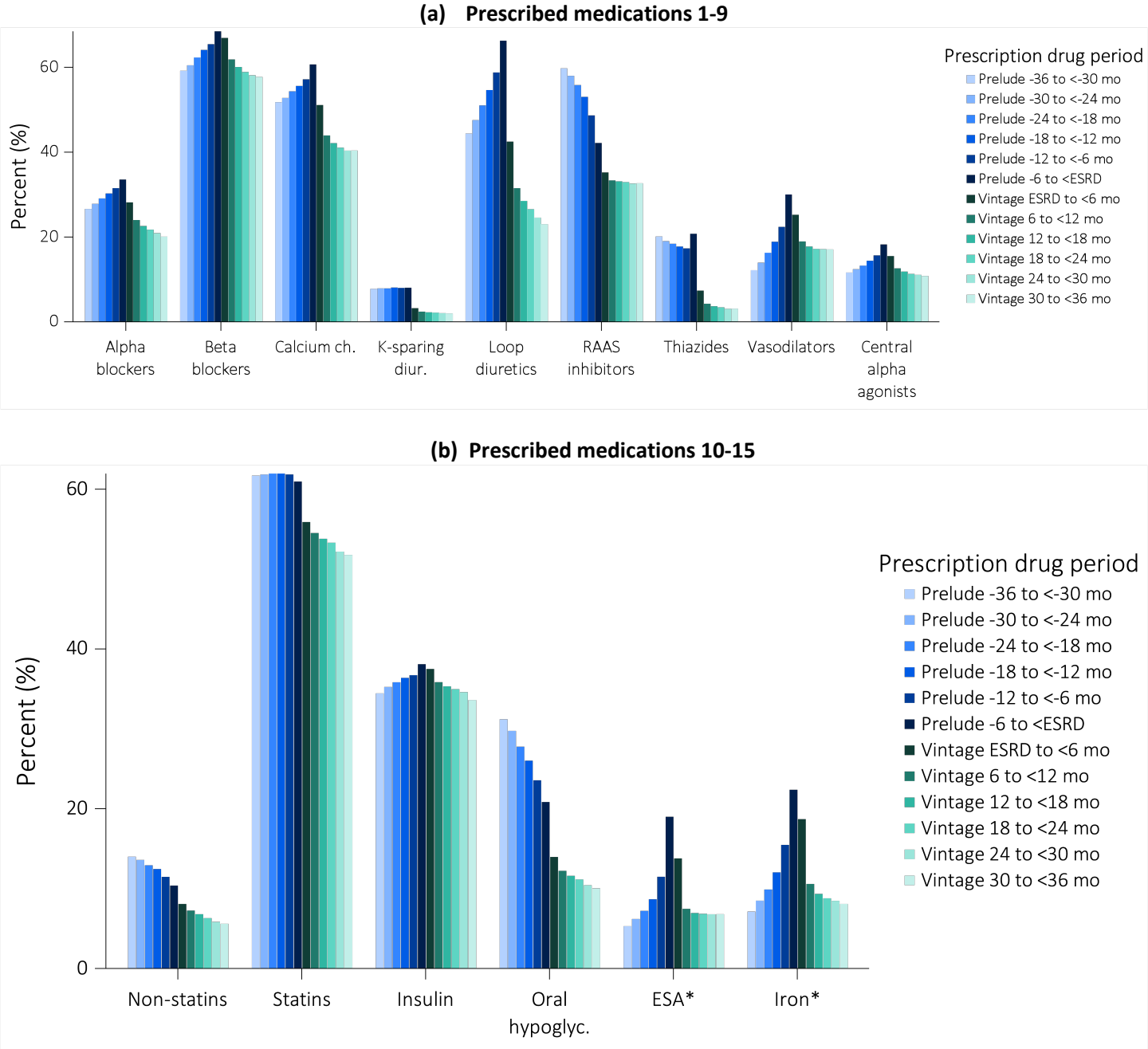
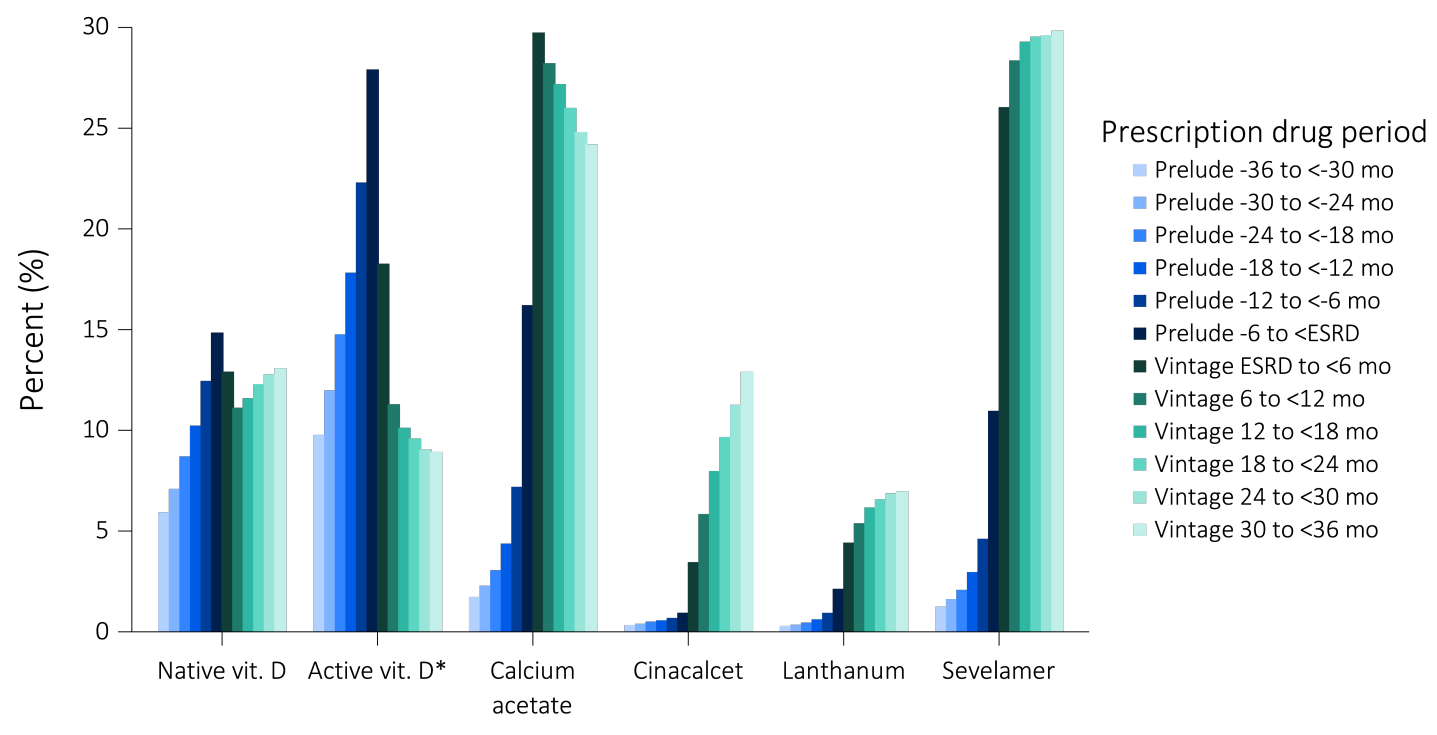


Figure 8.12 continued on next page.

vol 1 Figure 8.12. Granular prescribed medication data for incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015, with data up to -36 months prior to transition (prelude) and up to +36 months after transition (vintage) (data were abstracted from 84,004 Veterans) *(continued)*

(c) Prescribed medications 16-21



**Data on EPO, iron and active vitamin D medication use in the vintage period were affected by these medications being administered in commercial HD units, and therefore, were probably not well-captured by either CMS or VHA databases. Abbreviations: ESRD, end-stage renal disease; mo, month; Ch, channel; diur, diuretics; Hypoglyc, hypoglycemics; ESA, erythropoietin stimulating agents; and Vit, vitamin.*

HOSPITALIZATION PATTERN DURING TRANSITION TO ESRD

Data on hospitalizations for the 102,477 Veterans who transitioned to ESRD over 7.5 years (10/2007-3/2015) were collected from both inpatient and outpatient visits from VHA, CMS, and USRDS data sources. There were 89,552 patients, or 87% of all 102,477 ESRD transitioning Veterans, who were hospitalized at least once during a period of -5 years prior to (prelude) and +2 years after transition to ESRD (vintage). Table 8.4 shows a distribution of these hospitalization counts—77,709 (86%) were hospitalized during the prelude period, which includes Veterans who were hospitalized (1) only before, and (2) both before and after, transition to ESRD; and 12,453 (14%) were hospitalized only after but not before transition to ESRD. Among the Veterans who were hospitalized during the prelude period, 63% (n=48,414) were also hospitalized during transition to ESRD. Finally, of the Veterans who were hospitalized during the prelude and transition to ESRD periods, 40,690 (84%) were also hospitalized after the transition to ESRD.

vol 1 Table 8.4. Hospitalization events in 89,552 incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015

Hospitalized Prelude?	Hospitalized at time of ESRD?	Hospitalized after ESRD?
Yes N=77,709 (86%)	**Yes*** N=48,414 (63%)	**Yes** N=40,690 (84%)
		No N=7,724 (16%)
	No N=28,685 (37%)	**Yes** N=9,111 (32%)
		No N=19,574 (68%)
No N=12,453 (14%)	**Yes**** N=2,372 (19%)	**Yes** N=2,372 (100%)
		No N=0 (0%)
	No N=10,081 (81%)	**Yes** N=10,081 (100%)
		No N=0 (0%)

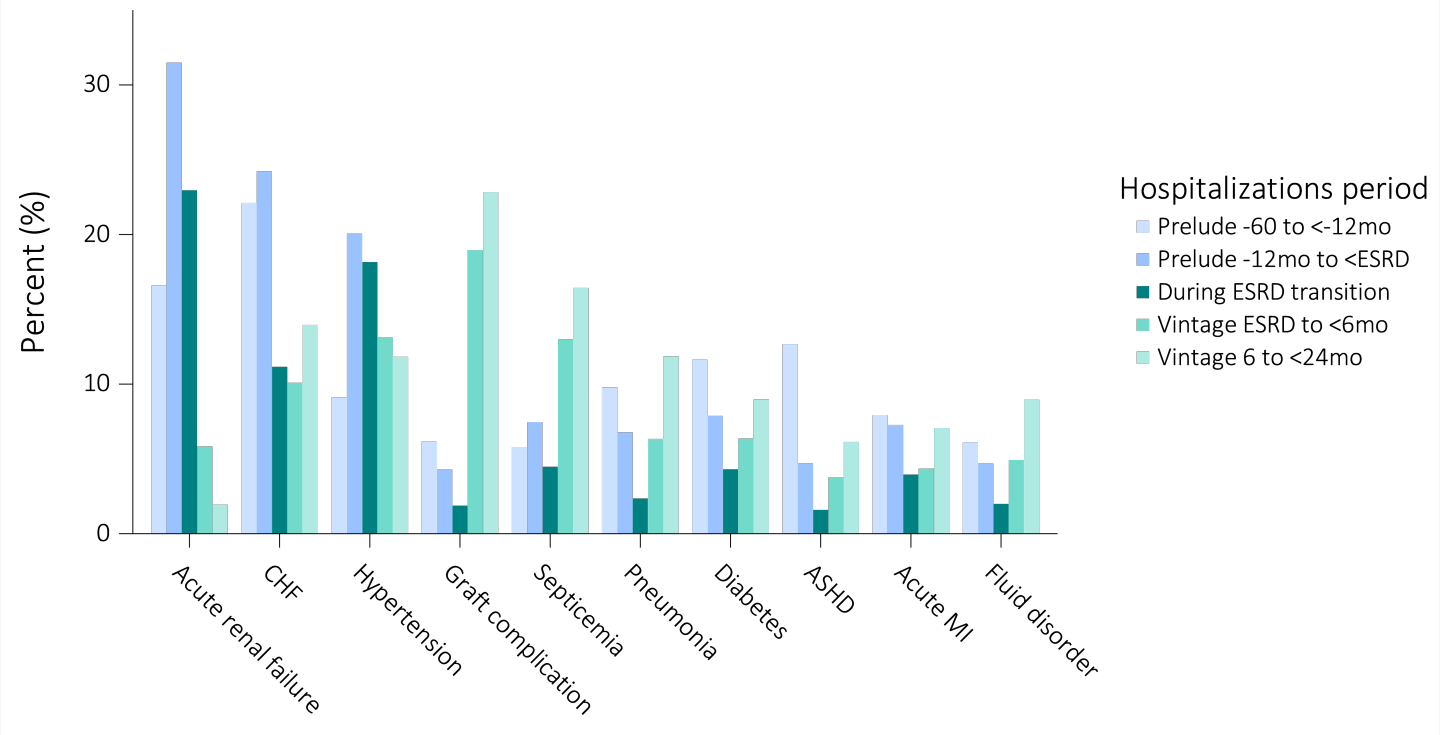
*Data source: VHA Administrative data, USRDS ESRD Database, CMS Medicare patient and Outpatient data. Data ranging from -60 months prior to transition (prelude) to +24 months after transition (vintage). *Among Veterans who were hospitalized during the transition to ESRD, included were hospitalizations that occurred (1) only during, and (2) both during and before, transition to ESRD. **Veterans who were hospitalized during the transition to ESRD were admitted only on the first day of dialysis treatment. Abbreviations: ESRD, end-stage renal disease.*

Cause-specific hospitalization events were also analyzed based on the primary diagnosis. Figure 8.13 shows the top 20 causes of hospitalization among 89,552 Veterans who transitioned to ESRD over the 7.5-year period (10/2007-3/2015), and who had at least one hospitalization event from -5 years prelude to +2 years vintage surrounding the transition intercept. These hospitalizations were then divided into five temporal categories. The two prelude periods consisted of the final 12 months of prelude, and the time prior to these 12 months, where the patient discharge day was considered as prior to the transition to ESRD. The two vintage categories were the first six months of ESRD, and thereafter, where the admission day was after transition to ESRD. The fifth time group consisted of the hospitalization that included the ESRD initiation event or preemptive kidney transplantation—any hospitalization that began in the prelude and ended in the vintage.

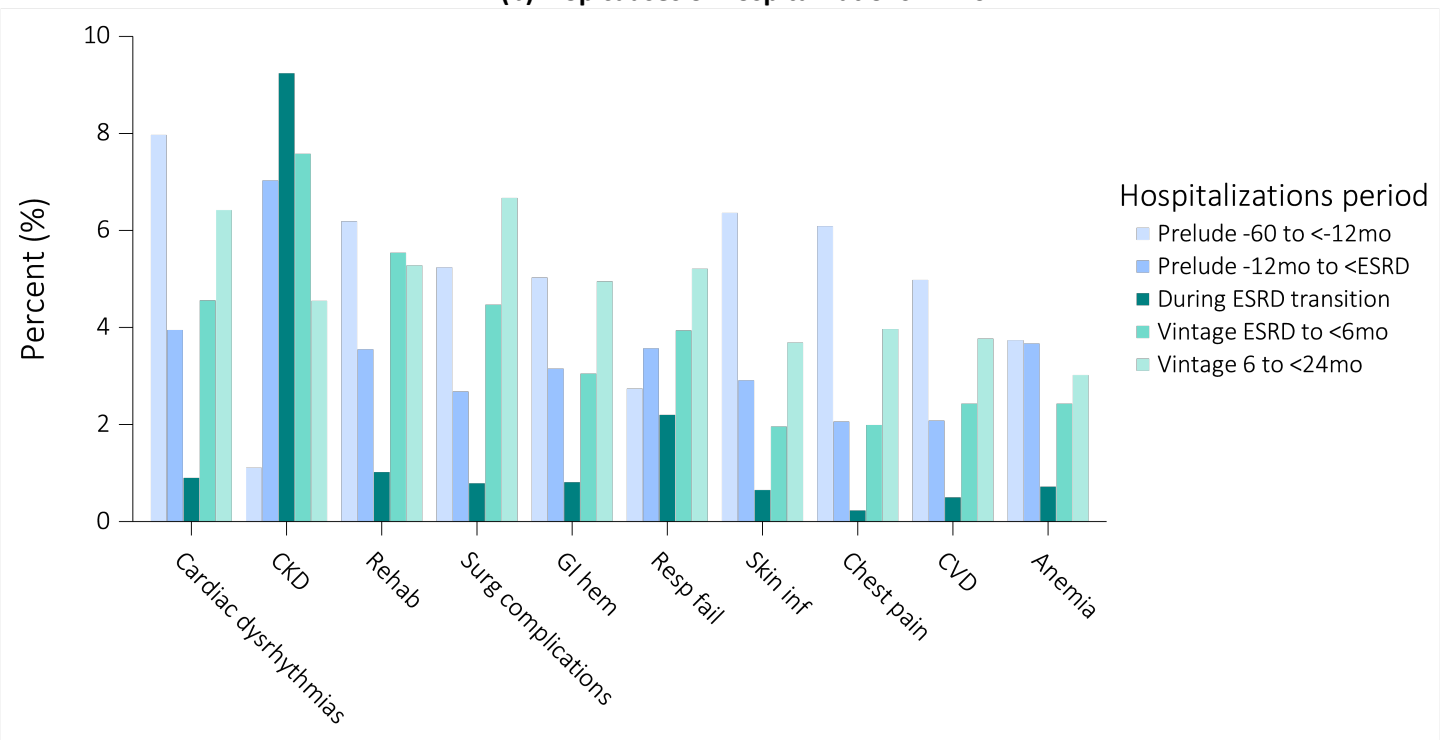
The top 20 causes of hospitalization included AKI, CHF, HTN, dialysis access complications (graft complication), septicemia, CKD, pneumonia, DM, atherosclerotic heart disease (ASHD), fluid overload (fluid disorder), acute MI, cardiac arrhythmias, rehabilitation, surgery (surgical complication), anemia, gastrointestinal (GI) hemorrhage, respiratory failure, skin infection (skin inf.), chest pain, and cerebrovascular disease (CVD). Of note, septicemia-related hospital events increased dramatically after ESRD transition. The most common causes of hospital admission that also included the ESRD transition day were AKI, HTN, CHF, and CKD.

vol 1 Figure 8.13. Top 20 causes of hospitalizations in 89,552 incident ESRD Veterans who were hospitalized at least once during the 60 months prior to ESRD transition (prelude) up to 24 months after ESRD transition (vintage).

(a) Top causes of hospitalizations 1-10



(b) Top causes of hospitalizations 11-20



Abbreviations: ASHD, atherosclerotic heart disease; CHF, congestive heart failure; CKD, chronic kidney disease; CVD, acute cerebrovascular disease; ESRD, end-stage renal disease; GI Hem, gastrointestinal hemorrhage; MI, myocardial infarction; mo, month; Resp Fail, respiratory failure; Skin Inf, skin infection; Rehab, rehabilitation; and surg, surgical.

Hospitalization events during each of the five aforementioned periods are ranked in Table 8.5. Congestive heart failure (CHF) and acute kidney injury were the most common primary reasons for hospital admission prior to ESRD transition (prelude period), whereas dialysis access complications were the most common cause after ESRD transition (vintage period). For hospitalizations that included the ESRD transition events, acute kidney injury (AKI) was the leading cause.

vol 1 Table 8.5. Ranking of the top 20 causes of hospitalization in 89,552 incident ESRD Veterans who were hospitalized at least once during the period of -60 months prior to transition (prelude) to +24 months after transition (vintage)

Cause of hospitalization	Whole cohort	Prelude 60 months to <-12 months	Prelude 12 months to <ESRD	During ESRD Transition	Vintage ESRD to <6 months	Vintage 6 months to <24 months
Acute renal failure	**1**	2	**1**	**1**	8	
Congestive heart failure	2	**1**	2	3	4	3
Hypertension	3	6	3	2	2	5
Graft complication	4	12	11	11	**1**	**1**
Septicemia	5	14	5	5	3	2
Pneumonia	6	5	8	8	7	4
Diabetes	7	4	4	6	6	6
Atherosclerotic heart disease	8	3	9	12	15	11
Acute myocardial infarction	9	8	6	7	13	8
Fluid disorder	10	13	10	10	10	7
Cardiac dysrhythmias	11	7	12	14	11	10
Chronic kidney disease	12		7	4	5	15
Rehabilitation	13	10	15	13	9	12
Surgical complications	14	15	19	16	12	9
Gastrointestinal hemorrhage	15	16	16	15	16	14
Respiratory failure	16		14	9	14	13
Skin infection	17	9	17	18		18
Chest pain	18	11				16
Acute cerebrovascular disease	19	17			19	17
Anemia	20		13	17	20	
Chronic obstructive pulmonary		18	18			20
Urinary tract infection		19	20		18	
Osteoarthritis		20				
Other circulatory disease					17	19
Cancer of kidney and renal pelvis				19		
Aortic; peripheral; and visceral artery aneurysms				20		

Data source: VHA Administrative data, USRDS ESRD Database, CMS Medicare Inpatient and Outpatient data.

Trends during Prelude Period (Prior to ESRD Transition)

Selected prelude (pre-ESRD) trends in laboratory data for up to five years prior to transition are shown below. Figure 8.14 shows the pre-ESRD trend in average blood hemoglobin in 55,329 Veterans who transitioned to ESRD over 20 quarters, or five years. Mean blood hemoglobin dropped from 13 g/dL to below 11 g/dL over the prelude period of progression from CKD to ESRD.

vol 1 Figure 8.14. Trend in blood hemoglobin level during the prelude (pre-ESRD) time over 20 quarters in 55,329 Veterans who later transitioned to ESRD during 10/1/2007-3/31/2015.

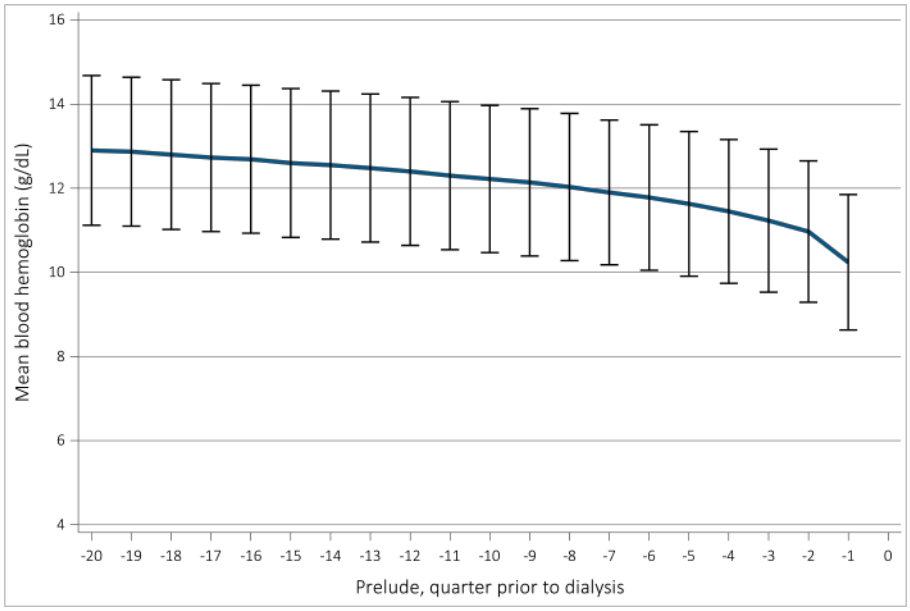


Figure 8.15 shows the pre-ESRD trend in averaged serum phosphorus in 29,362 Veterans who transitioned to ESRD over 36 months or three years. Serum phosphorus increased from 4 to above 5.5 mg/dL immediately prior to transition to ESRD.

vol 1 Figure 8.15. Trend in serum phosphorus level during the prelude (pre-ESRD) time over 36 months in 29,362 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

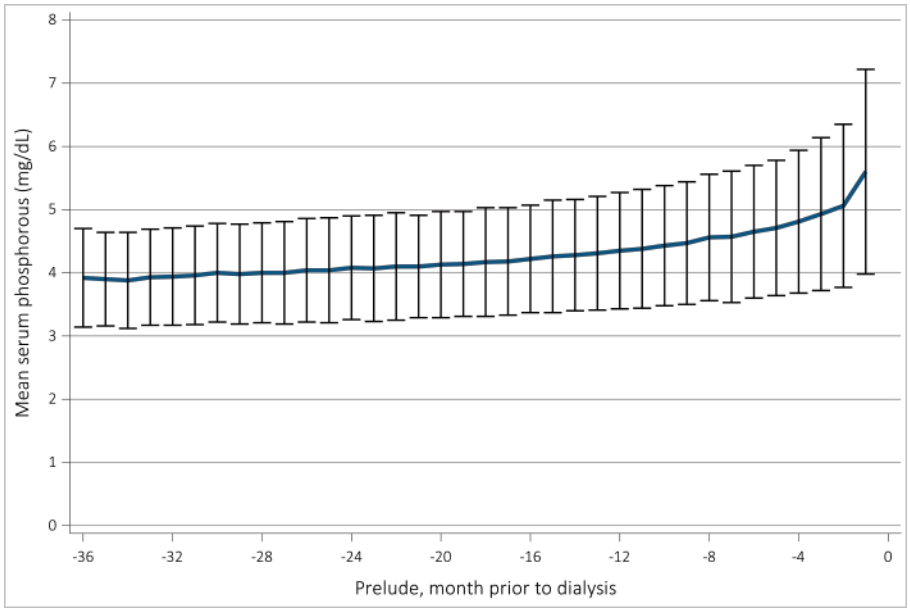
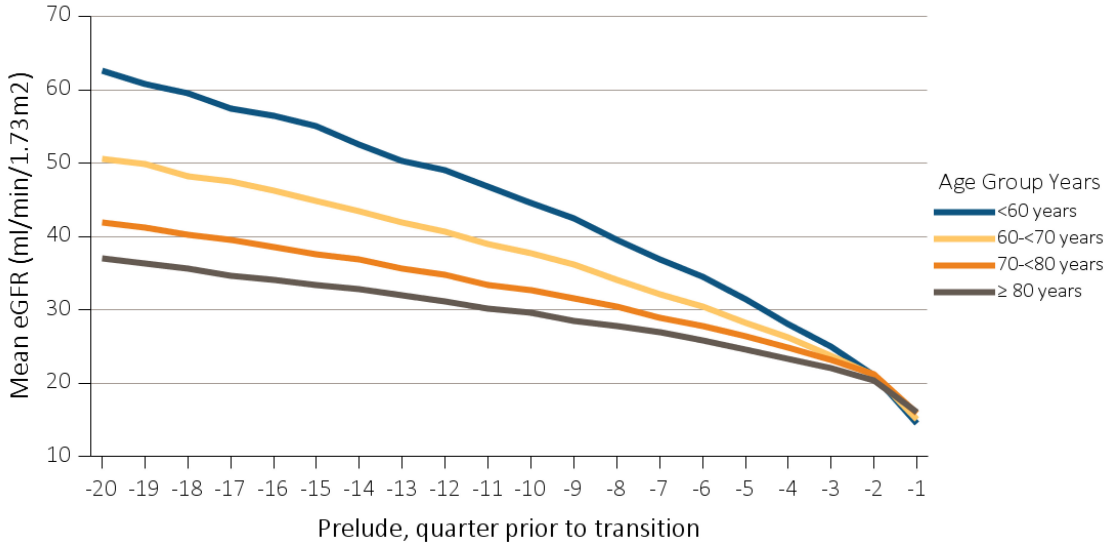


Figure 8.16 shows the pre-ESRD trends in average eGFR calculated by the CKD-EPI creatinine equation over 20 quarters (five years) for 57,615 Veterans who transitioned to ESRD, stratified by age and cause of ESRD. Figure 8.16.a shows that CKD patients who transitioned at an older age had a slower rate of progression than younger patients. Figure 8.16.b suggests that those with DM as a cause of ESRD had a faster CKD progression.

vol 1 Figure 8.16. Trends in eGFR during the prelude (pre-ESRD) time over 20 quarters in 57,615 Veterans who transitioned to ESRD during 10/1/2007-9/31/2015. (a) Stratified by age at incidence,(b) Stratified according to ESRD etiology

(a) Prelude eGFR stratified by age at incidence



(b) Prelude eGFR stratified according to ESRD etiology

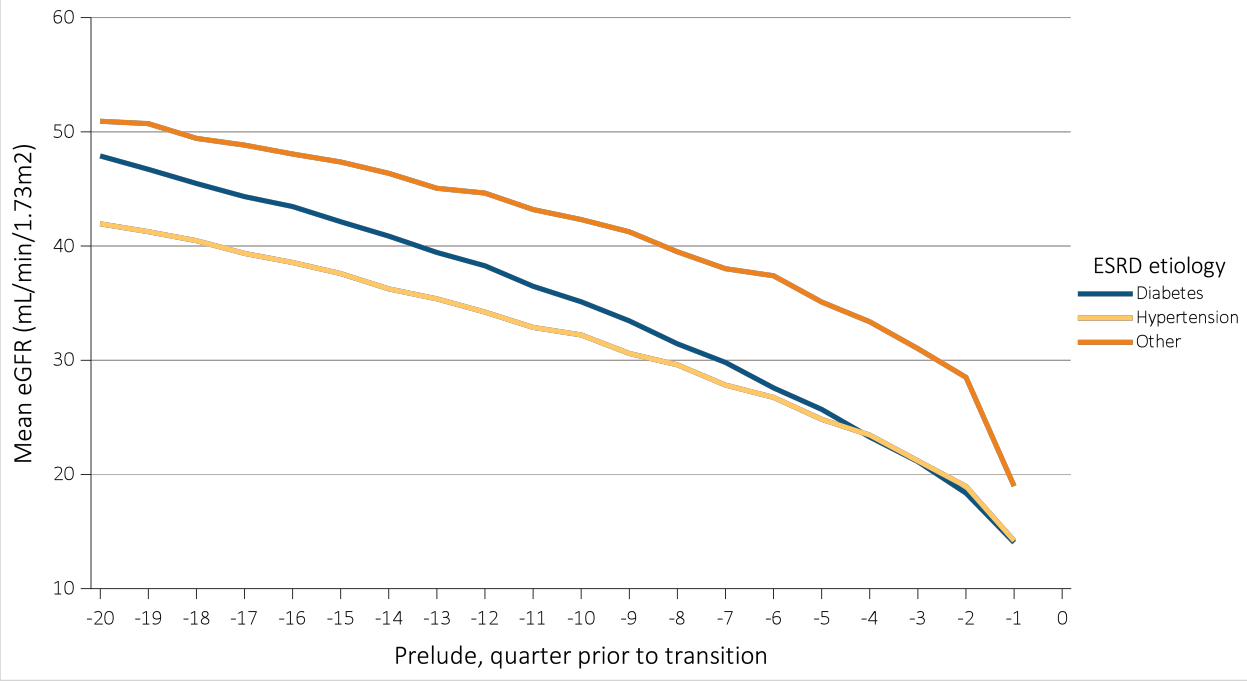
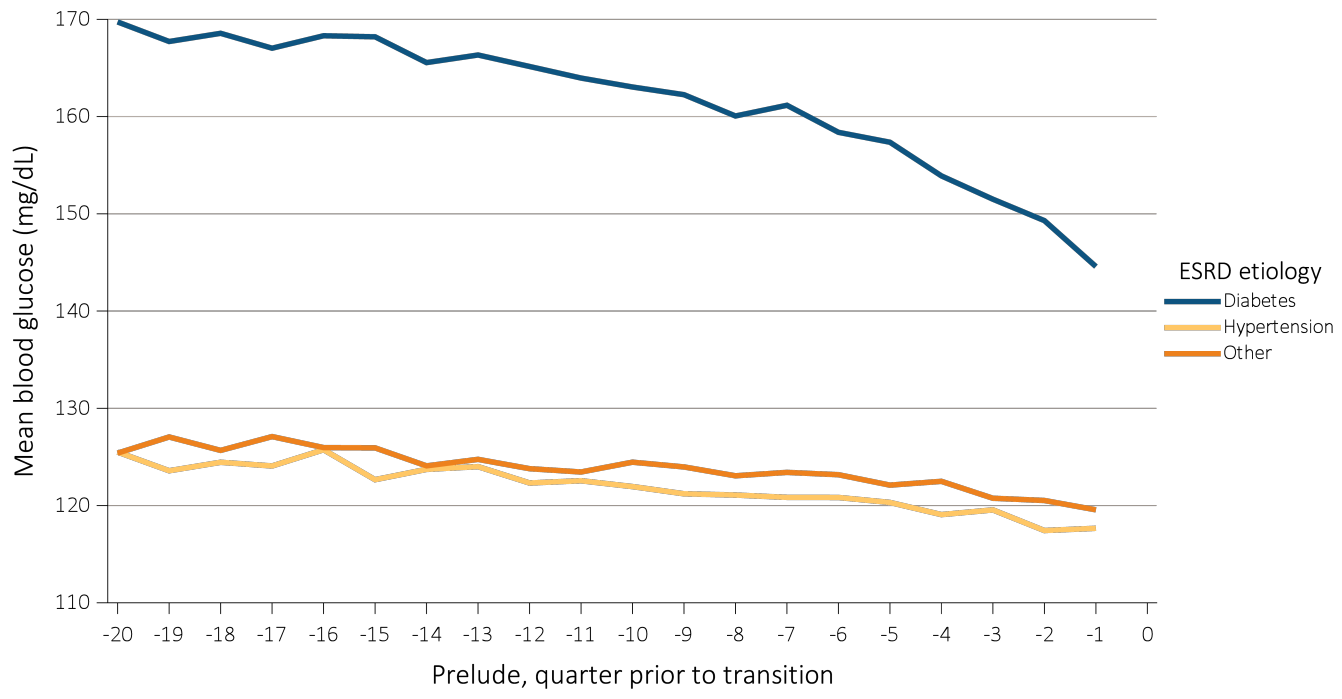


Figure 8.17 shows the pre-ESRD trend in glucose level by ESRD reason for 57,267 Veterans who transitioned to ESRD over 20 quarters, or five years. Patients whose ESRD was due to DM appeared to exhibit a gradual fall in serum glucose levels over time, as their CKD progressed to ESRD. Blood glucose levels did not change among patients whose ESRD was not due to DM.

vol 1 Figure 8.17. Trend in blood glucose level during the prelude (pre-ESRD) time over 20 quarters in 57,267 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

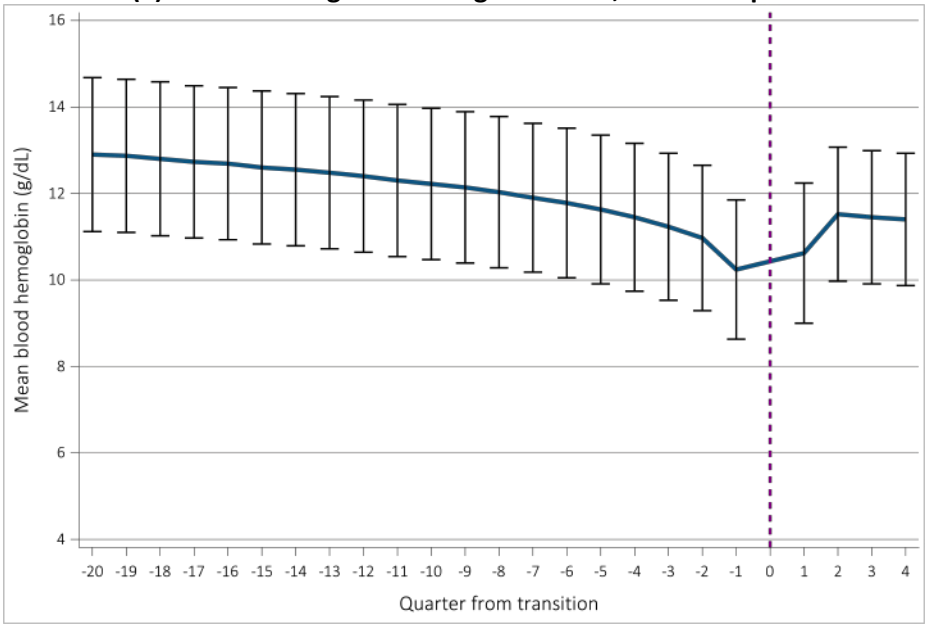


Comparing Laboratory Trends during Prelude (prior to ESRD Transition) and Vintage Periods (after ESRD Transition)

The changes in clinical and laboratory values that occur when a patient with non-dialysis dependent CKD transitions to RRT are not well understood. Hence, in this year's TC-CKD chapter, we have compared trends in select relevant measures between the prelude and vintage periods. Figure 8.18 shows the pre- and post-ESRD trends in average blood hemoglobin levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and four quarters (N=58,281), respectively, and (b) over eight quarters each (N=54,526). In Figure 8.18.a, mean blood hemoglobin dropped from 13 g/dL to almost 10 g/dL over the prelude period (-20 quarters), then increased from above 10 g/dL to less than 12 g/dL over the vintage period (+4 quarters). Figure 8.18.b shows that blood hemoglobin dropped from 12 g/dL to almost 10 g/dL over the prelude period (-8 quarters), and then increased from above 10 g/dL to a steady level below 12 g/dL over the vintage period (+8 quarters).

vol 1 Figure 8.18. Pre- and post-ESRD trends in average blood hemoglobin levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=58,281), and (b) 8 quarters each (N=54,526).

(a) Blood hemoglobin during transition, -20 to +4 quarters



(b) Blood hemoglobin during transition, -8 to +8 quarters

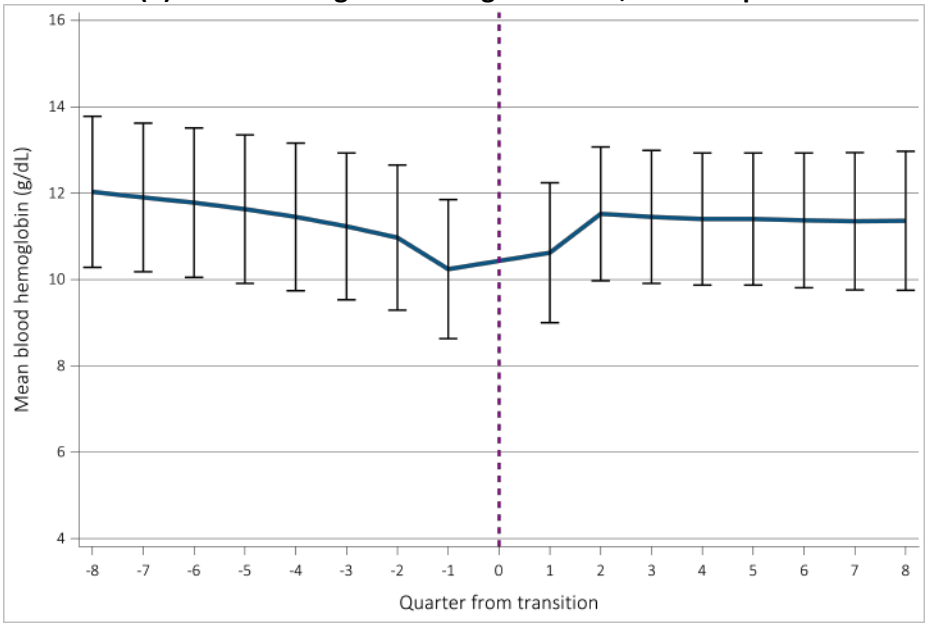


Figure 8.19 shows the pre- and post-ESRD trends in average sodium levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=60,372), and 8 quarters each (N=56,729), respectively. Figure 8.19.a shows that mean sodium levels remained relatively steady at around 139 g/dL over the prelude period (-20 quarters), and then dropped to 138 g/dL in the vintage period (+4 quarters). In Figure 8.19.b, mean sodium levels remained at a steady average above 139 g/dL over the prelude period (-8 quarters) and then dropped to a steady average of 138 g/dL over the vintage period (+8 quarters).

vol 1 Figure 8.19. Pre- and post-ESRD trends in average sodium levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=60,372) and (b) 8 quarters each (N=56,729).

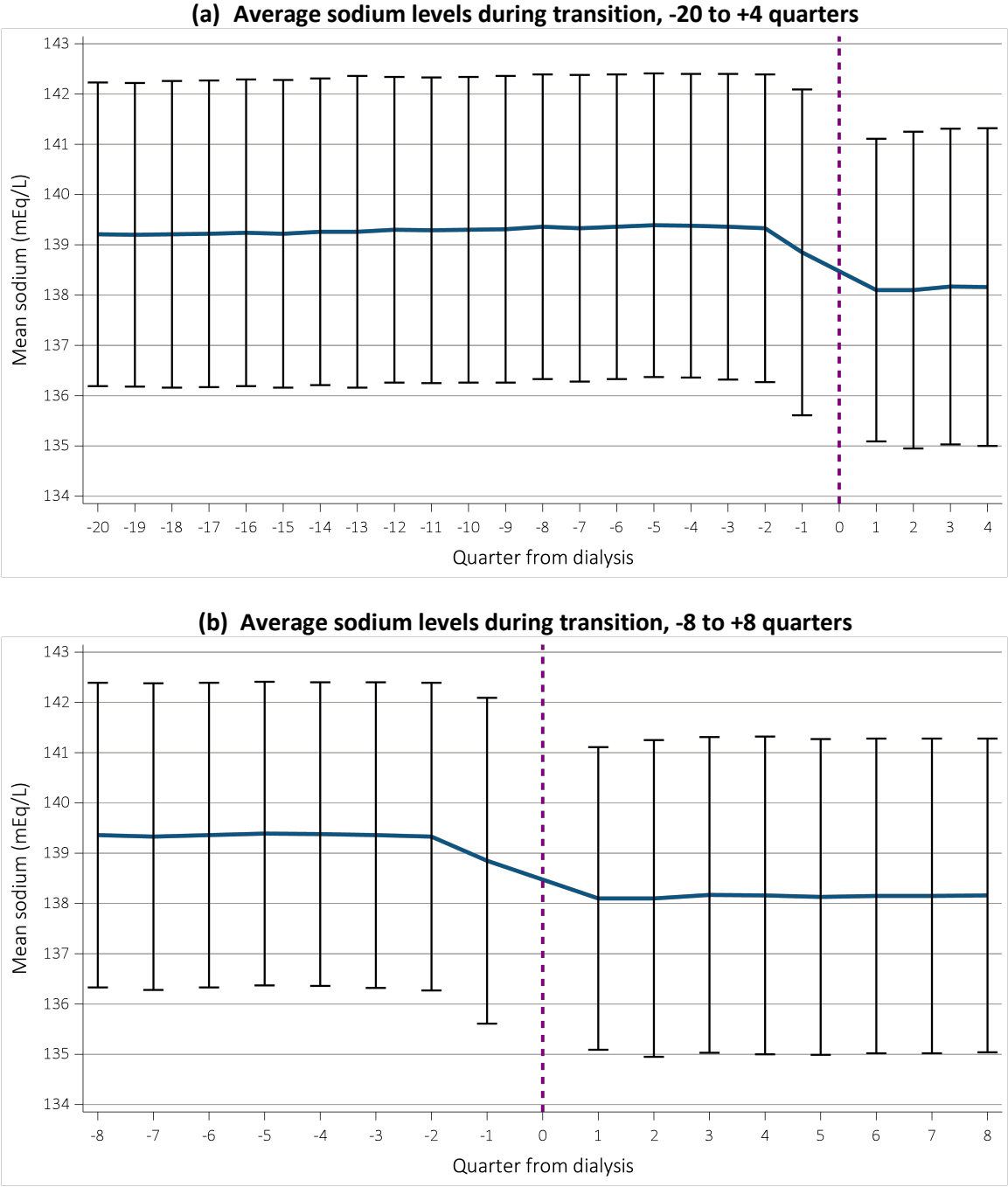
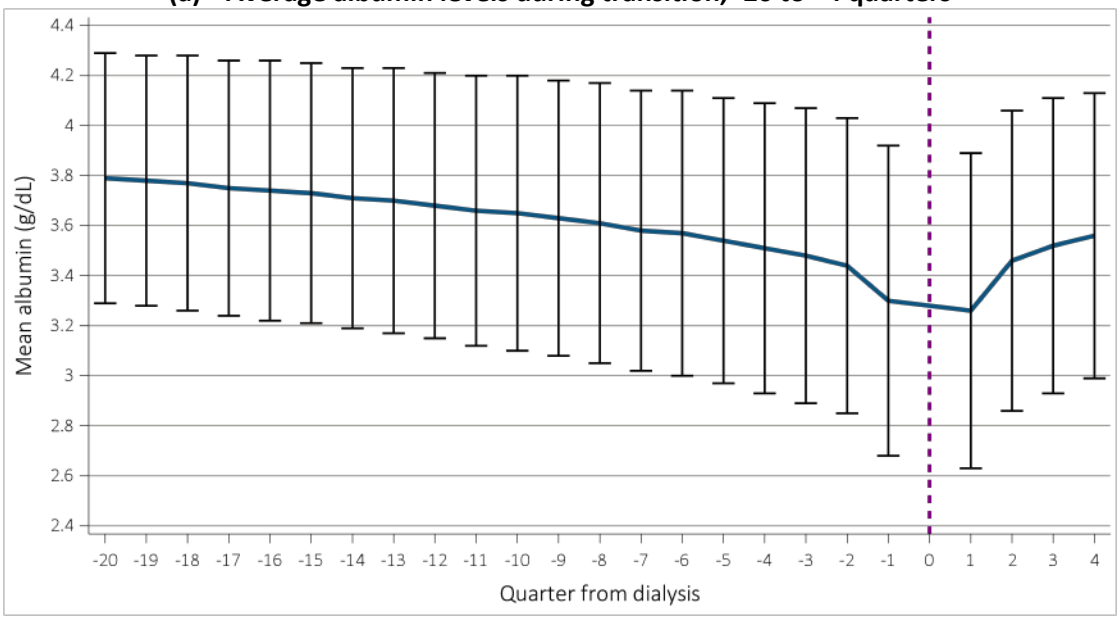


Figure 8.20 shows the pre- and post-ESRD trends in average albumin levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=57,277), respectively, and (b) 8 quarters each (N=53,634), respectively. In Figure 8.20.a, mean albumin levels declined from 3.8 g/dL to less than 3.4 g/dL over the prelude period (-20 quarters), and then increased to almost 3.6 g/dL in the vintage period (+4 quarters). Figure 8.20.b shows that mean albumin levels decreased from 3.6 g/dL to less than 3.4 g/dL over the prelude period (-8 quarters), and then returned to a starting pre-ESRD level of 3.6 g/dL over the vintage period (+8 quarters).

vol 1 Figure 8.20. Pre- and post-ESRD trends in average albumin levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=57,277) and (b) 8 quarters each (N=53,634).

(a) Average albumin levels during transition, -20 to +4 quarters



(b) Average albumin levels during transition, -8 to +8 quarters

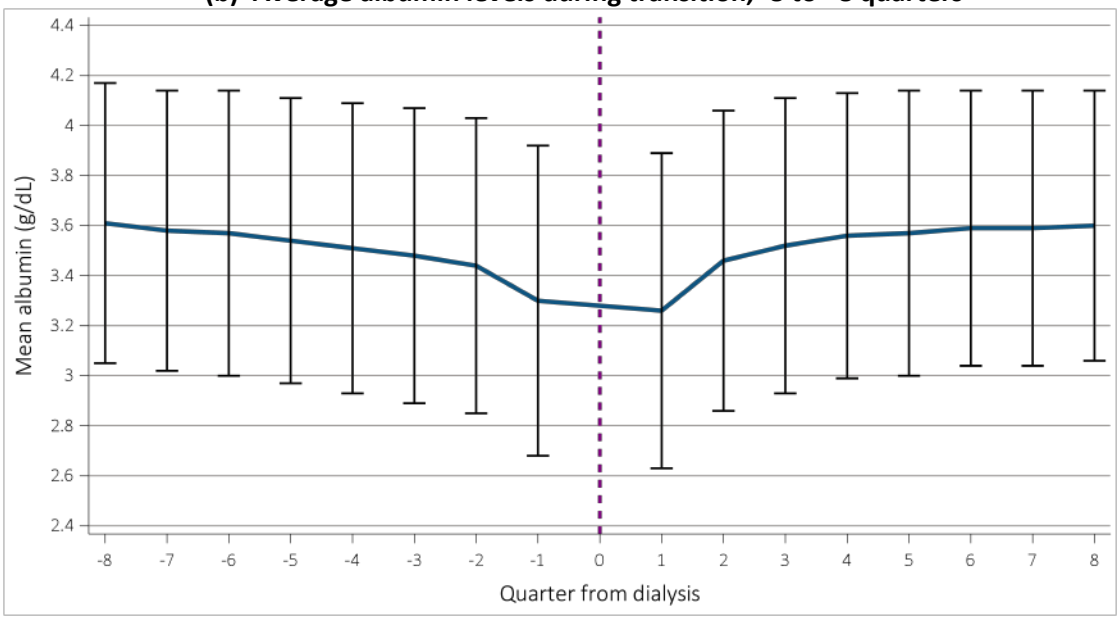
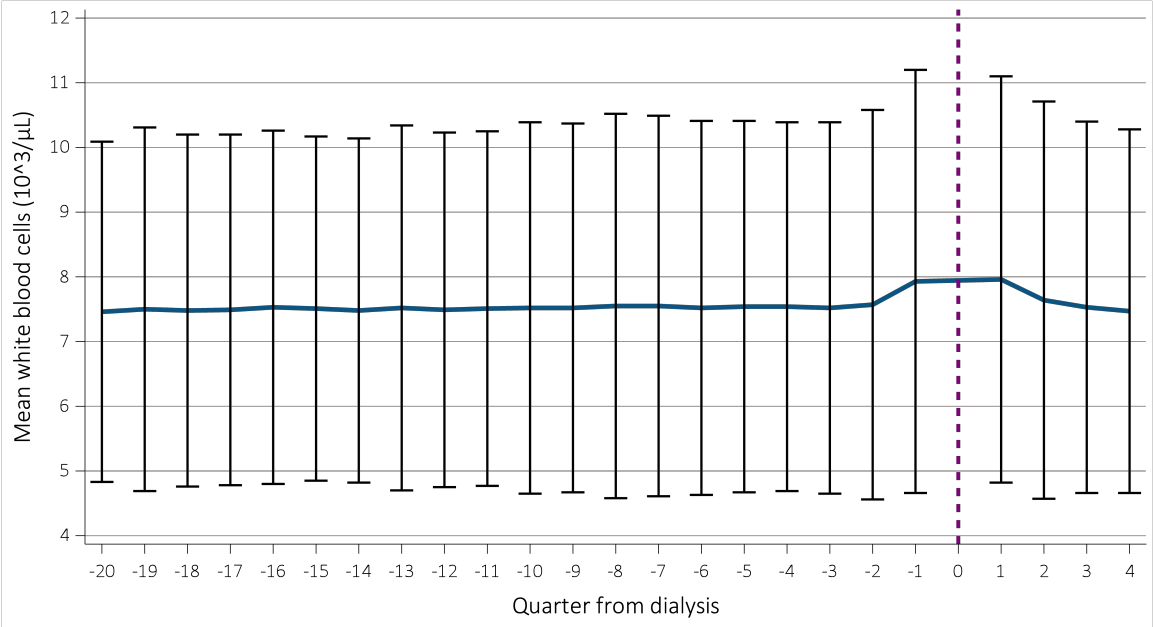


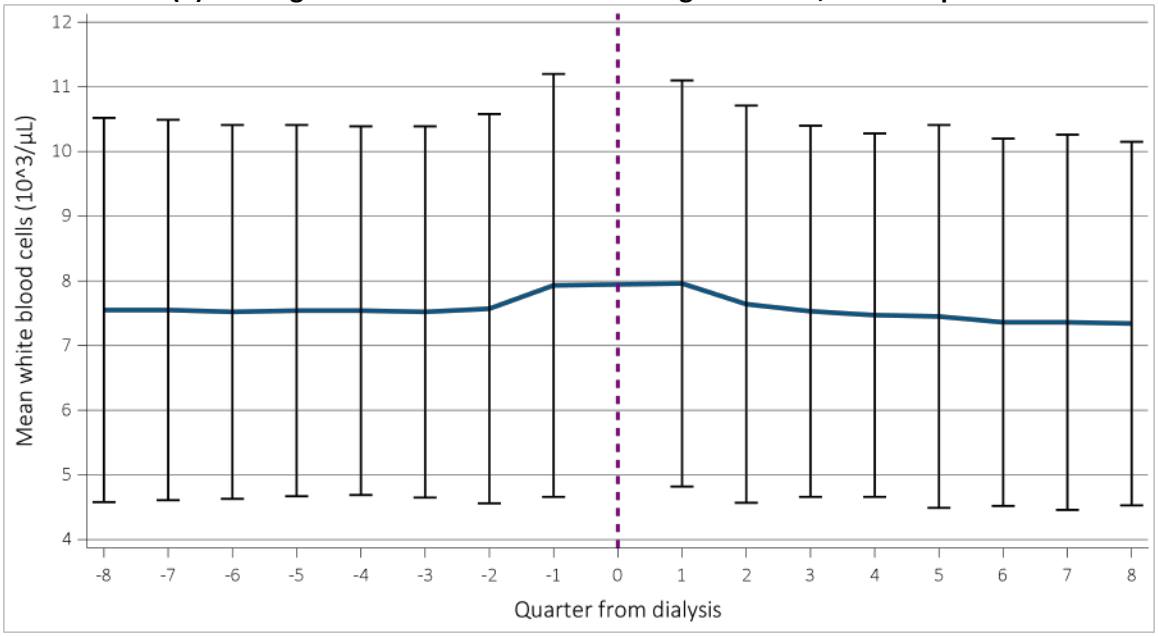
Figure 8.21 shows the pre- and post-ESRD trends in average white blood cells counts (an indirect surrogate of inflammatory conditions) in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=58,322), and (b) 8 quarters each (N=54,811). In Figure 8.21.a, mean white blood cell levels remained consistent at 7.5 103/μL, but increased to 8.0 103/μL over the 20 quarters prior to transition to ESRD, and then returned to pre-ESRD levels over the 4 quarters after transition to ESRD. Figure 8.21.b shows that mean white blood cells levels remained steady at 7.5 103/μL, but increased to 8.0 103/μL over the 8 quarters prior to transition to ESRD, and then returned to slightly lower than pre-ESRD levels over the 8 quarters after transition to ESRD.

vol 1 Figure 8.21. Pre- and post-ESRD trends in average white blood cells levels in Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over (a) 20 and 4 quarters (N=58,322) and (b) 8 quarters each (N=54,811).

(a) Average white blood cells levels during transition, -20 to +4 quarters



(b) Average white blood cells levels during transition, -8 to +8 quarters



Vol 1 Figure 8.22. Pre- and post-ESRD trends in blood glucose levels by ESRD-reason for (a) 60,103 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over 20 and 4 quarters, and (b) 56,455 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 over 8 quarters in each period.

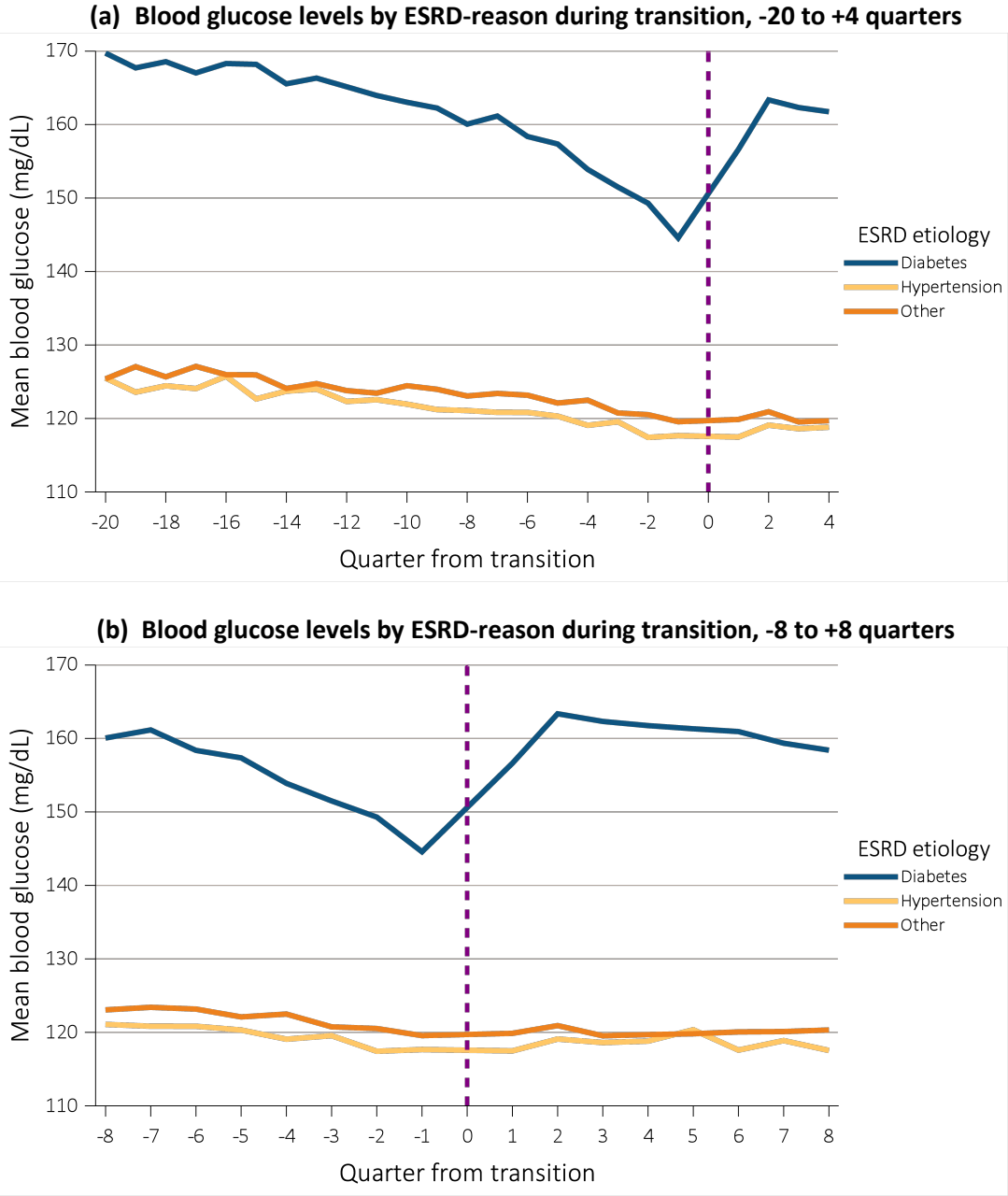


Figure 8.23 shows the pre- and post-ESRD trends in averaged serum phosphorus in 33,739 Veterans who transitioned to ESRD during 10/1/2007 to 3/31/2015 over 36 months or three years and 12 months or one year. Serum phosphorus increased from 4.0 to above 5.5 mg/dL immediately prior to transition to ESRD, and decreased to a steady level below 5.0 mg/dL after transition to ESRD.

vol 1 Figure 8.23. Trend in mean serum phosphorus level during the prelude (pre-ESRD) and vintage (post-ESRD) times over 36 and 12 months, in 33,739 Veterans who transitioned to ESRD during 10/1/2007-3/31/2015.

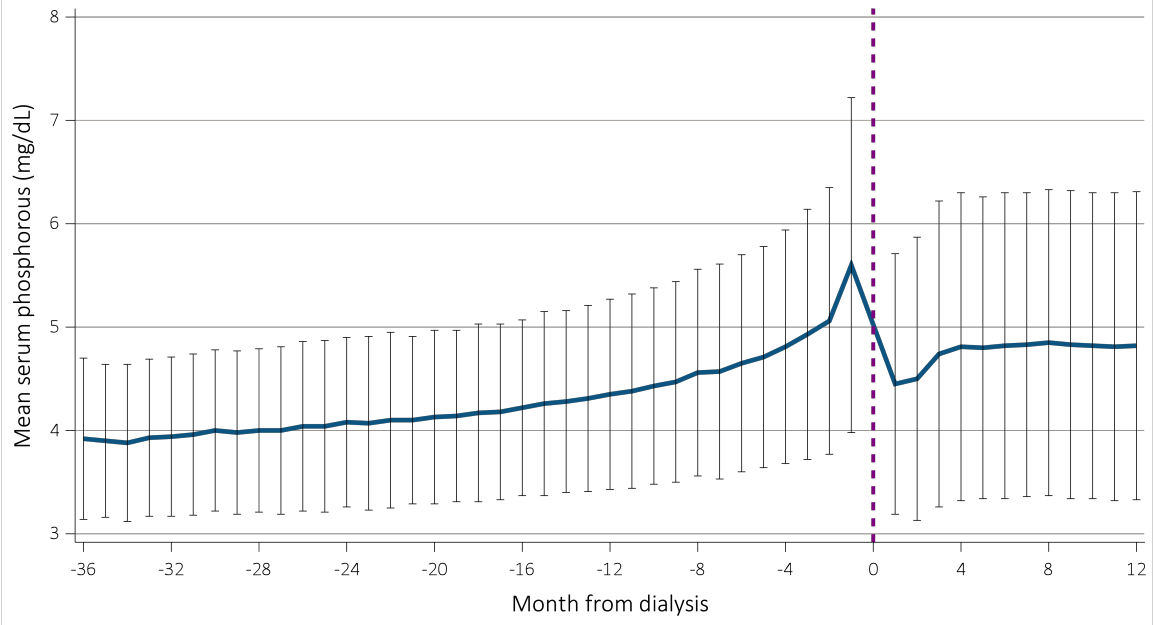
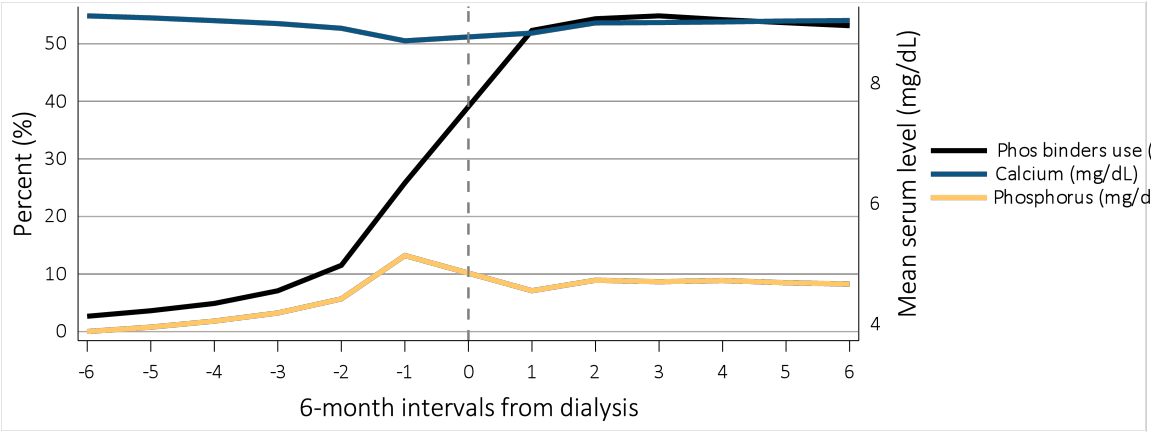


Figure 8.24 shows the trends in prescribed phosphorus binders, mean serum phosphorus level, and mean serum calcium level for incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 (N=84,004; N=37,789; and N=60,007), with data up to -36 months prior to transition (prelude) and up to +36 months after transition (vintage). The use of phosphorus binders starts to increase rapidly about a year before transition to ESRD and continues to climb for up to a year after transition. Concurrently, as the use of phosphorous binders increases surrounding the time of transition, serum phosphorus levels decrease and serum calcium levels rise.

Vol 1 Figure 8.24. Trends in prescribed phosphorus binders, mean serum phosphorus level and mean serum calcium level for incident ESRD Veterans who transitioned to ESRD during 10/1/2007-3/31/2015 (N=84,004; N=37,789; and N=60,007), with data up to -36 months prior to transition (prelude) and up to +36 months after transition (vintage).



Each unit on the x-axis represents a 6-month interval. Negative signs represent time prior to transition to dialysis, and positive signs represent time after transition to dialysis.Abbreviations: phos, phosphorus.

Data from Kaiser Permanente of Southern California

California is the most populous (38 million) and racially/ethnically diverse U.S. state. Southern California (SC) is the most populous mega-region of California with 23 million people (60% of California's population), and bears four of the nation's 50 most populated cities (Los Angeles, San Diego, Fresno, and Long Beach). It encompasses the Los Angeles Metropolitan region, including the >17 million people in Los Angeles and Orange Counties combined, and is the fifteenth largest economy in the world. In addition to substantial socioeconomic diversity, SC has remarkable racial/ethnic diversity that is reflective among the Kaiser Permanente Southern California member population.

Kaiser Permanente Southern California (KP-SC), the largest Kaiser Permanente region, is an integrated health care system that provides comprehensive health services for over 4.2 million members. Table 8.6 displays demographic characteristics of the KP-SC member population compared to the 2010 U.S. census and California populations. The KP-SC member population, like the California-specific total population, has greater racial/ethnic diversity as compared to the nation. The proportion of Hispanic patients at KP-SC matches that of the California-specific total population. KP-SC also has a larger proportion of non-Hispanic Black, and a smaller proportion of non-Hispanic Asian patients than the California-specific total population. The proportion of males to females and distribution by age appears similar to both the U.S. census and California populations.

vol 1 Table 8.6. Demographic characteristics of the Kaiser Permanente Southern California member population compared to the 2010 U.S. census and California populations

	KPSC (%)	U.S. census 2010 (%)	California 2010 (%)
Sex			
Male	48.2	49.2	49.7
Female	51.8	50.8	50.3
Age			
Under 5 years	5.8	6.5	6.8
5-17 years	19.1	17.5	18.6
18 to 24 years	8.7	9.9	10.5
25 to 44 years	26.1	26.6	28.2
45 to 64 years	28.2	26.4	24.9
65 years and over	12.1	13.0	11.4
Ethnicity			
Hispanic	37.6	16.3	37.6
Non-Hispanic	53.0	83.7	62.4
Unknown	9.4	^	^
Race			
White	47.7	76.2	40.1
Black/African American	9.8	14.6	5.8
American Indian/Alaska Native	0.4	0.9	0.4
Asian	9.1	5.6	12.8
Native Hawaiian/Pacific Islander	1.0	0.2	0.3
Other/Multirace	5.1	2.5	2.8
Unknown	26.3	^	^

Data source: Kaiser Permanente Southern California Electronic Health Records, U.S. Census Bureau. Active KPSC Members (all medical centers) on June 30, 2010. Abbreviations: KPSC, Kaiser Permanente Southern California; US, United States. ^Data not available.

Transition to ESRD in Kaiser Permanente of Southern California

The Kaiser Permanente transition to ESRD (TC-CKD) database is maintained by the KP-SC Renal Business Group, in which all members undergoing dialysis or transplantation were tracked through the health system's Renal Program, and regularly reconciled with internal dialysis unit census and outside claims. Patients' demographic information—including race, ethnicity, sex, and zip code—were linked to the KP-SC Membership and Benefit Research Data Warehouse created by the Research and Evaluation (R&E) Department. This mainly relies on four KP systems: the Operational Data Store (ODS), HealthConnect (HC), the Enhanced Prenatal Services System (PSS), and the Membership Extract Enrollment Management (MXEM) files. Other data such as socioeconomic information (education and household income) were collected from the KP-SC Geocoding database created by the R&E Department, in which three sources, including the U.S. Census, Claritas (i.e. Nielsen) and American Community Survey (ACS) five-year summary were combined. Mortality data of the ESRD population were obtained from the KP-SC Mortality database, which combines multiple data sources, including the California State Death Master Files, California State Multiple Cause of Death Master Files (MCOD), Social Security Administration (SSA) Death Master Files, KP-SC Hospital and Emergency Room (ER) records, KP-SC Membership System, Perinatal Data Mart (PDM), and Outside Claims Processing System (OCPS).

Over the eight years between 01/01/2007 and 12/31/2014, 9,260 KP-SC members transitioned to ESRD, i.e. dialysis and transplant patients. Crude and adjusted incidence rates are shown in Table 8.7. KP-SC incidence rates were lower than the U.S. general population, likely due to several different factors. These include an earlier and more standardized comprehensive delivery of care for the CKD population, and a population that may have been comprised of a larger proportion of people who were healthier and employed. KP-SC members were 62.6 ± 14.6 years old (mean ± SD) and included 5,382 (58.1%) men and 3,878 (41.9%) women. Race/ethnic groups included non-Hispanic whites (2,750, 29.7%), Blacks (1,936, 20.9%), Asians (939, 10.1%), Hispanics (3,356, 36.2%), American Indians or Alaska Natives (19, 0.2%), Native Hawaiians or Pacific Islanders (129, 1.4%) and those of other race (64, 0.7%). According to KP-SC Renal Program records, the cause of ESRD was DM in 4,870 (52.6%) patients and HTN in 1,694 (18.3%). At transition to ESRD, 7,771 (83.9%) started on in-center HD, 1,236 (13.3%) started on PD (continuous ambulatory PD and continuous cycling PD), and 27 (0.3%) started on home HD. Among 7,798 patients starting on HD at transition, arteriovenous (AV) fistula was used in 2,875 (36.9%) and AV graft was used in 269 (3.4%) patients for initial dialysis access. Pre-emptive transplant occurred in 174 (1.9%) cases at transition. During the first three months, 455 (5.0%) of all incident dialysis patients died.

vol 1 Table 8.7. Crude and age- and sex-adjusted incidence rates among Kaiser Permanente Southern California members who transitioned to ESRD between 1/1/2007 and 12/31/2014

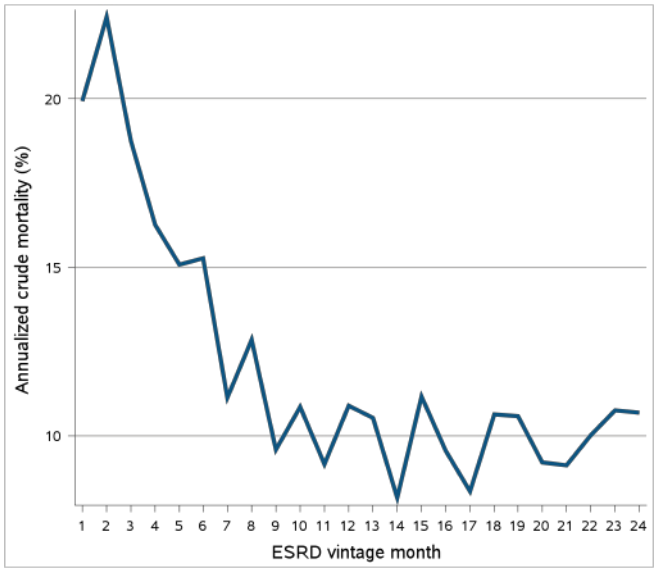
	Number of incident ESRD patients	Number of KP-SC members	Crude incidence/ 1,000,000 person years	Age-, Sex-adjusted incidence/1,000,000 person years
2007	1,122	3,183,804	352.4	379.9
2008	1,101	3,200,101	344.1	362.2
2009	1,233	3,216,209	383.4	397.9
2010	1,218	3,247,766	375.0	381.3
2011	1,124	3,387,552	331.8	336.0
2012	1,102	3,485,161	316.2	314.4
2013	1,139	3,551,617	320.7	310.9
2014	1,221	3,667,316	332.9	317.2

Data source: Kaiser Permanente Southern California Electronic Health Records, U.S. Census Bureau. The United States census 2010 was used as the standard population. Abbreviations: ESRD, end-stage renal disease; KP-SC, Kaiser Permanente Southern California.

Outcomes of Kaiser Permanente Southern California Patients who transitioned to ESRD

The annualized mortality rates among the 9,086 incident dialysis patients over the first 24 months of the vintage period are depicted in Figure 8.25. The higher mortality rates in the first several months bear resemblance to that observed among Veterans with incident ESRD and the U.S. ESRD population overall. Among patients dying early (two months after ESRD transition), 38.3% were hospitalized for AKI six months prior to ESRD transition compared to 19.4% who survived at least 12 months. Congestive heart failure was a primary cause of hospitalization six months prior to ESRD transition among the 27.0% of patients who died at two months compared to 11.4% who were alive more than 12 months. Table 8.8 shows the comparison of hospitalizations for CHF and AKI.

vol 1 Figure 8.25. Annualized unadjusted mortality of the 9,086 incident dialysis patients who transitioned to ESRD during 1/1/2007-12/31/2014 and were followed for up to 24 months



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease.

vol 1 Table 8.8. Comparison of hospitalizations for congestive heart failure and acute kidney injury for incident dialysis patients who died at two months vs. alive more than 12 months after ESRD transition

	Patients died at two months (N=167)	Patients survived more than 12 months (N=7,864)
	N (%)	N (%)
Primary cause of hospitalization in 6 months prior to ESRD transition		
Congestive heart failure	45 (27.0)	893 (11.4)
Acute kidney injury	64 (38.3)	1529 (19.4)
Hospitalization related diagnosis in 6 months prior to ESRD transition		
Congestive heart failure	95 (56.9)	2179 (27.7)
Acute kidney injury	134 (80.2)	3155 (40.1)

Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease.

TC-CKD Comorbidity Data prior to ESRD Transition at Kaiser Permanente Southern California

The comorbidity data for the prelude period were created from the KP-SC utilization database, which stores comprehensive patient diagnosis and procedure information from 1981 to the present. Pre-existing co-morbidities were determined by ICD-9-CM documentation in records from inpatient or outpatient settings in the three years prior to transition to ESRD. Among the top five comorbid conditions seen in Figure 8.26.a, more than 65% of the 9,086 incident dialysis patients at KP-SC had DM with or without complications. Over a third of the ESRD patients had peripheral vascular disease or myocardial infarction. Cancer affected 11% of the ESRD patients.

A macro originally developed at Manitoba Centre for Health Policy (MCHP) website was used to estimate Charlson Comorbidity Index (CCI) scores as shown in Figure 8.26.b. A revised, weighted CCI score that excluded renal disease was calculated according to the formula below:

CCI = 1* Myocardial Infarction + 1* Congestive Heart Failure + 1* Peripheral Vascular Disease + 1* Cerebrovascular Disease + 1* Dementia + 1* Chronic Pulmonary Disease + 1* Rheumatic Disease + 1* Peptic Ulcer Disease + 1* Mild Liver Disease + 1* Diabetes without chronic complications

+ 2* Diabetes with chronic complications + 2* Paraplegia or Hemiplegia + 2* Any Cancer

+ 3* Moderate or Severe Liver Disease

+ 6* Metastatic Carcinoma + 6*AIDS/HIV

The mean CCI was 4.1 ± 2.1 and 0.4% had a CCI of 10 or greater. The mean weighted CCI was slightly greater, 5.4 ± 2.6, and 5.6% of the persons with weighted CCI had a CCI of 10 or greater.

vol 1 Figure 8.26 Selected (a) comorbid conditions for calculation of the (b) Charlson Comorbidity Index, prior to transition to ESRD in 9,086 incident dialysis patients during 1/1/2007-12/31/2014

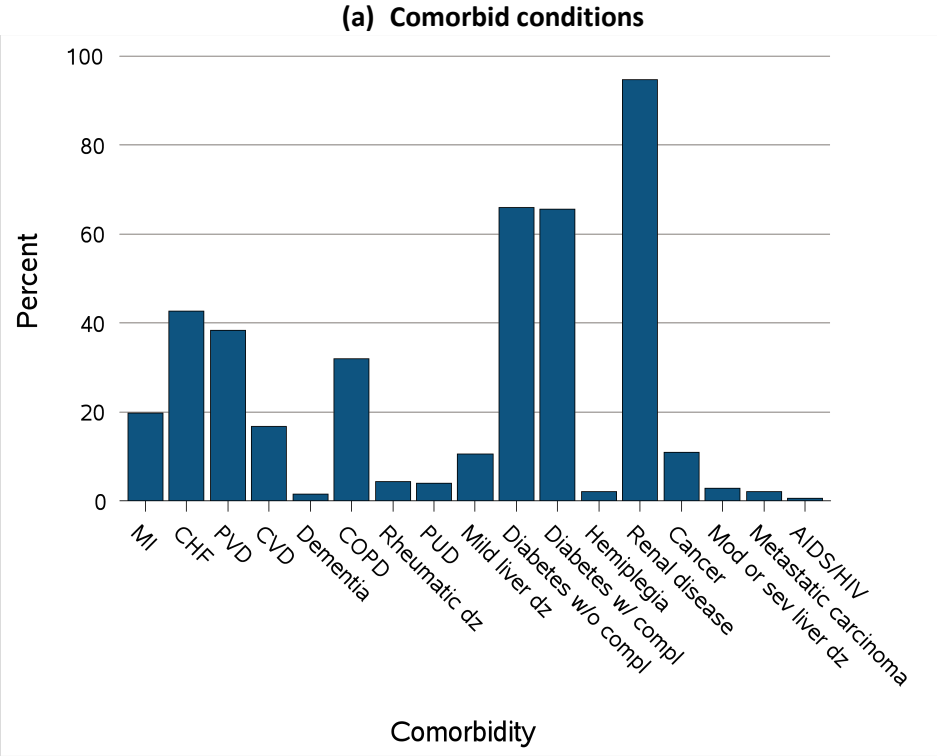
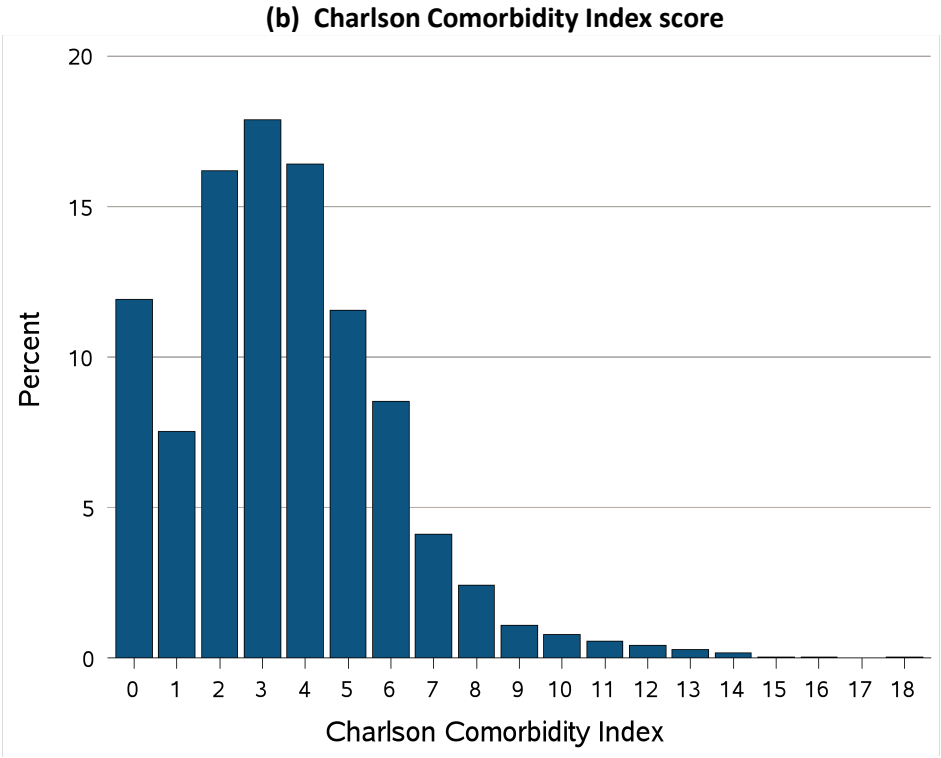


Figure 8.26 continued on next page

vol 1 Figure 8.26 Selected (a) comorbid conditions for calculation of the (b) Charlson Comorbidity Index, prior to transition to ESRD in 9,086 incident dialysis patients during 1/1/2007-12/31/2014 *(continued)*

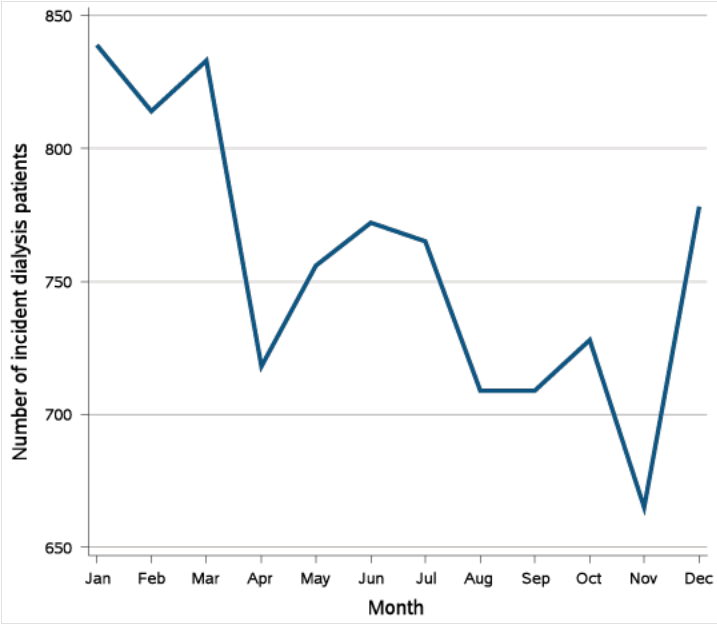


Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: CHF, congestive heart failure; compl, complications; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; dz, disease; ESRD, end-stage renal disease; MI, myocardial infarction; Mod, moderate; PVD, peripheral vascular disease; PUD, peptic ulcer disease; sev, severe.

Seasonal Trend among Kaiser Permanente Southern California Incident Dialysis Patients who Transitioned to ESRD

The seasonal trend of the 9,086 incident dialysis patients who transitioned to ESRD is shown in Figure 8.27. A greater number of patients transitioned to ESRD in the winter months of January, February and March, compared to the rest of the year. The least number of incident dialysis patients were in the month of November, where less than 700 patients transitioned to ESRD.

vol 1 Figure 8.27 Seasonal trend among 9,086 incident dialysis patients who transitioned to ESRD during 1/1/2007-12/31/2014

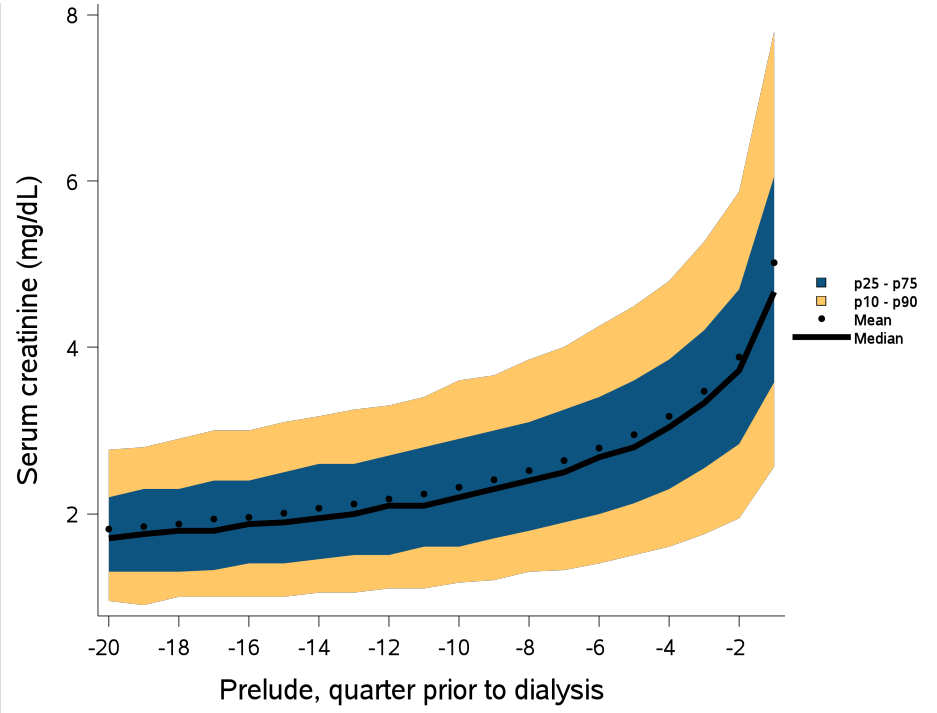


Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; Jan, January; Feb, February; Mar, March; Apr, April; Jun, June; Jul, July; Aug, August; Sep, September; Oct, October; Nov, November; Dec, December.

PRELUDE AND VINTAGE LABORATORY TRENDS OF TC-CKD DATA IN KAISER PERMANENTE SOUTHERN CALIFORNIA

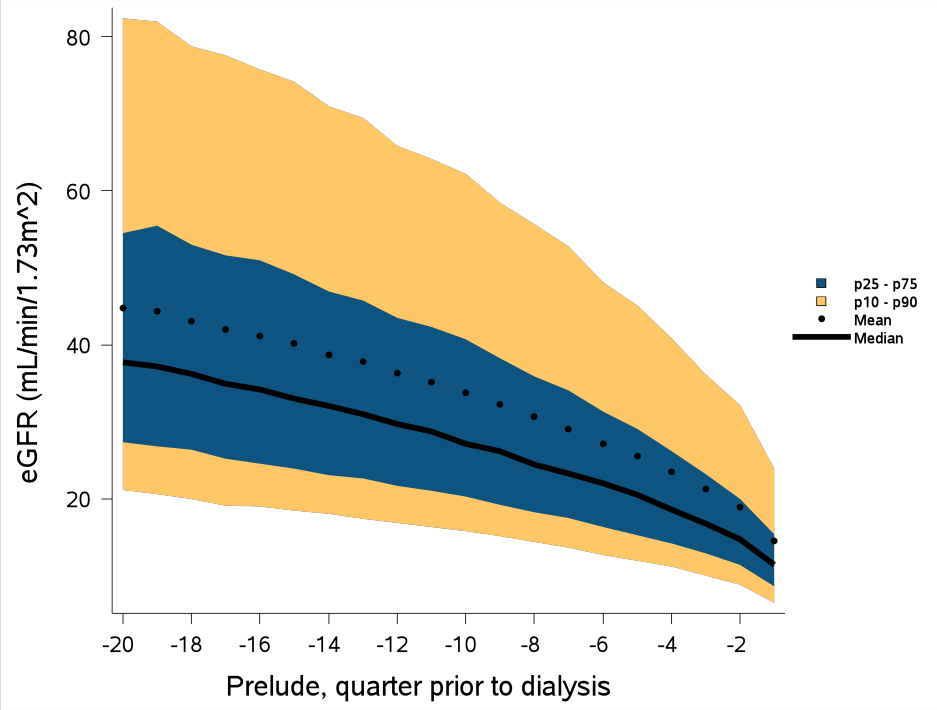
These data were extracted from the KP-SC Laboratory database that tracks inpatient and outpatient laboratory orders and results, spanning over 20 years. Figures 8.28 and 8.29 show prelude variables (including serum creatinine and eGFR) averaged by 91-day quarters (n=20 quarters) among the 9,086 patients who transitioned to dialysis. In the 90 days immediately prior to transition, serum creatinine levels remarkably increased and eGFR levels decreased. Furthermore, the age-stratified eGFR trend over 20 quarters shows that older CKD patients had a slower progression rate than younger patients (Figure 8.30). KP-SC started at lower eGFR rates, by about 10 mL/min/1.73m^2 for each age group compared to the VHA population, but showed a similar age-related eGFR trend.

vol 1 Figure 8.28 Trend in serum creatinine level during the prelude (pre-ESRD) period over 20 quarters among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



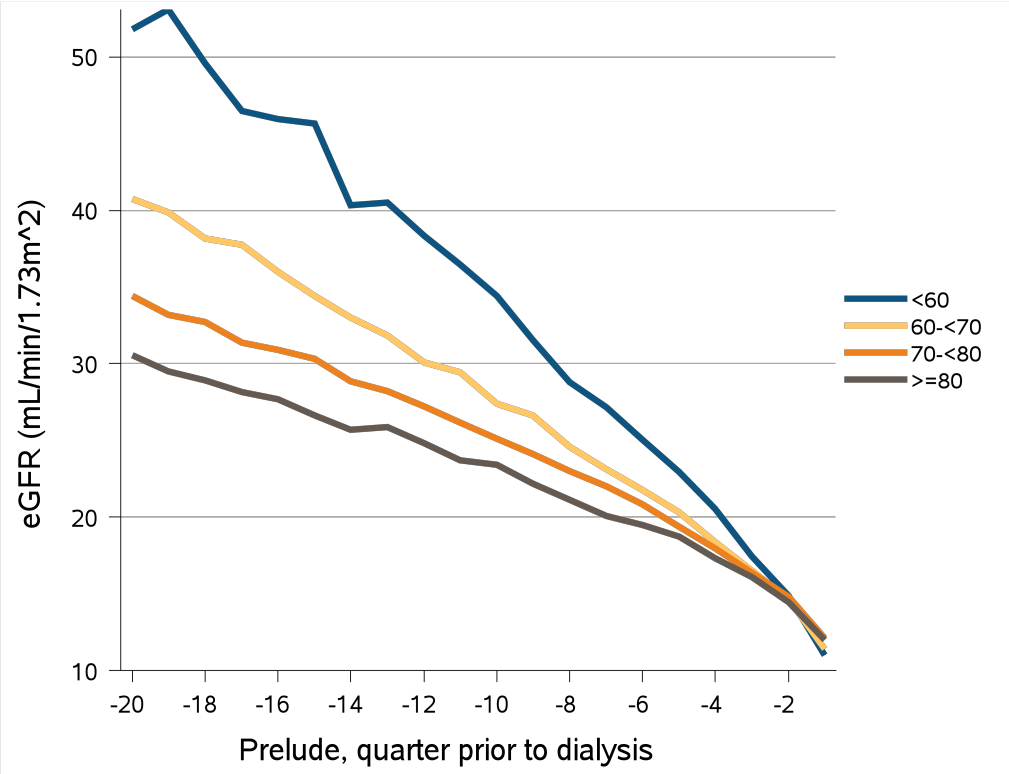
Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; mg/dL, milligrams per deciliter; p, percentile.

vol 1 Figure 8.29 Trend in eGFR during the prelude (pre-ESRD) period over 20 quarters among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: eGFR; estimated glomerular filtration rate; ESRD, end-stage renal disease; mL/min/1.73m², milliliter per minute per 1.73 meters squared; p, percentile.

vol Figure 8.30 Trends in eGFR during the prelude (pre-ESRD) period over 20 quarters among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014, stratified by age-at-incidence

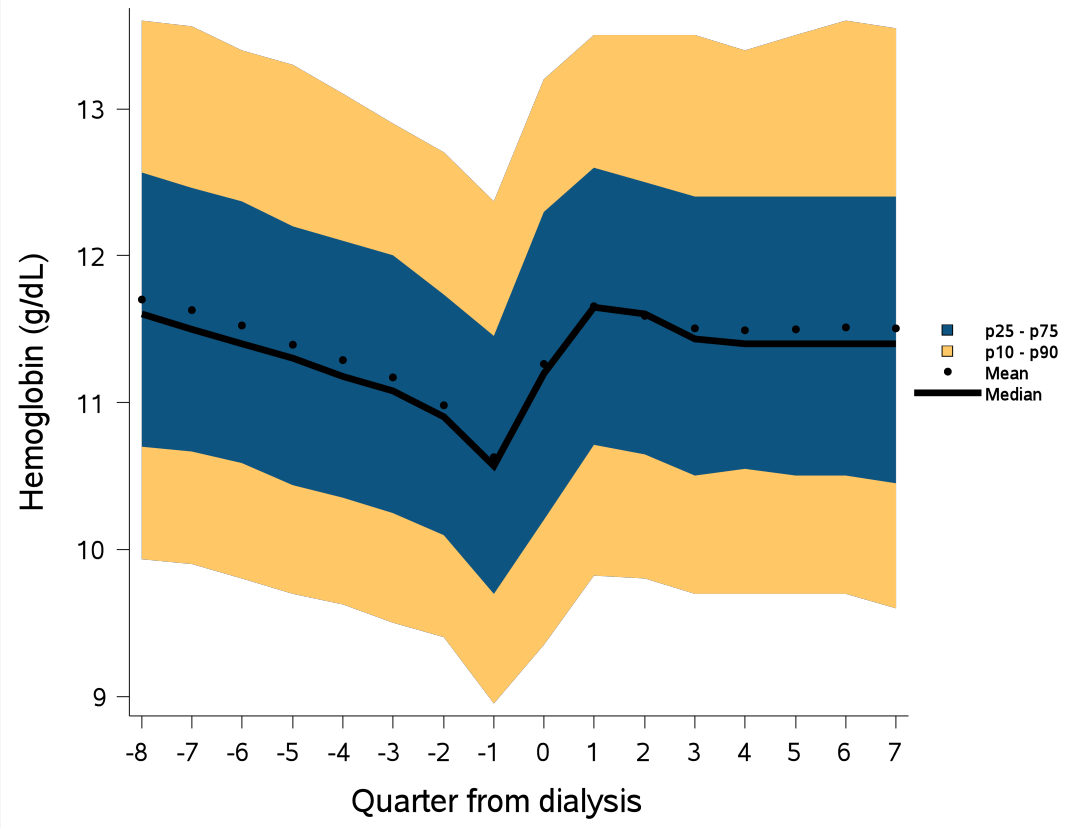


Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: eGFR; estimated glomerular filtration rate; ESRD, end-stage renal disease; mL/min/1.73m², milliliter per minute per 1.73 meters squared.

Among the 9,086 patients who transitioned to ESRD, the next set of figures show selected KP-SC laboratory data for hemoglobin, hemoglobin A1C, phosphorus, parathyroid hormone, and albumin levels during the prelude (pre-ESRD) and vintage (post-ESRD) periods over eight prelude (quarters -8 to -1) and eight vintage (quarters 0 to +7) quarters (see Figures 8.31, 8.32, 8.33, 8.34, and 8.35).

Mean hemoglobin levels gradually decreased from 11.70 g/dL to a nadir of 10.63 g/dL in the prelude period of progression from CKD to ESRD. Immediately after transition to ESRD, a slight increase in mean hemoglobin to 11.26 g/dL was observed in the first quarter (quarter 0), followed by a rise to a peak of 11.65 g/dL in the second quarter (quarter 1). Subsequent mean hemoglobin decreased in vintage quarter 3 and later appeared stable (Figure 8.31).

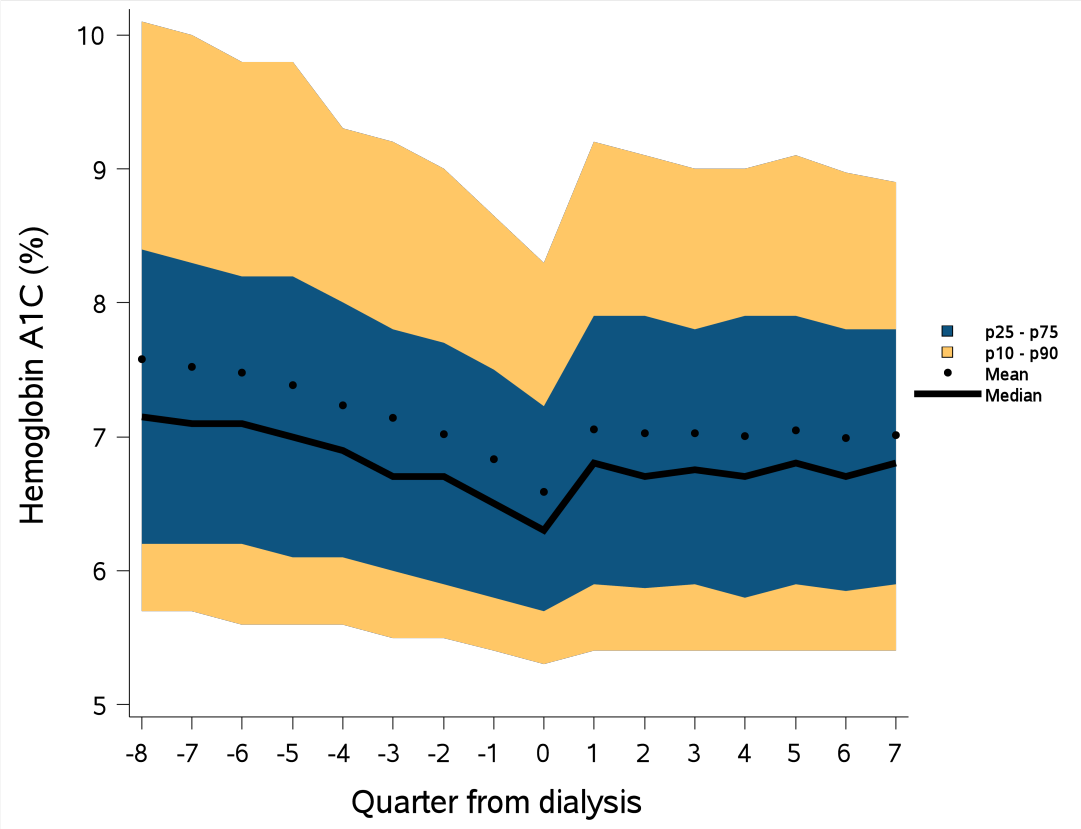
vol 1 Figure 8.31 Trend in hemoglobin levels (g/dL) over 8 quarters each in the prelude (pre-ESRD) and vintage (post-ESRD) periods among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; g/dL, grams per deciliter; p, percentile.

In Figure 8.32, mean hemoglobin A1C levels dropped from 7.58% to 6.83% in the prelude period, then slightly decreased even further from 6.83% to 6.59% immediately after transition to ESRD. In the second quarter, post transition (quarter 1), mean hemoglobin A1C levels rose to 7.06% and remained stable afterwards in the vintage period.

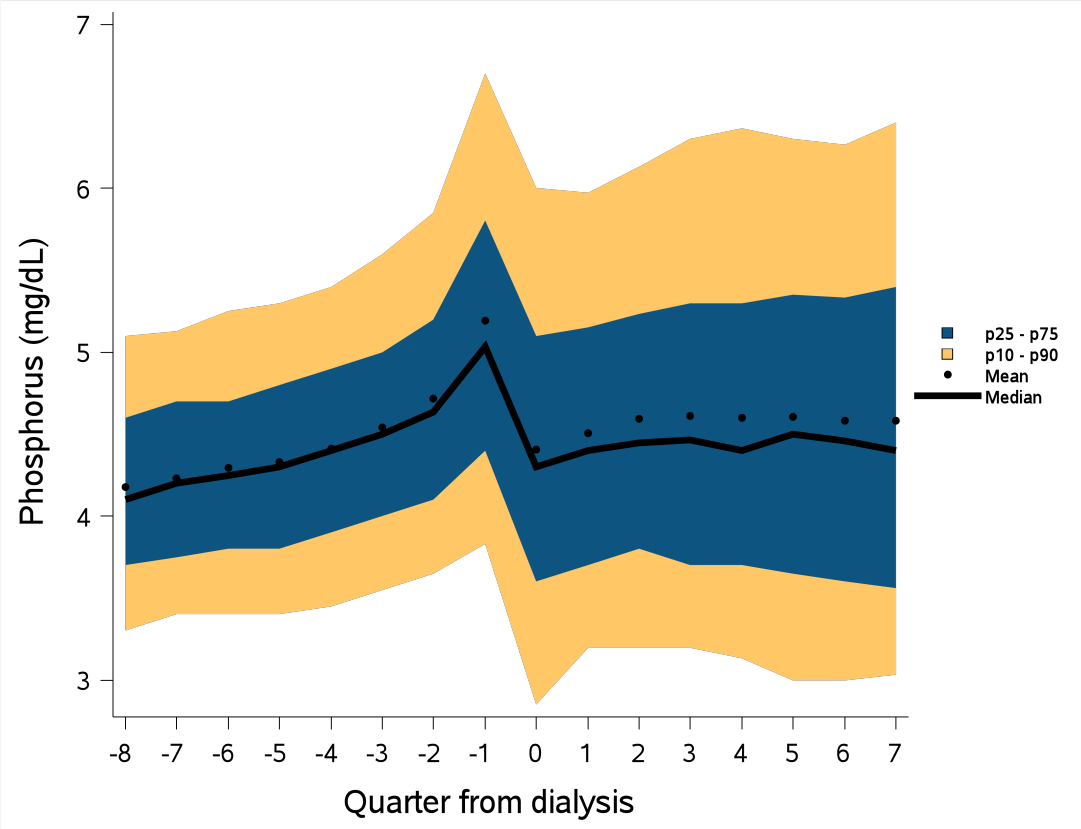
vol 1 Figure 8.32 Trend in hemoglobin A1C levels (%) over 8 quarters each in the prelude (pre-ESRD) and vintage (post-ESRD) periods among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; p, percentile.

Mean phosphorus levels increased in the prelude period from 4.18 mg/dL to 5.19 mg/dL (Figure 8.33). Immediately after transition to ESRD, mean phosphorus decreased from 5.19 mg/dL to 4.40 mg/dL. In the third quarter post transition (quarter 2), mean phosphorus increased to 4.59 and remained stable in the vintage period.

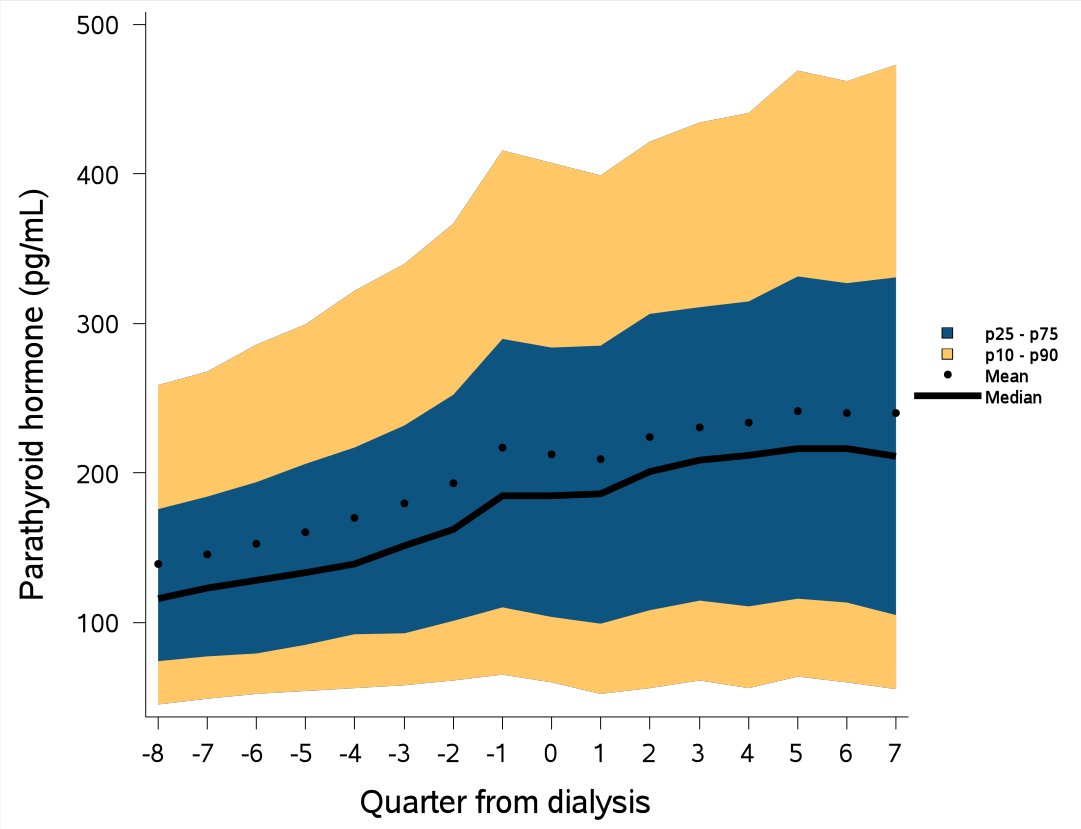
vol 1 Figure 8.33 Trend in phosphorus levels (mg/dL) over 8 quarters each in the prelude (pre-ESRD) and vintage (post-ESRD) periods among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; mg/dL, milligrams per deciliter; p, percentile.

Figure 8.34 shows mean parathyroid hormone levels steadily increasing over the prelude and vintage periods from 139.22 pg/mL to 240.29 pg/mL. Transition to ESRD did not appear to modify the increased trajectory of parathyroid hormone over time.

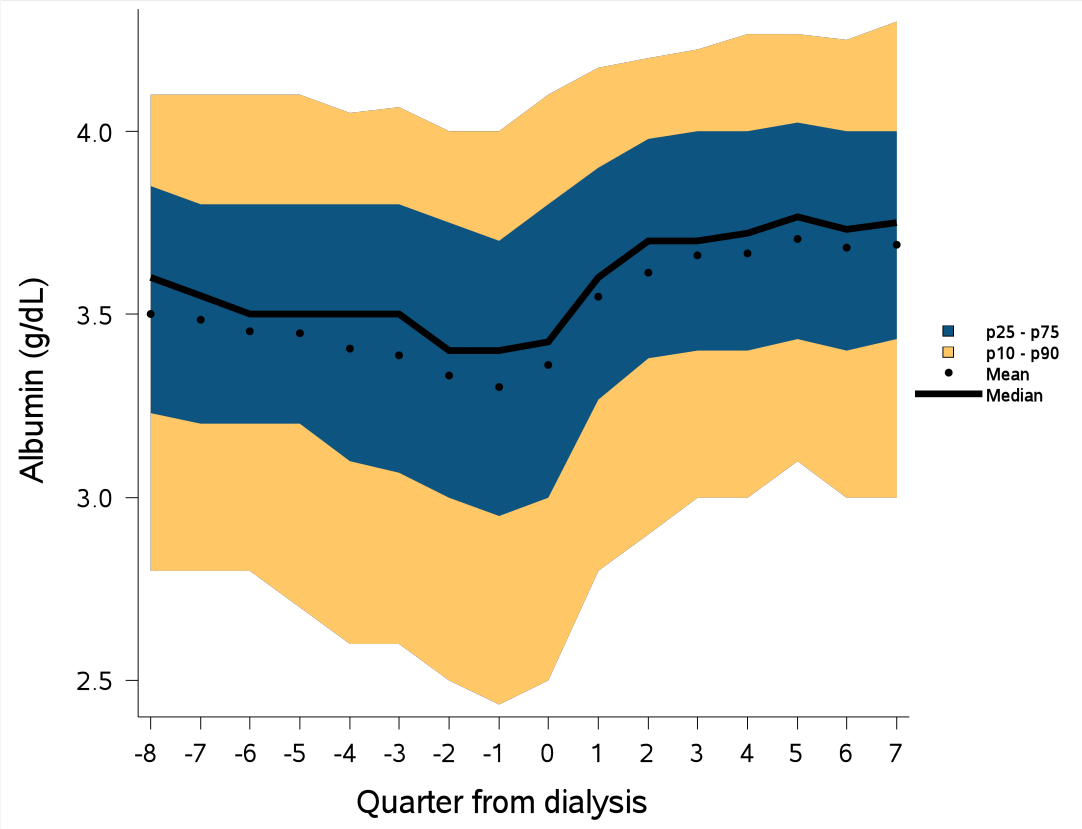
vol 1 Figure 8.34 Trend in parathyroid hormone levels (pg/mL) over 8 quarters each in the prelude (pre-ESRD) and vintage (post-ESRD) periods among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; pg/dL, picograms per deciliter; p, percentile.

Mean albumin levels dropped from 3.50 g/dL to 3.30 g/dL over the prelude period. Immediately after transition to ESRD, mean albumin increased to 3.36 g/dL in the first quarter to 3.66 g/dL in the fourth quarter (quarter 3) of the vintage period, and subsequently remained stable (Figure 8.35).

vol 1 Figure 8.35 Trend in albumin levels (g/dL) over 8 quarters each in the prelude (pre-ESRD) and vintage (post-ESRD) periods among 9,086 patients who transitioned to dialysis during 1/1/2007-12/31/2014



Data source: Kaiser Permanente Southern California Electronic Health Records. Abbreviations: ESRD, end-stage renal disease; g/dL, grams per deciliter; p, percentile.

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